Research evaluation

EVALUATION REPORT OF THE UNIT

IJM - Institut Jacques Monod

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université Paris Cité - UP Cité,
Centre national de la recherche scientifique - CNRS

EVALUATION CAMPAIGN 2023-2024
GROUP D

Rapport publié le 21/05/2024

High Council for evaluation of research and hgher education

In the name of the expert committee :

Alfonso Martinez-Arias, 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 Alfonso Martinez-Arias, Universidad Pompeu Fabra, Barcelona, Espagne
Experts:	Ms Ariane Abrieu, Centre national de la recherche scientifique – CNRS, Montpellier, France (representative of CoNRS) Ms Ina Arnone, Stazione Zoologica Anton Dohrn, Naple, Italy Mr Frederic Boccard, CNRS, Gif sur Yvette, France Mr Mathias Faure, CIRI – Centre international de recherche en infectiologie, Lyon, France (representative of CNU) Ms Brigitte Galliot, University of de Geneva, Switzerland Mr James Hombría Castelli-Gair, Spanish National Research Council - CABD, Seville, Spain Mr Ludger Johannes, Institut Curie, Paris, France Mr Christophe Le Clainche, CNRS, Gif sur Yvette, France Ms Armelle Lengronne, CNRS, Montpellier, France (representative of CoNRS) Mr Antonin Morillon, Institut Curie, Paris, France Ms Verena Ruprecht, CRG, Barcelona, Spain Ms Marisa Segal, University of Cambridge, United-Kingdom Ms Gerlind Sulzenbacher CNRS, Université Aix-Marseille, France (representative of supporting personnel)

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CHARACTERISATION OF THE UNIT

- Name: Institut Jacques Monod
- Acronym: IJM
- Label and number: UMR 7592
- Number of teams: 31
- Composition of the executive team: Dr. Michel Werner, Director ; Dr. Valérie Doye, Deputy director ; Ms. Christine Bénichou, Secrétaire générale

SCIENTIFIC PANELS OF THE UNIT

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

THEMES OF THE UNIT

The IJM has a wide research portfolio covering multiple aspects of basic biological research that broadly fall under three research axes: Genome and chromosome dynamics; Cellular dynamics and signalling; Development and evolution.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The IJM was founded in 1966 as the "Institut de Biologie Moleculaire", and celebrated its 40th year in 2022. In 2009, the Institute moved from the Jussieu Campus of Universities Paris VI and VII to its present location in the Buffon building at the Paris Rive Gauche Campus of University Paris Diderot-Paris VII in the centre of Paris.

RESEARCH ENVIRONMENT OF THE UNIT

The Institute is a mixed research unit (UMR 7592) between the Universite de Paris Cite and the CNRS. It is part part of the labex "Who am I", a PIA (Programme d'Investissement d'Avenir) interdisipliniray project that builds upon the activity of seven research units. Currently it comprises of 28 teams and four core facilities: an animal house, an imagining unit, a proteomic unit and one providing support for organoid culture and the engineering of cell lines that has been developed jointly with the "Epigenetic and Cell fate unit (EDC), a centre devoted to the study of cell fate transitions. There are also three 'technical units' that provide support for different aspects of genomics. The visit made clear that the unit has a very good atmosphere for research and that all teams are well integrated within a collaborative and helpful environment focused on high quality research.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	7
Maîtres de conférences et assimilés	21
Directeurs de recherche et assimilés	31
Chargés de recherche et assimilés	22
Personnels d'appui à la recherche	53
Sous-total personnels permanents en activité	**134**
Enseignants-chercheurs et chercheurs non permanents et assimilés	7
Personnels d'appui non permanents	33
Post-doctorants	26
Doctorants	56
Sous-total personnels non permanents en activité	**122**
Total personnels	**256**

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
CNRS	0	45	33
UNIVERSITÉ PARIS-CITÉ	27	0	19
AUTRES	1	8	1
Total personnels	**28**	**53**	**53**

GLOBAL ASSESSMENT

IJM is a relatively young institution in Paris. Although founded in 1966 as a consequence of the Nobel Prize to Jacob and Monod and aimed to usher in the then new science of Molecular Biology, it has undergone a number of transformations over the years, including the move from Jussieu to the Buffon building in 2009. The Institute has preserved its focus on molecular and cell biology and currently hosts 28 active teams that host 256 employees with 54 researchers (mainly from CNRS) and 31 professors/assistant professors (mainly from Université Paris Cité).

During the period of the evaluation, the director has been Michel Werner with Valerie Doye as deputy director. Both have worked to maintain and develop the high standards they inherited and they have fulfilled this aim. The IJM is a successful unit as shown, not only by the standards of its publications but also because of the quality of the groups, most of which score exceptional or outstanding in the evaluation. In addition, the members of the Institute obtained six ERC awards. Everybody we interviewed feels very happy in the institute and proud to be part of the community that clearly exists. This creates an excellent "*esprit de corps*" that we sensed during the visit and that is reflected in the collaborative environment as well as in the way people rally to solve the shortcomings that arise from insufficient support of the governing bodies (the University and the CNRS).

The existing institutional resource (CNRS and University) are strained (868 k€ for 2022 as a reference). The input of the CNRS has been decreasing over the period of the evaluation. Not only in terms of direct financial support but, most significantly in the provision of staff for the different groups. The committee raised this issue with the CNRS representative who explained that this was not something specific to IJM but a reflection of increasing limitations in the budget of CNRS. On the side of the University, while their financial contribution has not changed, it has not been increased in a manner that correlates with the global budget. Most significantly they are not addressing infrastructural problems in the building that create recurrent problems for researchers; decay in the building, electrical and temperature regulation problems.

The Institute has an excellent visibility and attractiveness. This is well-illustrated by >300 congress invitations, numerous managerial and evaluation activities (132 editorial activities, 31 responsibilities in learning societies, scientific committees (CoNRS, CNRS, ANR, University), success in national (labex, ANR, FRM…) and European grants (6 ERC, 3 European network) averaging 7M€ of competitive funding/year, 20 scientific distinctions (Prix Lacassagne du Collège de France, CNRS Bronze and Silver medal, Prix Bettencourt, 2 EMBO member election). The visibility is also reflected in an excellent level of attractiveness amidst young researchers that is reflected in the high number of applicants they have received for positions in the last calls and the high level of shortlisted and appointed candidates. Over the evaluation period, the unit has had an excellent attractiveness, recruiting six news teams, and obtaining nine CNRS CR, one Prof and four MCF positions, and hosted 52 PhD students and an average of 100 L and M students per year. Part of the attractiveness is a good mentoring system and the excellent atmosphere that we detected in our visit. If they could offer a good starting package, this would be superb. Major core facilities (including ProteoSeine and ImagoSeine) clearly contributes to the attractiveness. While the Institute is a place of excellent solid science with excellent National visibility, it lacks a figure or an achievement that singles it out internationally. The committee felt that for an Institution associated with Jacques Monod, it is not known as well as it should outside France. An effort should be made to redress this situation.

The scientific productivity is excellent with 659 publications, including 513 original articles, of which 56 % are studies led by IJM researcher. This is commensurate with the size of IJM, averaging >100 publications per year for 28 research teams. Quantitatively the number of original articles has improved from the last period: from 464 to 513. By contrast the number of review articles has decreased: 175 to 71, indicating a welcome emphasis on primary research. Reflecting the excellent solid science produced, a large number of articles were published in highly visible journals (Nature and several Nature journals, PLoS biology, Mol. Cell, Dev. Cell, eLife, Current Biology, PNAS, Science advances, Science signalling). Variation in quality is as expected: over the 25 teams for which a full evaluation was adequate, most teams have had an excellent or excellent to outstanding scientific

production (16), and five teams were evaluated as outstanding. Remarkable advances have been made in understanding the physical and biological mechanisms that govern cell behaviour and tissue organisation (Nature Physics, Nature Materials, Sci Adv), the mechanisms that position cell divisions during early embryonic development (Nature Physics, PNAS), and genome evolution in animal species during domestication and in human populations during the settlement of Europe (Nature Ecology & Evolution, PNAS, Sci Adv).

A possible, and perhaps only, "weakness" of the Institute within the context of increased support for applied science stems from its being very focused on basic research and knowledge that limits translating their excellent science into commercial and entrepreneurial activities, limited to three patents and two ERC Proof of concept grants to develop products with companies. Building on their specificity, the IJM largely communicates on the importance of fundamental research for societal progress to the general public through a large number of media interviews (38, France Culture, …), TV documentaries (5, Arte, …), and article in the general press (6, including in "Le Monde"). The unit also participate in multiple actions oriented towards young students (Apprentis chercheurs, Déclics, and Open days).

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The recommendations were divided into three sections: (1) logistics of scientific production, (2) Organisation and life of the unit and (3) Science, including strategy and support. The Unit has responded to each of these with specific actions and, for the most part, has been able to implement the recommendations with some follow-on improvements. For example, support has been put in place for researchers applying to large grant schemes e.g. ERC, and this is increasing the quality of the applications and the rate of success. Also, a general mentoring scheme for new PIs has been put in place, and this is being important in guiding them through the complex web of organisation and operation of the Institute; this clearly is having benefits in the quality of the research. Teaching support has been acquired and is being provided; this has freed personnel from teaching duties and allowed them to focus on research activities. At a more general level, a proper intranet system (Le Monod) has been put in place that facilitates internal communication and access to information.

However, some recommendations have been difficult to implement though, for the most part this has been due to circumstances outside the IJM influence. Most significantly, support for bioinformatics in the institute is being undermined by a lack of financial support for an engineer in bioinformatics (requested to the CNRS for 6 years in a row) and a loss of IT support staff which is not being replaced. Notwithstanding this, the unit has been proactive in developing bioinformatics with the hire of a *Maitre de conference* and a general push to teaching the subject and encouraging researchers to develop their own hubs. Nonetheless, this remains an important area that needs to be properly supported in a modern interdisciplinary institute like IJM. The *'initiative Platform for Omics Project-Université de Paris' (iPOP-UP)* developed jointly with EDC (Epigenetics and cell fate unit), IBPS (Institut de biologie Paris Seine) and Institut Cochin has been an attempt to address the shortcomings in this area but it doesn't really work.

An additional, but less important area, in which recommendations have been difficult to put in place has been the provision of space for meeting and lectures that remains limited.

There was a recommendation to foster interactions with other institutions as a way to increase the visibility of the interactions and to promote collaborations. There have been some developments here, with the iPOP-UP as a positive example but the most important would (and hopefully will) be the fusion with EDC which would be most important because of the obvious synergies between the institutions. Although not yet achieved, it remains an important target that would benefit the IJM.

On more positive notes, problems of the imaging facility that were highlighted in the review have been addressed with good investment in equipment, organisation and refurbishment (see more later) and the same is true of the proteomic facility.

Overall, and within the limitations of the funding schemes available and the complex nature of a multi-institutional landscape, the IJM has responded well to the recommendations and remain an attractive destination for young groups, as shown by the new hires.

B - EVALUATION AREAS

Considering the references defined in the unit's evaluation guidelines, the committee ensures that a distinction is made on the outstanding elements for strengths or weaknesses. Each point is documented by observable facts including the elements from the portfolio. The committee assesses if the unit's results are consistent with its activity profile.

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

Assessment on the scientific objectives of the unit

The scientific vision of the unit is to create a research environment that allows the exploration of the relationships between the levels intervening between molecules and organisms. To achieve this, the Institute has a broad portfolio of interests ranging from the molecular to the organismal level. This creates opportunities for a multidisciplinary approach that, in principle, are taken advantage of.

Assessment on the unit's resources

The unit has 256 personnel (28 research teams) distributed in one building that requires important refurbishment. The recurrent institutional support is strained (868 k€ for 2022 as a reference). The infrastructure and financial situation has been pretty much the same since the last review. There are excellent services with a special highlight in the proteomics facility which has received a big boost over the last few years and is recognised as an exceptional reference within the Paris area.

Assessment on the functioning of the unit

Despite some challenges (see below), the unit appears to work well. There is a very good spirit of cooperation and satisfaction with the functioning of the unit and the possibilities it offers to all groups. There was also satisfaction with the management team and, importantly, the core facilities. All members of the unit were unanimous in their feeling IJM is an excellent place to work in and be part of.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The unit focus is clearly on molecular and cell biology, along three broad research themes: 1-*Development and evolution; 2-Cellular dynamics and signalling; 3-Genome and chromosome dynamics.* The themes are bridged through two axes: quantitative biology and modelling, and molecular and cellular pathologies. This focus allows for reasonably clear scientific vision for the unit, although the transverse axes may not facilitate the caption of a unique scientific identifier for the unit. The scientific vision is thus broad but there is a plan to discuss it in detail in an upcoming PI retreat.

The unit aims at promoting scientific excellence. The teams are of high-level and this has been reinforced with the new appointments.

The unit is an excellent environment to do excellent science that is appreciated by all teams; this includes a high level of satisfaction in postdocs and students.

Weaknesses and risks linked to the context

From the scientific point of view there are no obvious shortcomings or weaknesses beyond the need to realign the vision which, as stated above, will be done in the forthcoming PI retreat.

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

Strengths and possibilities linked to the context

The unit has 256 personnel, 28 research teams, distributed in one building.

The Institute has very strong core facilities that have improved over the period under review. There has been a big investment in proteomics which has paid off and the facility, in addition to serve the IJM, is very well regarded and in demand within the Paris area. Investment has also been made in the area of imaging and image analysis as well as in a service, Enscore (shared with the EDC) that creates genetically modified cell lines and organoids for research. All this is reflected in the strength of the unit at the interface between cell and molecular biology at the quantitative level.

Weaknesses and risks linked to the context

The existing institutional resources (CNRS and University) are strained (868 k€ for 2022 as a reference). Including additional resources and exceptional incomes, the unit is running on a budget of 2.8M€ (for 2022 as a reference, excluding team competitive grants) with a current income of 2,847,918€ against an expenditure of 2,052,451€ that yields a positive balance. The situation of the balance has been pretty much the same since the last review, though the total income and expenditure have both increased. In order to remain competitive to the level deserved by its researchers, the functioning of an institute of the size and quality of IJM needs to be underpinned by good infrastructure, technical and administrative support and, in a highly competitive environment, this needs to be increased.

The two arms of the IJM, CNRS and the University appear to be in a phase of lowering rather increasing the support they provide. This is most clearly seen on the CNRS side which, in addition has diminished the appointments leaving CNRS groups without permanent researchers. Their budget contribution over the last five years has decreased by 15% but, importantly, the technical positions have gone down almost 50% from 49 to 26. This decrease, in the context of many people -particularly technical staff- leaving due to retirements or to the difficulties of living in Paris, create a problem for sustainable and competitive research.

From the side of the University, while the income has remained stable, their input in the maintenance of the building and its infrastructure is not optimal and suffers from understaffing and lack of support. There is a need for refurbishment and improvement of the electrical support that causes problems due to frequent cuts.

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

Strengths and possibilities linked to the context

The Institute is well run without major highlights.

There is a 'green committee' that looks into ensuring the environment friendly policies are put in place e.g. recycling and increasing the temperature of freezers.

Weaknesses and risks linked to the context

The visit confirmed the statement in the report that '*There is no coherent financial and personnel package policy by the CNRS or the Université Paris Cité for the installation of new teams*". This can be understood in the context of the waning financial support from the CRNS and is something that needs to be corrected.

The structure of the different groups, hierarchical structure, titles and remits are not clearly indicated in the website which leads to poor visibility of whoever is and is not a PI or a group leader.

There is also no proper structure or platform at the level of the Institute, in complement of governing bodies structures, to deal with mental health issue that have become paramount after the pandemic and this should be corrected.

While the PhD students are well represented and have visibility in the Institute, postdocs seem to lack a coherent grouping, guidance and activities that cater for their significant needs.

The committee also noticed during the visit (in December) that the temperature of the rooms in which the meetings were held were extremely high. Asked about this, the management said to be aware but that the control of the building is in the hands of the University.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The visibility and attractiveness of the unit is excellent as shown by the number and quality of the new recruits, the number of ERC applications in the second stage and awards (6) obtained, participation in EU networks and, significantly, the election of two group leaders to EMBO. Members of the IJM have also been awarded a number of national awards and participate in committees of science policy and evaluation at the national level.

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

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

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

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

Strengths and possibilities

The scientific visibility of the unit is excellent. Unit members have been invited to >300 congress invitations, ¾ international, and 270 seminar invite, and have organised 69 international conferences. Unit members also broadly contribute to managerial and evaluation activities, including 132 editorial activities, 31 responsibilities in learning societies, and participation to scientific committees (CoNRS, CNRS, ANR, University). The visibility is also attested by the success to national (labex, ANR, FRM…) and European grants (6 ERC, 3 European network), averaging 7M€ of competitive funding/year during the reporting period, and by over 20 scientific distinctions, including (Prix Lacassagne du collège de France, CNRS Bronze and Silver medal, Prix Bettencourt, 2 EMBO member election).

The Institute is an attractive place to do research for young scientists and this is recognised by the number of applicants in every call. The atmosphere of the place, the high calibre of the ongoing research and the state-of-the-art facilities act as good baits for people to join in. In addition, it has in place a program of activities to welcome new personnel to the institute in a manner tailored to the level of each individual career level. For new PIs, the IJM provides a 50K€ installation grant and a mentoring scheme that are appreciated and welcome. The mentoring scheme is a new thing from 2018. Over the period, the unit has had an excellent attractiveness, recruiting six news teams, and obtaining nine CNRS CR, one Prof and four MCF positions.

The unit is also highly attractive through its training implications. IJM hosted 52 PhD students and an average of 100 L and M students per year,

Major core facilities (including ProteoSeine and ImagoSeine) clearly contribute to the attractiveness. The facilities are open outside of IJM, and have benefited from major investment or reorganisation during the reporting period.

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

The current inability to provide permanent support positions to the new teams, but also to existing one, is an important issue. Solving this problem will make the institute more attractive and competitive. The lack of technical support is very obvious in the situation that the core facilities are run by scientists of the unit that thus

double their work. The most obvious case is the imaging facility headed by JM. Verbavatz, a researcher in the Institute and a teacher in the University, and RM. Mege, researcher.

The inability to provide a proper start up package limits the team-recruiting potential, in particular for mid-career or senior scientists. This is further stressed by the difficulty to recruit senior scientist at CNRS and the high teaching load for professors at the University. IJM is clearly an attractive place for young researchers that can make a difference in and for the future but much of how this develops will depend in the IJM being able to provide the administrative and support environment that they require.

The committee noticed that while the gender balance in the Institute is fair, there is no blueprint to work in the direction of gender balance, diversity and inclusion.

There is also no proper bioinformatics support for lack of resources.

Of perhaps major significance, while the level of science is very high, there is no figure of recognised high international standing that makes the institute stand out outside France.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production, as reflected in peer reviewed publications, is commensurate with the research potential of the IJM and has quantitatively improved when compared to the last period. Significantly, the number of original articles has increased while review articles has decreased, indicating a welcome emphasis on primary research. A large majority of teams produces excellent or excellent to outstanding science, which is illustrated by regular publication in highly visible journals (Nature and several Nature journals, PLoS biology, Mol. Cell, Dev. Cell, eLife, Current Biology, PNAS).

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

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

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

Strengths and possibilities

The research teams of the IJM produce high caliber excellent science. During the reporting period, 659 publications were produced, including 513 original articles, of which 56 % are studies led by IJM researcher. This is commensurate with the size of IJM, averaging >100 publications per year for 28 research teams. Quantitatively the number of original articles has improved from the last period: from 464 articles to 513. By contrast the number of review articles has decreased: 175 to 71, indicating a welcome emphasis on primary research.

The overall quality of the research led by IJM teams is illustrated by publications in highly visible journals, including Nature (2), Nature Commun (3), Nature Physics (3), Nature Materails (1), Nature Eco&Evo (1), PLoS biology (1), Mol Cell (1), Dev Cell (8), eLife (13), Current Biology (2), PNAS (4), Sciences advances (4) and Science signalling (1). Variation in quality is as expected: over the 25 teams for which a full evaluation was adequate, most teams have had an excellent or excellent to outstanding scientific production (16), and five teams were evaluated as outstanding. Of note, the research has provided ground breaking advances Highlights include advances in understanding the physical and biological mechanisms that govern cell behaviour and tissue organisation (Nature Physics, Nature Materials, Sci Adv), the mechanisms that position axis and places of cell divisions during early embryonic development (Nature Physics, PNAS), and genome evolution in animal species during domestication and in human populations during the settlement of Europe (Nature Ecology & Evolution, PNAS, Sci Adv).

The scientific production as well as its leadership are well shared between IJM members. 200 original articles have PhD students as first authors and 70 original articles are signed by non-group leader researcher as corresponding or co-corresponding authors. Core facilities are being acknowledged in publications and this makes their work visible, and in some instances, supporting staff are included as authors.

The Open access policy is embraced and, in general, primary data is secured and accessible inside and outside.

There is an increasing positive attitude towards preprints, which are being used as a way to demonstrate that the research has been done and thus to justify the funding

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

None identified

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The unit has a focus on basic research and actively communicates on the importance of basic research towards the society, including schools and the general public. Commercial and enterpreneural activities remain low, but commensurate with the scientific focus of the institute.

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

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

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

Strengths and possibilities

The unit has a focus on basic research and largely communicates on its importance for societal progress to the general public. All teams participate in these activities. This can be seen in a large number of media interviews (38, France Culture,), TV documentaries (5, Arte, …), articles in the general press (6, including in "Le Monde"), poadcasts, and the launching of a Youtube channel at the occasion of the IJM 40th anniversary.

The unit also participates in multiple actions oriented towards young students: Apprentis chercheur, supported by the association 'l"arbre de la connaissance" hosting each year secondary school students,; Declics, supported by the Shlumberger foundation oriented towards high school students; and open science days during the Fete de la science.

Despite commercial and entrepreneurial activities being low according to the fundamental research focus, 3 patents and two ERC Proof of concept grants to develop products with companies were obtained.

The excellent proteomic facility and, to a lesser extent, the microscopy unit, could try to externalize their services to commercial outfits which would result in an increase in revenue for the Institute.

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

The level of non-academic involvement of the unit is minimal. Given the remit of the research groups, it is not clear how this can be changed.

ANALYSIS OF THE UNIT'S TRAJECTORY

The trajectory of the IJM over the period of the evaluation is excellent. The small issues raised by the last evaluation have been addressed and in the Scientific content and vision, the developments are good and in an upward trajectory. Young talent has been recruited, the core facilities have been reinforced with good input funding (special mention to the excellent proteomics unit) and the place is becoming a centre of excellence as reflected in the six ERC awards that, in a place with 28 teams is an excellent proportion.

Technical, administrative and building infrastructure and support, are real threats for the Institute. This is not due to oversights as the management team is well aware of the situation and has raised it many times with the governing bodies (CNRS and University), rather it is the lack of actions of these bodies that has maintained the impasse.

There is a new head and deputy head in place for the next period. The new Director was deputy director and thus knows well the ins and outs of the system and should be able to steer the Institute to continuing success. The new Deputy Director will contribute his interdisciplinary interests to the next five years.

Looking into the future, IJM is in an excellent position to develop the base that it has created over the last five years. It is important that they get support from CNRS and the University so that teams get the technical support (in terms of personnel) they need and also the building gets the support that can host the high-quality research carried out by the teams.

The Institute has to find a way to bolster the bioinformatics support and, at this, they should find a way to liaise with the EDC; here, acknowledging the lack of space to bring them into the Buffon building, it would be good to facilitate interactions between the two institutions, possibly through building a bridge joining the two buildings.

At the level of appointments, while there is good gender balance in the Institute, it is obvious that the new appointments do not go into this direction. There is awareness of this, and actions are being suggested in this report to address this issue.

Overall IJM is an excellent host for young researchers in the areas of cell and molecular biology and it will be interesting to see the direction of travel for the next five. This was not very clear during the visit beyond an aspirational statement about bridging gaps between molecules and organisms. The Institute is having a retreat early in 2024 where this matter will be discussed in depth and the committee stressed the importance of getting this blueprint at the forefront of the discussions.

RECOMMENDATIONS TO THE UNIT

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

The science in the Institute is excellent but it needs a clear vision for the next five years. The committee understands that early in 2024 there is a retreat in which this matter will be discussed.

A significant weakness of the Institute lies in the shortcomings of the physical and administrative infrastructure. These depend on the University and it is important that they are addressed.

Equally significant is the dearth of technical support that is affecting the running of the groups and the core facilities. This is within the realm of the CNRS and while there is no expectation that things will change, the case should be addressed. One solution that is being considered is that the Institute launch a private foundation as amidst other things, this would allow the Institute use the funds that it can accrue to solve the infrastructural problem.

The report highlights recurrent problems developing bioinformatic infrastructure and this is still a problem that needs to be addressed. While the focus of the Institute is not in genomics, bioinformatics is a basic tool of modern biological research and it should be properly represented.

The recruitment of PhD students appears to be a problem. This could be solved by creating an in-house PhD program and by increasing the visibility of the IJM.

The groups should be encouraged to communicate better the biomedical relevance of their work to compete with other branches of research more closely connected to human health.

Importantly, there is no blueprint to work in the direction of gender balance, diversity and inclusion. For example, only one of their last six appointments was female. The solutions to this situation will not come, only, by focusing on bias during recruitment processes. The approach that needs to be taken should rely on a strong culture of equality within the institute. The path to this is now well established and rests on four pillars:
- Communicating the values and rules in force within the institute
- Raising awareness of respect, sexism, diversity and inclusion among all members of the institute
- Dealing with misconduct
- Actively promoting gender equality, diversity and inclusion

For each of these pillars, simple steps can be taken. The IJM should build on the excellent work that has been done on this subject at the Institut Pasteur where there is an excellent blueprint.

Recommendations regarding Evaluation Area 2: Attractiveness

The Institute is an attractive institution but it needs to boost its international visibility as it is not well known outside France. It is curious that there is a series of international conferences called the "Jacques Monod' conferences and that the IJM has nothing to do with them beyond the occasional organisation of one by a member of the Institute. They should work at developing their brand.

The development of a strong equality and diversity culture within the Institute should boost their attractiveness and excellent reputation! No doubt, it is a good investment for people active there and for the institute.

Recommendations regarding Evaluation Area 3: Scientific Production

The unit is in a good trajectory in terms of scientific production. The main recommendation should be that, given the current time scale of peer reviewed publication, teams should be encouraged to post their findings as preprints and the different bodies to value this practice. Along similar lines, the teams should watch out and limit publication in "predatory journals".

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

The IJM should make better use of its brand name that represents an icon not only of French science but of world-wide history of molecular biology. One idea would be to organise an annual conference with an international participation.

Also, more effort should be made to showcase the significance of basic research in model systems especially when the group also addressed cross-over research in humans.

Team 1: Cell polarity in development and evolution

Name of the supervisor: Ms Juliette Azimzadeh

THEMES OF THE TEAM

The team studies centrioles and cilia and notably how rotational polarity is achieved. This property is important for motile cilia to generate directional fluid flows. Two complementary research axes are based on studies in flatworms (multiciliated epithelia and field polarisation) and in mammalian cell cultures (centriole structure and rotational asymmetry). In the flatworm, locomotion depends on a multiciliated epidermis, and genes were identified that affect the direction of locomotion. The team also investigates the structural properties of centrioles and their fundamental roles in ciliogenesis, cytoskeleton organisation, and cell polarity.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report recommended that:

1- *It is urgent that the team publishes primary research papers.* Primary research papers have now been published with the PI as principal author: eLife 2022, Biol Cell 2020, Dev Cell 2019.

2- *The team leader should aim to develop public outreach activities.* A review for the general public has been published in Médecine/Sciences in 2021, and middle school students have been hosted (stage de 3ème).

3- *The team leader should focus on publishing ongoing work and leverage these publications in order to raise funds to allow the team to reach a sustainable size.* Six contracts were running during the contractual period under review, including ANR as coordinator. Total available funding amounted to 784 k€. The team has grown to five members, including a newly obtained staff technician position and a postdoctoral fellow from 2013-2018.

4- *It is probably wise to cancel -or at the least to postpone- parts of the future plans (e.g. spiral cleavage)*. The scope of research themes was focused. Spiral cleavage was not addressed in the contractual period under review.

5- *Mentoring from a senior scientist would strongly benefit the team leader.* In Section 1-6.2 it is mentioned that "Newly recruited group leaders are asked to choose two mentors". Not clear from the report whether this was the case for in this specific case.

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	1
Sous-total personnels permanents en activité	**2**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	**3**
Total personnels	**5**

EVALUATION

Overall assessment of the team

The team has an excellent to outstanding visibility and scientific production in the field of centrioles and cilia, as illustrated by fourteen invitations to talk at national and international conferences, including the most prestigious ones (e.g., EMBO and Jacques Monod), and publications in reference journals (e.g., Dev. Cell, eLife, J. Cell Biol.). The team has increased its size in the contractual period under review, and the funding situation has been stabilised with six contracts that were active for a total amount of 784 k€, including new contracts with ANR and ARC having the PI as coordinator.

Strengths and possibilities linked to the context

The team has an established standing in the field of cilia and centrosomes. The PI has been invited to talk at14 national and international conferences, including the most prestigious ones, e.g., EMBO in 2021 and Jacques Monod in 2022. When compared to the previous contractual period, the team has been significantly consolidated by the securing of a staff technician position. 3 Master 2, 7 Master 1, 1 L3, 1 BTS, 2 PhD students and a postdoctoral students have been trained, which is a substantial achievement for such a small team. The personnel who left the team after their PhD or postdoctoral students training found positions in biotech companies. With 784 k€ of external function that was available in the contractual period under review (including the PI as coordinator on 2 ANR contracts), the team has been able to make ends meet.

The team has identified candidate genes for the assembly and positioning of centriolar appendages in multiciliated cells, and uncovered a component accounting for the rotational asymmetry of centrioles within the human centrosome, an outstanding observation against the backdrop of centriole appendages subscribing to 9-fold symmetry. The fact that contrary to the accepted view, human centrioles proved to exhibit molecular markers of rotational asymmetry is a remarkable finding adding to the team's notoriety. These excellent discoveries were published in highly recognised international journals with the team leader as last author (notably Dev Cell in 2019 and eLife in 2022), and constitute the basis for exciting ongoing research endeavours. Based on the choice of models, the team has an original position at the interface with the evo-devo and evolutionary cell biology communities. Collaborations with French and international colleagues allow the team to reach out for complementary expertise.

Weaknesses and risks linked to the context

Despite the progress that has been made with the recruitment of a staff research technician, the relatively small size of the team remains a weakness. This limits the possibility of the team to live up to its full scientific potential, and to obtain certain funding, such as team "labélisation" by ARC, Ligue, or FRM.

The team does not have interactions with the socio-economic world, which appears fully understandable in consideration of the team's current small size and the resulting need for focus.

Analysis of the team's trajectory

Based on its established standing in the field of cilia and centrosomes, the team proposes to study the polarisation of multiciliated cells and the rotational asymmetry of centrioles at the centrosome. To be able to perform transgenesis, the team will start to use the marine species Macrostomum lignano as a model. First data indicate similarities and differences in the whole-body patterns of centriole rotational polarity between the freshwater planarian and M. lignano, which will be exploited to gain molecular and evolutionary insights. The program builds on the strengths of the team and is sufficiently focused to be feasible within the limits of the current team size. Collaboration with a team at INP, Marseille, on expansion single-molecule localisation microscopy, ICM, Paris on zebrafish, at IJM on mouse embryos, and one team at the University of Leeds on appendage interacting proteins are geared at providing additional structural resolution and dynamics.

RECOMMENDATIONS TO THE TEAM

The team is strongly encouraged to pursue its exciting research in the field of cilia and centrosomes and to expand its potential through well-chosen collaborations. The latter should enable the team to reach out for additional collaborative grants such as PRC (and possibly PRCI) from ANR. The team should be further reinforced

through the recruitment of staff personnel at engineer and researcher levels and through the securing of additional means to attract talented postdoctoral students.

The team leader may consider boosting her visibility by small teaching commitments that might help increase recruitment of MSc/PhD students.

The discoveries reported by this team hold important implications to the understanding of ciliopathies. The team leader should consider opportunities to showcase this aspect of their theme more strongly in order to enhance visibility and foster access to funding opportunities broadly connected to molecular understanding of disease.

The work on the human centrosome might have translational possibilities. On the basis of a further consolidated team, one might encourage the team leader to consider such opportunities by reaching out to the biotech sector and general public.

Team 2: Evolution and development of metazoans

Name of the supervisor: Mr. Guillaume Balavoine

THEMES OF THE TEAM

The team has a long-standing tradition in the field of Evo Devo, aiming at the reconstruction of key steps in metazoan evolution. The team's primary areas of research in recent years have been the development of segmentation and the genesis of the neurological, circulatory, and stem cell systems. The primary model system used by the team is the marine annelid Platynereis, for which a number of genetic tools (including FUCCI, cell cycle and beta-Catenin reporter lines) are being created to track the biology of stem cells.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report recommended:

1- *To use the positive momentum of the 2017 publications and the upcoming Wnt story for: i) a presentation campaign at international meetings; ii) round of grant applications, including striving to attract a permanent staff scientist position.* This was addressed (three invited international conferences and one ANR PRCI grant 2017-2022).

2- *To use the positive momentum of the 2017/18 publications and the new folks joining the lab as initiator of sustained growth*. This wasn't addressed.

3- *Focusing on tool usage rather than tool development.* This was only partially addressed.

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

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

EVALUATION

Overall assessment of the team

The team has a strong track record and is internationally recognised in the Evo-Devo field, as evidenced by invitations to present at conferences and collaborative grants. The team has produced a substantial body of very good primary research, managed to obtain funding through 2022, and continues to be active in public outreach through programs like "Déclics" and "Pint of Science". However, committee could not appreciate the work at its full value because of confidentiality. Last but not least, the team has strong ties to several foreign partners but little domestic cooperation.

Strengths and possibilities linked to the context

The team has a very good visibility at the international level with 3 invited conferences. Its very active contribution in building genetic tools in non-conventional animal experimental systems largely contributes to this visibility. The team leader contributed to a review with international collaborators.

The scientific production is very good with two original articles (eLife, 2017) and BMC Evol Biol , 2020). One of the main research axis is developing methods to make the worm Platynereis the primary model for reverse genetics in spiralians.

The public dissemination of evolutionary discoveries and knowledge is highly valued by the team leader who has an excellent record of non-academic initiatives.

Weaknesses and risks linked to the context

Despite attempts to increase the size of the team, including researchers or student), the team didn't manage to reach a reasonable size, and reached a minimal size with only the team leader at the end of the current reporting period.

The panel couldn't fully assess the quality of a potentially high impact recently submitted manuscript because of a confidentiality issue.

Analysis of the team's trajectory

RECOMMENDATIONS TO THE TEAM

The team will be relocating to the University Paris-Saclay in 2024. The team should take advantage of the move to invest in attracting PhD students and exploring various funding opportunities at the national, European or international level, in order to create a team dynamic.

Team 3: Mechanotransduction: from cell surface to nucleus

Name of the supervisor: Mr. Nicolas Borghi

THEMES OF THE TEAM

The research of the team is focused on epithelial tissue mechanobiology with the goal to study the mechanisms by which cells generate and sense mechanical forces. The team has an interdisciplinary approach and the research bridges the fields of physics and biology.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

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

1- The team should identify strategies to increase their international visibility and attract more students and postdoctoral students. A recent publication in J. Cell Biol. is very encouraging and may demonstrate that the team is moving in the right direction. Little things like a proper webpage of the lab in English and a Google Scholar profile might already help. The team has demonstrated efforts to promote its visibility as through collaborations and conferences and is encouraged to maintain these activities in the future.

2- The team leader should continue to develop a strong team. The team leader has been able to maintain permanent members and recruit new postdoctoral fellows and a PhD student.

3- The team should identify one or two key questions they want to address and focus their efforts on those. Integrating mechanotransduction by different mechanosensors across length scales and collaborating with theorists might be a good way forward to provide the group with a unique selling point in a rapidly growing, competitive field. We strongly recommend to assign a mentor to the team. The team has convincingly consolidated specific research lines and established a coherent research plan.

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

EVALUATION

Overall assessment of the team

The team has a proven track record in the development of advanced quantitative imaging methods, biosensors and micromanipulations tools and is internationally recognised in the field of cell and tissue mechanobiology. The team has made very good to excellent contributions that advanced our understanding of mechanotransduction mechanism at cell adhesion sites and force transmission to the nucleus, presented in several key publications and review articles. Solid resources of national funding were obtained and the team has been engaged in teaching and outreach activities. Finally, the team has established collaborations with a number of partners promoting the transfer of technology developed by the team and its application in various biological questions and model systems.

Strengths and possibilities linked to the context

The team has a strong established profile in the field of mechanobiology and is very well internationally recognised. While the team has a rather small size, it has maintained the permanent research staff and attracted new postdoctoral fellows and a PhD student. The group acquired substantial funding, particularly several ANR grants and PhD funding support. Four PhD students have published scientific articles, reviews and book chapters. The team has an excellent visibility with sixteen invitations to scientific conferences and co- organised four conferences. The team further had active scientific contributions in peer-reviewing of papers and grants and participations as an evaluation panel member for grant programs and assistant professor recruitment.

The team scientific productivity has been very good to excellent, with eleven original articles as a corresponding or co-corresponding author in visible international journals including Development, PLoS One, 2x JCB and Nucleic Acids Res. The publications reflect the efforts of the team in advancing imaging technologies for multi-scale live cell microscopy at the sub-cellular and tissue level. Primary research work further contributed to significant insight into epithelial tissue biology and the role of mechanical forces in cell adhesion and force transmission to the nucleus, with relevance to epithelial tissue architecture, migration and gene regulation. The number of co-author articles supports the collaborative efforts and wider research network established by the team. The scientific output of the team further reflects the cross-disciplinary scientific focus and is consistent with the long-term vision of the team.

The team has been strongly engaged in teaching activities and participated in different outreach activities.

Weaknesses and risks linked to the context

While the team has maintained its overall size, a further growth of the teams appears beneficial to promote its productivity. Significant international funding has not yet been acquired by the team and could enhance the visibility and attractiveness of the team for the recruitment of cross-disciplinary researchers.

The team also has a proven record in technology development resulting in several co-authorship articles, the publications as a corresponding author could be further strengthened in this area.

Interaction with industry and other sector appear to be not fully exploited and could be beneficial considering the focus on technology development by the team.

Analysis of the team's trajectory

The team's trajectory aligns with the research expertise in mechanobiology and will strengthen efforts in the area of epithelia tissue homeostasis and plasticity. The research trajectory will particularly focus on investigating the mechanisms controlling cell adhesion and nuclear mechanotransduction. The investigation of ERK functions in the nucleus in controlling cell and nuclear mechanics will represent an interesting continuation of previous research. A new direction will further be opened in the area of cell metabolism and host-pathogen interactions that will promote further collaborations and expand the expertise of the team. A persistent focus will also be placed on developing new tension sensors and probes for live cell imaging, including Fret/Flim microscopy, along with the development of microscopes. Overall, the research vision of the team is ambitious and follows an exciting cross-disciplinary approach that can advance fundamental questions of tissue biology from a multi-scale angle.

RECOMMENDATIONS TO THE TEAM

The acquisition of international funding and the continued engagement with the international scientific community should promote the development of the team and its international attractiveness.

The team should target efforts in the development of tools and technologies to specific questions aligned with the core interest of the team. Publications in the area of tools and method development as a lead author can further strengthen the profile and visibility of the team.

First author research articles of research staff are also encouraged to promote their career development.

Team 4: DNA replication of pathologies

Name of the supervisor: Mr. Jean-Charles Cadoret

THEMES OF THE TEAM

The team investigates DNA replication dynamics and cancer in eukaryotes, focusing on understanding the role of replication stress in genome instability through two main axes: i) the study of DNA replication dynamics, and ii) the disturbance of replication in cancers, in particular in the context of treatments with therapeutic molecules.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

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

1- *Promote High-impact publications with lab members acting as senior authors, while not neglecting their successful collaborative style*. This point has been improved: one researcher has published 1article as last author, and the team leader published four articles as co-corr. or co-last author (Embo J. 2017; Embo J. 2021; NAR genomics and Bioinformatics 2020 and Int J Mol Sc. 2021). The lab's collaborative efforts have strengthened: twelve collaborations leading to eight publications.

2- *The team should strive to train a larger number of PhD students if possible*. This has been addressed with three PhD students trained. However, the team's senior researcher does not have her HDR diploma, which compromises her supervision of students.

3- *Sharing bioinformatics expertise with other IJM members may be a very good direction to consider increasing the team's impact*. This has not been addressed, but it is offset by the large number of collaborations, linked to the team's expertise in acquiring and analysing genome-wide replication data.

4- *Plan and implement a research programme with a unique angle that will sharpen his independent research profile*. The team is addressing this point by developing a novel research line, investigating DNA replication program alterations with anti-cancer therapeutic molecules. This initiative aims to enhance the team's visibility.

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

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

EVALUATION

Overall assessment of the team

The team develops research projects deciphering DNA replication dynamics in cancer cells, with or without anti-cancer treatments, using a combination of wet and dry experiments. Both the scientific quality of the work and production are very good to excellent considering the small size of the team. The team's visibility is excellent, as attested by the large number of collaborations, the recruitment of PhD students, and the successful acquisition of funding. The team non-academic activity is excellent, with extensive teaching commitments.

Strengths and possibilities linked to the context

The team has an excellent visibility and recognition, attested by the very large number of fruitful national and international collaborations (12), the co-organisation of two national conferences ("DNA replication and replicative stress: from fundamental mechanisms to cancer" 2022; "Replicon club" 2021) and the participation in scientific evaluation (Ligue contre le Cancer, HFSP program) and committees (Doctoral school Paris Saclay, thesis jury (17)). Three (3) PhD students were trained, two defended and one is ongoing, which is excellent. The team has a good ability to raise resources from national agencies ((2) INCA as a partner, (1) idex "Dynamique de la Recherche" as a coordinator, (3) Gefluc (1 as a partner, and 2 obtained by a researcher of the team), one ANR as a coordinator and one grant from "Legacy Larzat".

The team consistently produces very good to excellent research, combining wet and dry experiments, which is the strength of the team. In particular, significant progress has been achieved in creating user-friendly and freely accessible software, START-R (Simple Tool for Analysis of Replication Timing with R). This web-based interface enables the analysis of diverse replication dynamics parameters across various genetic contexts, benefiting both the team and collaborators. In addition, the team investigates (i) natural replication fork pausing and (ii) the impact of anti-cancer drugs on DNA replication. Using diverse methods such as genome-wide replication timing analysis, ChiP-seq, DNA fiber spreading, and cell fractionation, the research is conducted through productive national and international collaborations. The team has a very good publication record, totalling nineteen publications. The team leader contributed as co-corresponding or co-last author to fourarticles (EMBO J. 2017; EMBO J. 2021; NAR genomics and Bioinformatics 2020; Int J Mol Sc. 2021) and one preprint on Biorxiv (co-corresponding, 2022). Additionally, he is a co-author on 4 collaborative works (BioRrxiv 2020, BioRxiv 2022, Sci. Rep. 2021, Nat. Com 2018), wrote one review (Int J Mol Sci. 2021), and one book chapter (Edition de Boeck, 2018). Other lab members contributed with one last-author article (Aging, 2017), two articles from a previous lab, four collaborative works (Mol Psychiatry 2021, J Natl Cancer Inst. 2019, Transl Psychiatry 2019, Sc Rep. 2017), and one book chapter (Edition de Boeck, 2018). Publications involve all team members across various research axes.

The teaching activity is excellent including significant teaching roles such as co-responsability for the summer school 'Chemistry-Biology Interface,' M1 European Genetics module, and leadership in the 'Stabilité du génome et épigénome' UE for the European Master of Genetics. He also contributes to the pedagogical commission of the EUR G.E.N.E and co-organises the online training course 'NGS&Cancer' for Cancéropole IdF since 2020. The team has collaborated with Agilent Technologies on a publication.

Weaknesses and risks linked to the context

While the team has been successful in attracting PhD students, there is a need to recruit additional PhD students and permanent technical staff. The team leader is heavily involved in collective responsibilities (heavy teaching duties) and in the management of intensive collaborative work. While these aspects are positive, they pose a significant challenge to the team's focus on its own projects. These functions can be also compromising for the mentoring of students which relies currently solely on the team leader, as one researcher has left the team, and the senior researcher of the team does not have yet her HDR diploma. The team needs to strengthen its permanent staff with a senior researcher to help with the supervision of students. Securing funding for the team is also crucial and should be prioritised promptly.

While all the research axes developed by the team have demonstrated productivity, there is a potential risk of not sustaining this level of output due to a reduction in the team size. All the publications signed by the team leader in a senior position are co-corresponding or co-last author. While this reflects the success of many

collaborations, it should be noted that the team leader has not yet established himself completely independently in the context of his own projects.

It is essential for all team members to actively participate and contribute to outreach activities.

Analysis of the team's trajectory

The proposed trajectory builds upon the foundation laid by previous successful projects and preliminary data. It centres on two primary focuses: (i) examining the impact of PARylation on the DNA replication process and (ii) investigating the dynamics of the replisome in standard or replicative stress conditions.

Based on unpublished results indicating that anti-PARylation drugs (which are used since a decade to treat cancers) perturb DNA replication dynamics, the goal of the 1st project is to understand how PARylation is involved in the activation of the replication origins and/or in the elongation by the replisome. The recent acquisition of expertise to collect synchronised cells by elutriation will enable this project to be carried out successfully. The project will be based on the use of a wide combination of approaches (genome-wide analysis of the replication program, mapping of PARP enzymes onto chromatin, identification of their partners, DNA combing, iPOND and nascent strands DNA analysis).

The second project is based on their observation that during S phase, the replication machinery naturally pauses frequently, at loci enriched in SNP and CNV. The goal of this project is to understand what leads to the pausing of replisomes and weather this is the cause of the genomic instability associated to these loci.

The proposed trajectory should enable the team to elucidate the cellular consequences of anti-PARylation anti-cancer drugs and explore the functional connections between DNA replication and spontaneous replicative stress. In essence, this research is crucial for understanding the intricate relationship between replication and genome instability, potentially guiding improved utilisation or development of anti-cancer drugs.

RECOMMENDATIONS TO THE TEAM

The team size is small to sustain its project. There is a need to recruit additional PhD students, permanent technical staff and ideally recruit a permanent researcher. The preparation of the HDR by the senior researcher of the team should be considered as soon as possible to contribute to the supervision of PhD students.

Given the fragility of human resources and the team leader's substantial teaching commitments, the committee is concerned by the feasibility of pursuing both lines of research, especially considering the numerous ongoing collaborations. Focusing on one project and exploring it in depth would help to establish the team leader's identity.

The committee encourages for seeking funding opportunities and initiating collaborative ANR projects, involving collaborators or other researchers within the French network.

The committee recommends increasing attendance to international conferences in the area of DNA replication and genome instability to become more visible in this field.

Team 5: Mitochondria, metals and oxidative stress

Name of the supervisor: Mr. Jean-Michel Camadro

THEMES OF THE TEAM

The research of the team focuses on fundamental processes governing iron metabolism and oxidative stress using yeast and human cell lines and employing transcriptomics, innovative quantitative proteomics and computational biology approaches.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

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

1- *The team might increase the efforts to publish at least some results in more visible, or even general audience, journals.* The team published 39 research articles and three review and book chapters. Many of the research papers appeared in journals dedicated to methods, thus intrinsically specialised.

2- *The panel had the impression of a relatively fragmented research program; considering the size of the team, the team leader should consider focusing on a smaller set of fundamental discoveries that could help to achieve output of higher impact.* The team has forwarded a focused research plan for the period 01/2023-07/2024 (date when the team will close), based on the core expertise of the team members.

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

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

EVALUATION

Overall assessment of the team

The team has very good to excellent national and international visibility which stems largely from their expertise in proteomics. The team can forward an excellent scientific output with 39 primary research articles, along with three review and book chapters, produced over the period. The team could secure major sources of funding, they are actively involved in training and interactions with the socio-economic world. Finally, they provide considerable services to the academic and scientific community.

Strengths and possibilities linked to the context

This is a well-established team with very good to excellent visibility. The team leader is part of national and international boards and scientific coordinator of the IJM ProteoSeine facility. Pierre Poulain, who joined the team in 2017, is an active member of the French Bioinformatics community and Valérie Serre is the Head of the Life Sciences Department and member of the CSS1 from the Inserm. The team was able to secure substantial funding for the period under evaluation from ANR, H2020, the "Association Française Ataxie de Friedreich', the labex "Who am I" and via teaching activities. Four PhD students obtained their thesis during the period under evaluation, all of them published, with three of them having one or two articles as first author. The team trained also three Master2, one Master1 and six students from different levels. A major asset of the team is the complementary expertise in biochemistry, microbiology, human genetics and computational biology.

The team's scientific production has been excellent with 39 research articles (18 of them with team members as first and/or last authors) in a variety of different journals, a great number of which specialised in methods. The team has continued physicochemical characterisation of frataxin, a ubiquitous protein whose mutations in humans are associated with Friedreich ataxia and addressed important fundamental questions related to the origin of oxidative stress, the dynamics of post-translational modifications and proteome changes in patient cells. These studies were complemented by investigations of iron-metabolism in frataxin-deficient model yeasts. The team revealed novel mechanisms of adaption to low iron concentrations in phytoplankton. They also developed "Simple Light Isotope Metabolic Labeling", an original method for the quantification of protein abundance variations in complex mixtures, along with algorithms for signal processing. SLIM-labelling can be applied to bacteria, nematodes and human cells and can be used for the quantification of intact proteins in top-down proteomics experiments. All developments and analysis tools are made available to the scientific community.

Members of the group present since many years their research progress at the annual meeting of 'Association Française Ataxie de Friedreich' and they actively interact with Friedreich's ataxia patients.

Weaknesses and risks linked to the context

A large activity of the team members is dedicated to teaching and administration. A team member passed away in 2021 and as a consequence the team has lost the competence in handling radioactive iron, which heavily impacts the development of certain research projects related to studying iron metabolism. The team has never obtained permanent technical support. The team will close mid-2024 when Jean- Michel Camadro will retire.

Although the team is very productive, most publications are submitted to medium-profile and specialised journals.

Analysis of the team's trajectory

The short- and medium-term projects have been planned in view of a one-and-half year term. All topics are a continuation of research carried out in the past, namely the characterisation of the molecular basis of Friedreich's ataxia, analysis of thiol-dependent responses to different physiological oxidative stresses and methods developments in massive data analysis and mass-spectrometry. Following the passing away of the team member studying iron metabolism in marine microalgae, this theme will not be pursued, except to complete a publication. In the long term the team leader plans to be available for consulting the ProteoSeine proteomic facility regarding strategic decisions.

RECOMMENDATIONS TO THE TEAM

The team will close mid-2024 when the team leader will retire. No recommendations can thus be given, except of wishing the PI a joyful émeritat/retirement and all the team members success in their future research environments. A special thanks to the PI for having been instrumental for the establishment of the high-end ProteoSeine proteomic facility at IJM, a high-quality entry point for proteomic analyses in the larger Paris area.

Team 6: Regulation of cell-fate specification

Name of the supervisor: Mr Jérôme Collignon

THEMES OF THE TEAM

The team is interested in understanding how cells respond to signalling during specification. They have been especially interested in how cells respond to the TGFß family signal Nodal in the preimplantation mouse embryo and during mouse primitive streak formation. They also have analysed how Nodal influences human melanoma progression. Their approaches are genetic, imaging, molecular and more recently omic.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

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

1- *The possibilities for outreach activities should be developed, for instance by taking part in IJM initiatives such as "Apprenti chercheurs".* Three team members have started participating in school directed initiatives such as Apprentis-Chercheurs and another team member has participated in the Délics action.

2- *Their interdisciplinary collaborations should continue.* The team is very active at setting collaborations with other teams of the unit and external laboratories.

3- *Ex vivo models, such as micropattern devices should be developed to increase the screening potential before mouse embryos need to be used.* The team has introduced gastruloid analysis for ex vivo studies.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**4**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**4**
Total personnels	**8**

EVALUATION

Overall assessment of the team

The team is performing very good research on a number of interesting issues focusing on Nodal protein signalling and its interaction with other TGFß molecules during development. The team has modernised its approach, introducing single cell techniques and gastruloids. The team international visibility is very good.

Strengths and possibilities linked to the context

The visibility of the team is very good to excellent. The team has trained five PhD students during the reporting period, as well as five master students. The team leader regularly reviews for highly visible journals, attesting international visibility in the field. The team is strong at setting collaborations within the unit and with external laboratories.

The scientific production of the team is very good, with ten published papers, but only a single truly led by the team (Stem cell reports (2022)). They have introduced the organoid model in the lab that allows the use of less animals and is less expensive. They have started working on cancer related projects that may help them widen their funding possibilities.

Weaknesses and risks linked to the context

The team obtained a discrete to medium amount of funding, around 400k during the six-year period evaluated, with a major Inca grant that terminated in 2018.

This is a small team composed at the end of the running contract of two permanent staff, one engineer and one PhD student. Most publications were collaborations, including a Development paper and three Scientific reports papers. Publications led by the team includes a Stem cell reports paper in 2022 and a BioRxiv publication in 2021 (that has been published in 2023 in the Noncoding RNA journal). There is room for improvement in the publication record.

The team lacks bioinformatic expertise for all the omic approaches they have planned.

Analysis of the team's trajectory

The team is going to abandon the preimplantation project after the PhD working on this project will defend in 2024, to concentrate in the two other team projects.

The first will analyse how the Nodal and BMP TGFß signalling molecules interact. The response to both signals is mediated by SMAD proteins, although each signal is mediated through the activation of different members of the family (Smad2 and 3 for Nodal vs. SMAD 1 and 5 for BMP). To analyse the consequences of the activation of Nodal or Nodal combined with BMP, the team is going to use gastruloid cells induced to form either anterior, posterior or intermediate fates, analysing them employing SCRNAseq, ATAC seq, IP and CUT &Tag. This will be done in collaboration with one team at IJM and two Institut Curie teams that will be in charge of the bioinformatics. Using gastruloids diminishes the need for mice, although it is to be seen how the gastruloid results apply to embryos in vivo. To confirm the validity of the gastruloid approach, the team will analyse later the replication of their results in mice embryos. This project should elucidate the molecular basis of primitive streak specification.

The second project will investigate the function of Ladon in melanoma tumour progression. This project follows up the recent team's finding of an antisense transcript that comprises Nodal's second exon and neighbouring intron sequences. Expression of this transcript is correlated with tumour proliferation and metastatic capacity. Ladon contains MIR and Alu homology sequences and homology with MYCN and a lncRNA involved in tumour progression. The objective here is to find out how Ladon modulates the tumour and finding out what regions of the transcript mediate its function. The team is interested in finding what the function of Ladon in normal development is, as well as testing its possible involvement in other types of cancer.

RECOMMENDATIONS TO THE TEAM

The team is at a critical point. After introducing novel approaches in the lab they have to aim at publishing their new interesting results in more visible journals to be able to get more sizeable grants. As some of the work will be done in collaboration with other teams, it is important that the team members appear as corresponding/first authors to demonstrate their leadership in the project. The team should aim at increasing its size with postdoctoral fellows and PhD students.

Team 7: Regulation of microtubule in multi-cellular animals

Name of the supervisor: Mr. Paul Conduit

THEMES OF THE TEAM

The team studies microtubule nucleation using drosophila as a model system. They use a combination of genetics, cell imaging, biochemistry and structural biology to study gamma-tubulin ring complexes assembly, recruitment and activation at specific microtubule organising centres (MTOCs).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

N.A.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	**2**
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	**5**

EVALUATION

Overall assessment of the team

The team adapted very quickly to the French system since in three years, the team leader secured funding, recruited staff with whom he published original publications that will move the field forward. The team leader is also involved in IJM lab life, and is regularly invited to meetings and reviewing, showing how renowned and respected he is in his field. Overall, the team was evaluated excellent to outstanding.

Strengths and possibilities linked to the context

The visibility of the team is outstanding. The team leader established his own team in Cambridge in 2015 before joining IJM in August 2020. Over the past three years, his remarkable achievements include securing significant funding exceeding one million euros from prestigious sources such as ANR, ATIP-Avenir, and idex ("Chaire d'excellence"). He recently got awarded the "Impulscience" grant (similar level of funding than an ERC). Additionally, he successfully recruited five persons including a permanent assistant professor, two Ph.D. students, and two postdoctoral students researchers. He is regularly invited to international meetings in his field (Centrosomes or Microtubules EMBO workshops, Drosophila meetings in France and UK) and to give seminars in Europe. He reviews articles for Nature Cell Biology, Current Biology, eLife, JCB and PLoS Biology.

The scientific production of the team is excellent to outstanding. Since 2018, the team leader has made significant contributions to the field, evidenced by six publications where he served as the last author (one still in BiorXiv). One of them follows up an observation he made as postdoctoral students revealing that in Drosophila syncytial embryos, daughter centrioles exhibit a tendency to assemble specifically towards the nuclear envelope (Open Biol 2022). While still in Cambridge, they identified Mozart 1, a conserved gamma-TURC protein, showing its specificity for certain MTOCs and its confinement to sperm cells (Curr Biol. 2018). The team thus demonstrated that there are differences in gamma-TURCs composition, thereby helping to assemble cell-specific arrays. The team then employed Crispr-dependent knock-in techniques, successfully introducing GFP into the endogenous gamma-tubulin locus in neurons. This innovative method allowed them to observe the asymmetric localisation of gamma-TURCs to the cis-side of golgi stacks within the soma (eLife 2020). This asymmetric positioning induced a directional preference for microtubule growth towards the axon and away from the dendrites, shedding light on crucial cellular mechanisms. Surprisingly, they also uncovered that gamma-TURCS are not essential for microtubule nucleation at centrosomes due to the presence of Msps (JCB 2023). An equally significant revelation was the demonstration that autoinhibition of Cnn binding to gamma-TURCS plays a critical role in preventing abnormal microtubule nucleation, consequently averting cell division defects (JCB 2021).

While the team acknowledges that it had a limited contribution to society so far, he already got involved in collective tasks with the IJM ("Green IJM", "Seminar Organising Committees).

Weaknesses and risks linked to the context

It will be crucial for the team to attract more permanent staff, particularly a lab-manager, and possibly other permanent researchers.

Analysis of the team's trajectory

The team is following two research axes. The first, already underway or set to commence soon, focuses on unravelling the regulation and activation mechanisms of the gamma-TURC by Cnn. Thanks to a collaboration with I2BC, they are hoping to decipher the structural basis for Cnn auto-inhibition via interaction between its CAI and CM1 domains. Using purified gamma-tubulin complexes and TIRF microscopy, they plan to study how Cnn binding stimulates gamma-TURC nucleation activity.

The second axis will investigate the regulation of microtubules within neurons. Building upon the observation that gamma-TURC is dispensable for golgi-dependent microtubule nucleation, they will investigate how the resulting lack of asymmetry affects overall microtubule polarity within neurons. They identified what they called "dendritic bubbles" where Cnn and gamma-tubulin concentrate and they are testing the hypothesis that microtubules are nucleated within these bubbles independently of gamma-TURCS. They will use molecular modelling to test whether asymmetric nucleation and plus-end directed motor guiding along adjacent parallel microtubules are sufficient to explain overall microtubule polarity in neurons. The requirement for Augmin to nucleate microtubules nucleation with or without gamma-TURCS will be investigated.

In the long term, their research trajectory encompasses probing the regulation of microtubule nucleation during early neuronal development, examining the role of gamma-TURCS in mature adult neurons, and scrutinising microtubule nucleation regulation during periods of neuronal stress.

RECOMMENDATIONS TO THE TEAM

Continue to perform great science!

Team 8: Evolution and genetics

Name of the supervisor: Ms. Virginie Courtier

THEMES OF THE TEAM

The team's general aim is to bring new data and new perspectives on the evolution of living beings. This is addressed in two major axes: one, involving wet lab experiments using closely related species of Drosophila, focusing on the evolution of larval glue proteins studied as a model for bio-adhesion and on the evolution of the genitalia; and a second axis involving reflection and computer analyses on general topics about genetics and evolution, such as the genetic basis of evolutionary changes, new biotechnologies (gene drive) and SARS-CoV-2 origin.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hcéres evaluation (italics) were:

1- The committee's recommendation is that they keep up their exciting work and the promotion of discussion in the science community and the broader public. This has been addressed by giving several talks at research conferences and interviews/discussions for newspapers, radio stations, associations, etc, by serving as a member of national committees, and by sitting in various Editorial Boards and Scientific Advisory Boards.

2- One suggestion is to invest in the creation of an even more international environment, attracting more researchers from outside the French system to join the team. Recruitment of more PhD students would be a plus. This has been addressed by recruiting three PhD students and several Master and other students and by attracting more researchers who joined the team in 2022 and 2023.

3- The team's main challenge in delivering its ambitious research vision will be to keep their forward momentum going as they reach the end of their ERC grant. Prompt publication of the highly promising ongoing work is therefore essential to secure further funding. This is largely addressed by publishing 22 research papers and 13 reviews and book chapters. However, no major grants were obtained yet after termination of the ERC starting 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	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**4**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	1
Doctorants	1
Sous-total personnels non permanents en activité	**3**
Total personnels	**7**

EVALUATION

Overall assessment of the team

With multiple invitations to present at conferences and seminars, the team has demonstrated excellence and recognition on a global scale in the field of genetics and evolution. The team has created a corpus of quality primary articles in addition to book chapters and reviews. This corpus of work is also being contributed to by researchers from outside of France who were attracted to the group due to the reputation of the team leader, who has also made outstanding contributions to outreach and public engagement. Securing additional funding for the future may be facilitated by a more concentrated focus on one of the many research topics addressed.

Strengths and possibilities linked to the context

The team visibility is outstanding. The team has had a strong production in the discussion of important societal issues including the origin of Covid19 and the risks and promises of new Crispr-Cas9 tools for establishing gene drives. Their main scientific focus on comparative evolution is very original, analysing populations in the wild, and also studying the bases of genitalia development and evolution and how the morphological changes may impact different copulatory behaviours analysing if morphological changes and the particular behaviour of the animal are associated. The team has created a website where it recollects all the published data on genetic variants involved in various evolutionary changes that is open to the general community. The team leader also has written several papers with a societal impact on the risks and possibilities of using Crispr-Cas9 genetic drive biotechnological tools. The team leader is engaged in several societal committees (CNRS Comets, OPECST (office parlementaire d'évaluation des choix scientifiques). 13 reviews and book chapters were published. Numerous honors have been awarded to the team leader in recognition of her contributions to science and society, including the Lacassagne Prize from Collège de France and the Chevalier de l'Ordre national du Mérite title. Moreover, she has been Elected EMBO Member in 2022.

The team has had an excellent scientific production featuring 22 research papers (including 12 BoiRxiv), with half of them being in lead position. The team has studied how various Drosophila characters evolve among close species. They have focused in: i) the glue genes that are required for pupal adhesion to the substrate but are also involved for predator protection; ii) the evolution of the male genitalia that has a certain asymmetry in different close species that still allow hybridisation and thus the identification of the molecules involved in this variation; they have managed to induce Crispr/Cas9 mutagenesis in some of these species, which allowed reversing the genitalia polarity but did not affect the behavioural position during copulation.

The team leader has an outstanding activity in science and society which includes Comité d'éthique du CNRS and Office parlementaire d'évaluation des choix scientifiques et technologiques as well as lecturing at Collège de France.

Weaknesses and risks linked to the context

The team has missed a great opportunity to generate a strong CV to allow them to apply for competitive grants at the end of the ERC starting period.

The team has produced many papers but, with some exceptions (including a Current Biology paper), not in the most highly regarded journals.

Analysis of the team's trajectory

The team is going to continue the study of Drosophila glue proteins in different species. Besides its interest from the evolutionary perspective, this work may give rise to new bio-adhesives. They will continue their work on the genitalia evolution comparing close species and analysing different genes to test if they are responsible for some of the observed phenotypes.

The team is also continuing their work to decipher the origin of the virus responsible for Covid19. They organise a meeting on the topic every three months.

The team leader will give a series of conferences on *Evolution and the Living World* at the College de France collecting them in a book. This is a very interesting intellectual tour de force that she will have to make compatible with her other research.

The team will also analyse the effects of gravity on development. Although this has been analysed previously on experiments where flies were sent to the space station, in this project they will analyse how exposing the animals to continuous variable gravity force changes during development affects different properties like intestine permeability, bilateral growth precision, and aging. This is very original although quite challenging as the relevance of such changes in development under normal conditions are unclear.

Another aspect that will be analysed is ageing, considered as an end-of-life process. This also is an original point of view of this pervasive issue.

RECOMMENDATIONS TO THE TEAM

The team analyses extremely original issues that may give very interesting results, but they must dedicate more effort to apply for research funds. While the diversity of topics and evolutionary questions covered are very intriguing and could be attractive for funding agencies fancying high risk - high gain projects, a more focused approach based on robust preliminary data should be also used to secure significant funds to perform their work.

Team 9: Non-conventional functions of nuclear pores

Name of the supervisor: Ms. Valérie Doye

THEMES OF THE TEAM

The team research focuses on the non-conventional role of nuclear pore proteins in human cells, mESC cells, Drosophila, Zebrafish, and iPSC-derived organoids, through three main axes: the study of (1) the crosstalk between nuclear pores and kinetochores, (2) the implication of nucleoporins in pluripotent stem cells differentiation, and (3) the impact of nucleoporins mutations in tissue-specific human genetic diseases.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hcéres evaluation (italics) were:

1– Recommendations on scientific production and activities: "the group is encouraged to continue along these lines." This has been addressed with the team publishing eleven papers with team members as last author in high-ranking journals (Mol. Cell, Nat. Comm, Cell Reports, J Cell sci., EMBO reports…)

2– Recommendations on the team's organisation and life: "Benoit Palancade's independence as group leader of his own research team" This was achieved by the creation of a new team at the IJM, with the PI who responded to an international call. In addition, a researcher recruited in 2019 at the CNRS has also left the team to start her team at the IGH in Montpellier.

3– Recommendations on scientific strategy and projects): "The team should continue to address important questions and produce quality science." This has been addressed as the research team actively explores and poses original and critical questions.

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

EVALUATION

Overall assessment of the team

The team develops cutting edge research projects deciphering the non-conventional role of nuclear pore proteins. Both the scientific quality of the work and production are excellent to outstanding considering the small size of the team. The team's visibility is excellent to outstanding, as attested by its international recognition, the recruitment of PhD students & of researchers, and the successful acquisition of funding. The team non-academic activity is excellent, with biotech collaborations and the local organisation for IJM of the "Apprentis Chercheurs" program.

Strengths and possibilities linked to the context

The team has an excellent to outstanding visibility and recognition, attested by invitations to communicate at international meetings (5 invited conferences), the organisation of the international conference 'Nucleocytoplasmic Transport' (Spain) and the participation in evaluation committees (Hcéres, Scientific council of the INSB (CNRS)). Three PhD students defended their theses. The team has undergone a dynamic flux of permanent scientists, which is indicative of its dynamism, first with the fusion of the team with another team (2 researchers) and the recruitment of one permanent CNRS researcher, and secondly, with the departure of two permanent researchers who have started their own teams and two permanent staff who have retired. The team has an excellent ability to raise resources from national agencies ((2) Equipe labellisée FRM 2015 and 2020; (3) ARC foundation; (1) Ligue Nationale Contre le Cancer; (1) idex université Paris Cité), and obtained two doctoral contracts and two postdoctoral students contracts (labex "Who Am I?"). Moreover, (1) Transversal Project grant from labex "Who Am I?" to establish the Enscore platform has been co-obtained by the team leader. All the permanent researchers have obtained funding.

The team consistently produces excellent to outstanding research, demonstrating high levels of both productivity and the quality of their work. In particular, major advances have been made in studying the contributions of Y complex nucleoporins to nuclear pore assembly and gene regulation during mESC growth and differentiation, and in understanding the molecular determinants of Cenp-F localisation to nuclear pores and kinetochores. The work is carried out through multidisciplinary approaches (quantitative microscopy approaches, genetics, transcriptomic analyses, *in silico* structural modeling (national collaboration)), is based on the use of different cell models (mainly human cells, mESCs, IPS/organoids, and Drosophila, Zebrafish) and on the frame of many fruitful national and international collaborations. The team has an excellent to outstanding scientific production in terms of publications, with thirteen high-quality publications, eleven being signed in leading positions including five by the team leader (Mol. Cell, 2 Nat. Commun, Cell Reports, EMBO reports, Sci. reports, J Cell Sci., Open Biol. …) and two resulting from collaboration within the unit or with an international team. Moreover, one review article (Med. Sci.) and 1 preprint (BioRxiv 2023) have been published. Publications involve all the team members, and all the research axes.

The non-academic activity is excellent with biotech collaborations (EMD Millipore) for the commercialisation of two antibodies generated by the team. The team participates in science outreach programs such as "Apprentis chercheurs", and organises visits for the general public of the Enscore organoid facility ('Visite insolite' of the CNRS).

Weaknesses and risks linked to the context

While the team has been successful in attracting PhD students and securing their funding so far, there is a need to recruit additional PhD students. The team leader is heavily involved in collective responsibilities as the director of the unit and the co-director of the Enscore organoid facility. These functions are very positive, but can be compromising for the mentoring of students which relies currently solely on the team leader. The team needs to strengthen its permanent staff with a senior researcher to help with the supervision of students. This should be ensured in 2024 by the arrival of a senior researcher with a permanent CNRS position and of an assistant engineer. It is also imperative to promptly secure funding for the team.

Although all the areas developed by the team are very productive, there is a risk of losing the ability to remain at the cutting edge due to the reduction in the size of the team (which is the result of retirements and the budding out of 2 new research teams).

Analysis of the team's trajectory

The suggested trajectory continues the path paved by previous successful projects, focusing on one main axis: exploring the involvement of ubiquitous structural nucleoporins in rare genetic diseases. The main goal will be to determine why, despite the universal role of nuclear pores in all nucleated cells, mutations in certain ubiquitous nucleoporins cause tissue-specific inherited human pathologies.

The team will focus on nucleoporin gene mutations causing steroid-resistant nephrotic syndromes (SRNS), and Galloway-Mowat syndrome (Gamos), both affecting specific neurons and kidney cells, the podocytes. The recent acquisition of expertise in differentiating iPSCs carrying these mutations into neurons and podocytes, in 2D or 3D (organoids), will enable this project to be carried out successfully. The project will be based on the use of a wide combination of leading-edge approaches (quantitative and super-resolution microscopy, RNA sequencing,), and on established collaborations with experts.

Data obtained previously using Nup133 inactivation in mouse embryonic stem cells provide avenues of investigation for phenotype analysis. Based on this knowledge, the team will establish a comprehensive set of assays to investigate the potential causes of phenotypes induced by NUP mutants in differentiated cells derived from iPSCs. This entails examining NPC assembly, evaluating nuclear trafficking efficiency, assessing the mechanical sensitivity of the nucleus, studying nuclear migration, and analysing gene expression. This project is poised to allow the team to delineate the cellular and molecular repercussions of NUP gene mutations, leading to the identification of novel factors and molecular networks influencing the differentiation and/or maintenance of specific cell types. The crucial inquiry into whether the phenotypes associated with NUP mutations arise from NPC or non-NPC functions of nucleoporins is pivotal for comprehending the tissue specificity of human pathologies.

In total, the team's project is both thrilling and feasible, given the extensive and longstanding expertise of the team.

RECOMMENDATIONS TO THE TEAM

The team should elaborate a strategy to attract PhD students and postdoctoral fellows to increase its manpower.

Given its visibility, the team should explore a wider range of funding sources.

Interaction with the society should be maintained.

Team 10: Programmed genome elimination

Name of the supervisor: Ms. Sandra Duharcourt

THEMES OF THE TEAM

The team is studying genome stability in particular during the programmed genome elimination in ciliate Paramecium tetraurelia. To get a better understanding of the fundamental mechanisms governing genome elimination, they address two questions: which parts of the genome are eliminated, and how does elimination occur. Three main axes are developed: 1-Identification of the eliminated sequences: annotation of the somatic and germline genomes, 2- Identification and functional characterisation of new factors involved in programmed genome elimination and 3- Somatic genome recognition (DNA Adenine methylation).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hcéres evaluation (italics) were:

1- The team should continue to pursue exciting and novel science. This is obvious with numerous milestone publications in the field and also national recognition.

2- The team should aim at recruiting a permanent researcher to assist the PI while increasing other team members' productivity. This has been partially addressed with the recruitment of an assistant professor in 2022 but would benefit of a full-time permanent scientist position.

3- One possibility for improvement might be to increase computational skills inside the group or strengthen interactions with local computational groups. For the moment it remains an important weakness in the team to get autonomy in computational approaches.

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

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

EVALUATION

Overall assessment of the team

The team has an excellent to outstanding scientific production given its modest size with a total of eleven publications (7 research articles in leading positions) frequently published in highly visible journals (Dev. Cell, Genome research, PLoS Genetics, PLoS Biology, Nat. Commun). The visibility of the team is outstanding with four PhD trained, the awarding of the CNRS Silver medal and capacity to attract funds with over 1,2M€ (including 2 ANR and 2 FRM team grants).

Strengths and possibilities linked to the context

The attractiveness and visibility of the team are outstanding with numerous conferences in international meetings (including 27 internationals; EMBO Workshop, Cold Spring Harbor Laboratory, Gordon), one national prestigious awards for the PI (CNRS Medaille d'argent 2022) and recruitment of six PhDs and two Post-doctoral researchers as well as an associated professor in 2022. The recognition of the team is also attested by their capacity to attract funding (2 ANR, 2 FRM-team grants to reach over 1.2 million euros).

The scientific production is excellent to outstanding given the size of the team with eleven publications (9 research articles including seven as main author and 3 reviews) in the best journals for the field (Genome research, PloS Biol., PloS Genet., Nat. Commun). The team studies genome instability in the context of the paramecium genome elimination and is highly visible in the field being a leader in developing approaches and understanding fundamental mechanisms. Two main axes have been developed from the identification of the genomic regions that undergo rearrangements to the functional characterisation of the regulatory factors. These two axes are now completed by an emerging topic in the team focused on the identification of signal(s) that marks the somatic genome participating to these processes. The study of adenine methylation is pursued by a former team member, now assistant professor in Japan.

Finally, the outreach activity of the PI is excellent with special focus on young people training or research activity incitative (Declics, high school teachers).

Weaknesses and risks linked to the context

The team has no major weakness, but would certainly benefit from an international funding as ERC or HFSP to secure a mid-term expertise on genomic computational activities that are now essentially performed by collaborators. The outstanding research looks limited to the model organism and might benefit of diversification towards other models.

Analysis of the team's trajectory

Three axes will be developed in the future with the two first as a follow up of the last term.

1- Identification and annotation of the eliminated sequences (France Génomique consortium – C. Rubio Ramón) using *de-novo* genome reconstitution by short and long reads.

2- Mechanisms of genome elimination focusing on PRC2 reconstitution, roles of histone marks and the SUMOylation focusing on Complex reconstitution (EZI1) and Histone mark binding proteins (Mass spec) as well as on the role of the Sumo pathway in genome elimination (targets identification).

3- Regulation of sRNA dynamics is a novel axis consisting in understanding how the complex population of SRNAS representing the entire germline genome is sorted out in the maternal somatic nucleus by comparison with the entire somatic genome. In particular they will focus on a role for PRC2 in sRNA selection (uncovered by the team) and perform a functional analysis of protein(s) involved in sRNA selection by gene candidate approach (Ptiwi09) and the role of the ubiquitin pathway in sRNA selection.

The trajectory is sound and robust and capitalised on the expertise of the team and the actual collaborations. The first axis will need a lot of computational analysis.

RECOMMENDATIONS TO THE TEAM

The team should certainly continue the high quality and rigorous science that they produce.

The team should also try to accommodate more with valorisation of their research (protecting some methodologies).

The most important recommendation would be to secure a bioinformatic permanent position in the team to get autonomy in this large and growing part of their activity. Such recruitment could be performed by an international funding, allowed by the team's proven excellence. On this aspect, a high-risk high gain project could be to diversify to other models, with more genomic complexity.

Team 11: Cell division and reproduction

Name of the supervisor: Mr. Julien Dumont

THEMES OF THE TEAM

The team probes the mechanisms for chromosomal segregation in meiosis and early embryonic mitotic divisions, with special attention to the function and regulation of microtubules, using the nematode worm *C. elegans* as a model. The team has pursued three interconnected axes revolving around oocyte meiosis, namely spindle function and dynamics, chromosomal segregation and oocyte meiosis in a non-model nematode. A fourth axis centres on the first mitotic division of the *C. elegans* zygote.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hcéres evaluation (italics) were:

1- To continue producing high quality science and obtaining competitive funding. This has been addressed as the team generated a strong publication record over the last five years (16 publications in total) that includes at least four first/last author research articles contributed by multiple members of the team (eLife, Dev. Cell, Nat. Commun). Also, outstanding funding support over the same period from multiple sources (ANR, FRM, ERC consolidator, among others) has continued.

2- To hire new PhD students. This has been addressed but the recommendation remains relevant. Over the period under evaluation three new PhD students joined the team. Out of five trained during the period, three have finished and two are scheduled to depart by the end of 2023. Thus, none would remain past early 2024.

3- To improve international visibility of the team leader. Over the last five years, the team leader has received invitations for six international conferences and eight national/international seminars and has received other national recognitions.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**3**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	3
Post-doctorants	1
Doctorants	3
Sous-total personnels non permanents en activité	**7**
Total personnels	**10**

EVALUATION

Overall assessment of the team

The team has an excellent to outstanding track record and is internationally recognised in the field of meiotic and mitotic cell division, with invitations to present in conferences and seminars. The team has built a body of high-quality primary articles, along with review and book chapters, has continued to secure major sources of funding and maintains a presence in outreach/public engagement, including various modes of interactions with high school students and public. Finally, the team is well-connected with a number of collaborators, thus expanding their research scope.

Strengths and possibilities linked to the context

This is a well-established team with outstanding visibility sustained by a track record for research quality and productivity. Financially, the team is in a great position as it continues to secure major sources of funding (ANR, FRM, ERC consolidator, among others) and has managed to keep a consistent group size. Despite the relatively limited number of permanent staffs in the team, seven Master 2, six Master 1, four L3, 2 BTS and five PhD students have been trained over the period under evaluation and both the team leader and the assistant professor pursue teaching activities. Moreover, the team leader has received multiple invitations to present at international conferences and seminars as well as national recognitions. Enhanced impact stems from productivity involving international, national/IJM collaborators enabling a wider agenda within the field of cell division mechanics.

Scientific production
The team productivity has been excellent to outstanding with thirteen research articles (at least four first/last author research articles contributed by multiple members of the team published in eLife, Dev. Cell, Nat. Commun) and other scholarly outputs —1 review article and two methods book chapters. Collectively under the oocyte meiosis research axes, a series of elegant multidisciplinary studies featuring state-of-the-art microscopy have made remarkable contributions for understanding mechanisms residing at the microtubule-kinetochore interface versus the central spindle that govern spindle dynamics and chromosomal behaviour. Intriguing observations were made in two further studies (listed as Ms in prep): first, a novel structure perhaps contributing to chromosomal segregation, the so-called "interkinesis envelope" appearing at the transition between meiosis I and II in *C. elegans* oocytes; second, maternal centrosome inheritance (outstandingly stemming from centrosome persistence during oocyte meiosis) in a parthenogenetic nematode. The mitotic division research axis yielded novel insight into non-canonical roles of an otherwise well-studied spindle assembly checkpoint component for enforcing chromosome bi-orientation while another study uncovered a mechanism linking cell volume and microtubule dynamics for scaling spindle length to cell size over early embryonic divisions.

The prospects for non-academic engagement may be limited in view of the basic nature of the research undertaken. Nevertheless, the team has participated in a number of outreach initiatives targeted to high school students and the general public.

Weaknesses and risks linked to the context

Although the team has kept a consistent size over the period under evaluation, most temporary staff will be leaving by early 2024. Moreover, the team has no permanent technician/engineer and there is no planned replacement for two permanent staff member (1 researcher and engineer) who left. Taken together these constitute serious challenges to continuity.

It appears that the team suffered from loss of significant work due to a crash of their -80°C freezer. Considering the size of the group and the significance of such a loss, the question should be raised of whether there are contingency plans or sufficient risk assessment in relation to this critical area of resource management. It is also of interest to ask what is the support available to a team to plan how to avert such accidents.

Analysis of the team's trajectory

The team excels on their multidisciplinary approach to the study of mitosis and meiosis. Their accomplishments thus far provide solid basis to expect that the proposed work for the next five-year period will yield significant advances. The decision to focus on female meiosis already met with support in the previous evaluation as this was understood to be the most likely area for the team to make their mark. Indeed, in the last five years the

team has made key progress in characterising mechanisms underlying spindle and chromosomal dynamics in oocytes and has uncovered outstanding idiosyncrasies of oocyte meiosis in nematodes —a novel membrane-based structure and the persistence of centrosomes throughout oogenesis in the context of parthenogenetic reproduction.

In the next five years the team will combine genetic-based perturbation and in utero live imaging in *C elegans* to generate an integral view of the molecular players at the heart of a centrosomal spindle assembly as an organised network of regulators of microtubule nucleation and dynamics under the control of key cell cycle kinases. These studies will set the stage for analysis of the differences between spindle assembly at meiosis I versus meiosis II, in terms of molecular requirements and timescale.

The team is also proposing to pursue ongoing studies on meiotic kinetochore architecture and its dependence on centromere-associated proteins as well as expanding on their findings on segregation of chromosomes via microtubule pushing forces emanating from the central spindle as instructed by a candidate-based approach in progress to dissect the contribution of *C elegans* eighteen kinesin-like proteins.

Collectively this exciting programme is likely to yield crucial molecular insight to ultimately achieve a detailed timeline of interconnected processes along meiosis I and II given the existing expertise, network of collaborators and access to cutting-edge microscopy. Finally, the team will capitalise on this knowledge to explore contrasting mechanisms for meiotic spindle assembly and cytokinesis under parthenogenetic reproduction in *R. dutinus*. The departure from *C elegans* in these comparative studies sounds very timely and should convey novel leads to gain crucial evolutionary insight into the mechanisms underlying oogenesis although the proposal did not address how the possible significance to higher eukaryotic systems, including humans might be pursued.

RECOMMENDATIONS TO THE TEAM

The team should continue to capitalize on their strong productivity to translate their success into novel funding opportunities and enhanced visibility.

They should consider other scholarly contributions and boost media presence to enhance impact.

The team should endeavour to strike a robust balance between permanent staff and PhD recruitment.

In their strategic plan, the team should approach the challenge of coordinating funding cycles and team member turnover to boost continuity and help maintain a consistent team size.

Contingency plans for storage of critical resources/stocks/materials should be developed and risk-assessed to avert costly accidental loss in the future.

Team 12: Epigenomics and paleogenomics group

Name of the supervisor: Mr. Thierry Grange / Ms. Eva-Maria Geigl

THEMES OF THE TEAM

The project of the team focuses on the evolutionary processes occurring over the last hundred thousand of years by analysing the ancient genomes from fossils. The main objective is to explore the evolution of genomes during animal domestication or during the peopling of Europe to further apprehend the relationship between genotypes and phenotypes.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hcéres evaluation (italics) were:

1- *The team was encouraged to exploit the technology they have developed in order to pursue their interesting research questions together with their impressive collaborator network*. This was achieved over the past 5 years.

2- *It seems important to strive to obtain more technical staff support; all the more so given the team's investment in method development – for paleogenomic-related DNA extraction or bioinformatics methods*. The team obtained a two-year engineer position (IE CNRS in the frame of a collaboration).

3- *The good focusing of the research plans on two main areas (peopling of France and cattle domestication) will help in preserving the team's forward momentum. A strong drive to leverage recent progress and the potentially medically/agronomically attractive parts of the programme (genetics of complex (ancient) disease; cattle evolution) to apply for national and international funding will be essential to maintain a critical mass and provide the financial means to acquire technical support for the lab.* The team has continued to focus on these two main areas of research and has obtained new grants during the past 5 years, both international (H2020, CSA, Neomatrix) and national (ANR, Office Français Biodiversité).

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

EVALUATION

Overall assessment of the team

The research performed by the group is outstanding with important contributions. The team, which has developed methods to read ancient DNA, is internationally recognised for its work on genome evolution through the analysis of paleogenomes. Its visibility is excellent to outstanding as assessed by the publications, collaborations with archeologists, regular funding and invitations to international conferences. The non-academic contribution is outstanding with numerous articles, conferences and media performances for science popularisation.

Strengths and possibilities linked to the context

The team has an excellent to outstanding national and international visibility because of its seminal studies with original approaches to characterise genome evolution in domesticated animals and human populations as reflected by fruitful collaborations with archaeologists. The work has been funded by national and international agencies as principal investigator (2 ANR, 1 H2020) or as partner (1 ANR, 1 Office Français de la biodiversité). This is a well-established team composed of three permanent members (2 DR CNRS and 1 assistant-professor), five PhD students (3 defended), one postdoctoral students and one engineer during the period.

The production of the team is outstanding over the last six years with eleven papers as PI in very good journals: Nature Ecology & Evolution (2017), Science Advances (2019, 2020, 2022), PNAS (2020) and Mol Eco Resources (2017, 2018) or in more specialised ones: Diversity, PLoS One, Microbial Environmental Genomic, two papers in collaboration, seven reviews on paleogenomics. The team is working on genome evolution in two different reach lines, in animal species (bovines, equids, cats) during domestication and in human populations during Europe peopling. First, by comparing the nuclear and mitochondrial genomes of fossils up to 120,000-year-old, they traced the evolution of auroch (Bos) and bison populations, showing the effect of domestication on Bos genome evolution and reconstructing the phyleogeographic evolution of bison with an unknown ancestor of the today's European bison. Using mitochondrial genome, they revealed the evolution of wild auroch and domesticated cattle through time and space (Europe, Southwest Asia, North Africa) and the effect of climate change over the last 50,000 years and human interactions over the last 10,000 years (to be published). For equids, they compared the genomes of three species from Northern hemisphere, two domesticated (horse and African donkey) and one on the edge of extinction (wild Asian donkey -hemione); they unveiled the timing of expansion of domestic horse and hemione population history. For cats, by analysing mitochondrial genome, they reconstructed the history of the spreading of the North African and South-West Asian wild cat, the predecessor of the domestic cat, over the last 10,000 years. Second, they show how four cultural and populational transition periods during Europe peopling over the last 40,000 years affected the genome of human populations. Finally, by analysing ancient mitochondrial DNA, they demonstrated that a fragment of skeletal remains from the Denisova Cave is the larger, missing part of a fifth finger phalanx of a Denisovan type specimen. The team has also developed a number of methods to construct genomic libraries from highly degraded samples and detect circulating DNA in blood (3 publications).

The contribution of the team to society is outstanding with a national training course "Archeogenomics", 14 articles and 9 conferences of scientific popularisation, 19 media performances.

Weaknesses and risks linked to the context

The two PIs will retire in 2024 and 2025. It will be important to get the results already obtained published, especially those involving non-permanent members of the group.

Analysis of the team's trajectory

A number of projects (4) have been described which should be finished before mid-2025. They are in the continuity of the actual studies and rely in most cases on expertise of the group.

RECOMMENDATIONS TO THE TEAM

Since the team will not be renewed, it is important to publish before the end of 2025 the very original results obtained.

Team 13: Chromatin dynamics in mammalian development

Name of the supervisor: Mr. Maxim Greenberg

THEMES OF THE TEAM

The project of the team focuses on the epigenetic reprogramming that occurs during the early mammalian development. The main objectives are to characterise non-canonical roles of DNA methylation, such as the impact on 3D genome organisation, the influence on cis regulatory elements, and antagonism of gene silencing pathways in certain contexts.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has been created very recently (Fall 2019).

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	0
Sous-total personnels permanents en activité	**2**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	2
Sous-total personnels non permanents en activité	**4**
Total personnels	**6**

EVALUATION

Overall assessment of the team

The research performed by this young team is promising but it is too early to assess its quality as the team was created only in fall 2019. Nonetheless, the team has already acquired an outstanding visibility as assessed by obtaining several important funding including an ERC starting grant, as well as by the recruitment of postdoctoral students, PhD students and a permanent researcher. The team leader is internationally recognised for its work on the epigenetic reprogramming occurring during early mammalian development. The non-academic activity of the team is excellent with several initiatives with the general public and debates in society.

Strengths and possibilities linked to the context

The team has an outstanding visibility and attractiveness. This young team has been established in Fall 2019 and is composed of seven persons including two permanent members (2 CRCN CNRS), two postdocs, two PhD students and one engineer on short term contract. The team leader obtained an ERC Starting Grant in 2019. The team attracted recently two PhD students. The team obtained three funding for postdoctoral students (2 FRM

and 1 from ARC). One of the postdoctoral students was recruited by CNRS in 2022. The team has also produced three reviews in primary journals (Nature Genetics, Cell Dev Biol and Nature Review in Molecular and Cellular Biology) demonstrating the visibility. The team leader has been invited as speaker to two international conferences including an EMBO workshop on Epigenetics. Six seminars were given at international institutions during the period.

The publications reported in the document correspond to the work performed by the PI while he was still in postdoctoral students (Nature Genetics and eLife) or resulted from works performed in collaboration with groups of PA Defossez, V. Ribes and H. Kobayashi. The work described in the document, while promising, remains to be published. The team is working on non-canonical roles of DNA methylation in mammals occurring during early mammalian development. They use a a mouse embryonic stem cell differentiation system to analyse these processes together with an in vivo mouse model to establish the epigenetic memory of early embryonic events through life. Different lines of research are followed: i) genome-wide identification of specific regions (termed Switch regions or SWRs) subjected to the DNA methylation-based activation process occurring during embryonic development, ii) identification and characterisation of the factors required for SWR regulation in mammals, iii) probing the impact of DNA methylation on the 3D genome organisation, iv) dissecting the interplay between DNA methylation and H3K4 methylation, v) analysis of the regulation of mammalian enhancers by DNA methylation

The results obtained by the group since its creation identified about 3400 SWRs where DNA methylation supplants H3K27m3, and 111 potentially SWR-activated genes of which six are actively characterised. The impact on H3K27me3 distribution and gene expression is assessed upon altering the methylation state. These studies also unveiled that one variant polycomb repressive complex (PRC1.6) is required for polycomb to DNA methylation switching at a subclass of genes. In addition, they probed the CTCF dynamics during a specific period of early embryogenesis and identified about 1600 differential binding sites, of which 339 contain a methylated CpG in the predicted binding site; the work is still underway to determine how DNA methylation may orchestrate enhancer-mediated gene contacts during differentiation. Finally, two other projects have been initiated: the first one aims to explore the interplay between DNA methylation and H3K4 methylation while the second one aims to reveal the order of events, concerning chromatin marks deposition and DNA methylation, that occur during enhancer activation or decommissioning during embryonic development.

The team inclusion in the society is excellent with several initiatives towards the public (social media, guest in two popular science podcasts (Lonely Pipette and the Genomics Podcast)).

Weaknesses and risks linked to the context

The team has been created only four years ago and, as other young groups, has been particularly impacted by the Covid-19 pandemics (student loss and delay in postdoctoral students arrival).

Apparently, the group cannot rely on a permanent bioinformatic infrastructure and will need to recruit and train in bioinformatics a new member.

The mammalian epigenetics field is very competitive and there is a risk of competition with well-established groups at the international level.

Analysis of the team's trajectory

The team project will derive naturally from the results obtained by the team in the 2019-2022 period, described in detail above. Projects are very exciting, innovative and achievable considering the expertise and the cutting-edge methods employed by this young team.

RECOMMENDATIONS TO THE TEAM

The team is encouraged to focus its efforts on a limited number of projects.

It is also advisable to establish collaborations with expert groups with complementary skills.

Team 14: Polarity and morphogenesis

Name of the supervisor: Mr. Antoine Guichet

THEMES OF THE TEAM

The team studies the development of *Drosophila*, in particular the role of microtubules in cellular polarity (notably the positioning of the nucleus) and of actin in cell intercalation and cellular rearrangements (notably in relation to adhesion proteins). For cellular polarity, the link between membrane trafficking and polarity proteins and the role of independent microtubules sources and kinesin-1 to ensure the robustness of nuclear positioning were studied. For 3D cell remodelling, actin distribution was correlated with cell remodelling, and E-Cad endocytosis with cell intercalation. Finally, a versatile method to detect GFP-associated proteins by electron microscopy was developed.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hcéres evaluation (italics) were:

1- The team is encouraged to keep going with this innovative research. In addition to the ANR, the team is encouraged to apply for significant grants outside the French national system, such as HFSP. No funding contract outside the French national system was obtained in the current evaluated period.

2- The team should hire excellent Master and PhD Students as well as postdoctoral students, in accordance with the important asset represented by the presence of three MCFs. In the current evaluated period, six Master 2, fifteen Master 1, 6 L3, and five PhD Students were trained.

3- The team leader should carefully consider priorities in coming years, in order for the team to avoid over - committing itself in a challenging funding climate for basic research. The team has established clear research priorities fitting with its human resources. In the evaluated period, 283 k€ were obtained from external funding sources (ARC, La Ligue, Gefluc, idex) that have allowed them pursuing their scientific objectives.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**3**
Total personnels	**8**

EVALUATION

Overall assessment of the team

The team has excellent visibility in the field of cell polarity and tissue morphogenesis, as illustrated by thirteen invitations to talk at national and international conferences, including the most prestigious ones (e.g., EMBO and Biochemical Society). The team members have an excellent track record of nine articles as key authors (including Development, Nat. Commun and eLife) among a total of nineteen articles and reviews. The team size was kept constant with six PAR and three PhD students. The team has an outstanding involvement in teaching.

Strengths and possibilities linked to the context

The team has an established standing in the fields of cell polarity and tissue morphogenesis. The team leader has been invited to talk at thirteen national and international conferences, including the most prestigious ones, e.g., EMBO in 2017 and Biochemical Society in 2019, and meetings at leading universities and research centres such as European Molecular Biology Laboratories in 2018, Ecole Polytechnique Fédérale de Lausanne in 2018, and Münster University in 2018 and 2019. When compared to the previous contractual period, the team has been strengthened with the arrival in 2022 of Sylvain Brun, assistant professor UPC. During this period six Master 2, fifteen Master 1, 6 L3, and five PhD Students were trained.

The team has studied how microtubule-associated transport contributes to the polarised distribution of PAR3, how kinesin-1 organises microtubules to position the nucleus, how actin cytoskeleton dynamics influences cell rearrangement during the tracheal morphogenesis of the *Drosophila* embryos, and how GFP-associated proteins can be detected by electron microscopy. These excellent studies were published in highly recognised international journals (notably Nat. Commun and eLife), and constitute the basis for exciting ongoing research endeavours.

The team has an outstanding involvement in teaching with the organisation of Master 1 and Master 2 programs and teaching at the graduate and master levels. The team is also strongly involved in making issues of cancer research accessible to a general non-scientific audience, in the exchange between researchers and high school students, and in the 'Apprentis Chercheurs, l'arbre de la connaissance' program to team up middle and high school students with PhD students of the team to carry out one-year research projects.

Weaknesses and risks linked to the context

The amount of external funding, 283 k€, obtained in the current reviewed period (ARC, La Ligue, Gefluc, idex) appears quite limited, and although it is sufficient to perform the proposed research, does not allows reinforcing the team further by hiring postdoctoral students.

Currently, the team is not involved in interactions with the socio-economic world.

Analysis of the team's trajectory

Based on its established knowledge in the in the fields of cell polarity and tissue morphogenesis, the team proposes to study in Drosophila how several microtubule networks coordinate to control the polarised positioning of the nucleus in the oocyte, and how the actin cytoskeleton contributes to cell intercalation in the tracheal tubules during embryogenesis.

More specifically, the team plans to analyse how the microtubules organising from places different to the centrosomes (the nuclear envelop and the posterior cortex) are coordinated with other MTOC. It will be analysed how depleting each, either with optogenetic tools or genetically, affects nuclear localisation. It will then be studied how forces are applied to the nucleus during normal migration and in mutant conditions.

In parallel, the team will continue the analysis of how actin dynamics independent of myosin, influences dorsal tracheal branch reorganisation searching for its regulators. They will test a novel technique to depolymerize actin locally to see how this affects the whole branch in the collective migration, and use laser ablation to test membrane recoil.

This project will involve collaborations with one team at IJM to measure nuclear envelope deformation using a genetically encoded FRET biosensor of molecular tension, and with one team at Institut Fresnel (Marseille) who

recently developed a polarimetric technique to identify the nature of the actin networks. The proposed project appears to be well dimensioned for the size of the team.

RECOMMENDATIONS TO THE TEAM

The team is strongly encouraged to pursue its excellent research in the fields of cell polarity and tissue morphogenesis and its outstanding teaching activities.

Some collaborations are mentioned in the trajectory. It might be explored how these (or possibly others to be initiated) could enable the team to reach out for collaborative grants such as PRC from ANR. Such additional means might then allow to attract talented postdoctoral students to further augment the scientific output of all team members.

Team 15: Membrane dynamics and intracellular trafficking

Name of the supervisor: Ms. Cathy Jackson / Mr. Jean-Marc Verbavatz

THEMES OF THE TEAM

The team focuses on molecular mechanisms involved in the regulation of organelle dynamics and on functions of endoplasmic reticulum – organelle membrane contact sites.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has mostly addressed the recommendations provided in the previous report.

It was recommended to continue to publish in top scientific journals, which was done with a publication in 2018 in a high-profile journal (Nat. Commun.), and to increase the number of published papers which was also done (13 during the previous period, 25 during the current one).

Ambitious programs were also recommended to be maintained which was also achieved with 3 ANR grants obtained during the period.

Although recommended to be increased, the number of postdoc (1 before, 2 during the current contract) and PhD students (4 versus 3) remained similar.

It was also recommended to get a permanent technician. This was achieved in 2021. However, 2 staff researchers were not stabilised and left the team in 2019 and 2021.

Last, the team was encouraged to amplify its complementary approaches, which was achieved.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	1
Doctorants	1
Sous-total personnels non permanents en activité	**3**
Total personnels	**8**

EVALUATION

Overall assessment of the team

The scientific achievements of the team are of very good to excellent. Four articles were published in leader position in very good to excellent journals. Relative to the size of the team, attractiveness is excellent with three PhD students and two postdoctoral fellow trained, four reviews and a book chapter in leading position, contributions to scientific society committees and important national grants (4 ANR, FRM team label). The contribution to society is also excellent with participations to Declics and mentorship programs.

Strengths and possibilities linked to the context

The visibility of the team is very good. The team was invited to give fourteen talks including in international meetings (Faseb, EMBO). The team was involved in evaluation committees (Hcéres, Inserm, UK Research and innovation) and in scientific journal editorial board (Biology Open, PloS One; J. of Cell Sci.). The team is also involved in different scientific societies (Club exo-endo, Société Française des Microscopies, Collège des sociétés savants) and ethic committee on animal experimentations. Four reviews (Curr. Biol., Biology of the Cell, Front. Cell Dev. Biol., Curr Opin. Cell Biol.) and one book chapter were published in leading positions. The team has been supported by grants for a total of >1.4 M€ in the reporting period. Grants include national ones (4 from ANR with two as leader (2014 and 2021), two from Ligue nationale contre le cancer, one from FRM (team label 2016) and 1 from labex). The team has no international grants and industrial contracts. The attractiveness of the team is excellent. The team has trained three Ph.D. students, two having completed the thesis at the time of the report. Two postdoctoral fellows were also trained during the reporting period.

The scientific production of the team has been very good to excellent. The team is made up of two teacher-researchers (one full professor and one assistant professor) and two full-time researchers (one research director and one staff scientist) who have been working on the origin of membrane trafficking and the mechanisms involved in the communication of organelles. In addition, because of their highly specific individual expertise, team members contributed independently to a large set of collaborative projects (21 collaborative contributions). The team has described the involvement of Arf/GBF1 in the motility of mitochondria on microtubules. In a very recent work, accessible on BIORXIV, the team identified the endoplasmic reticulum (ER)-resident Vapa as an important regulator of motility and actin cytoskeleton organisation through the regulation of ER-plasma membrane stability and anchoring. Thanks to his extensive expertise in high-resolution imaging methods, one of the team's co-leader is heavily involved in the imaging facility of Institut Jacques Monod. Findings from the team were associated to 21 original articles, four with team members in leading positions in Nat. Commun., J. Virol., Scientific Report and PloS One.

The team contributed to research activities to society through their involvement in Declics and mentorship programs.

Weaknesses and risks linked to the context

The total number of original publications (4) in leading positions by members of the team is comparatively low for a team of two full-time researchers and two teacher-researcher, two PhD students and three postdoctoral students.

The departure of two staff scientists (2019 and 2021) could be seen as a weakness as they would have contributed to stabilise the team for the period to come, in terms of publication and potential to diversify grants.

Analysis of the team's trajectory

The team is going to pursue as during the previous contract with, as permanent staff, the four researchers (including two teacher-researchers) and a technical staff. The trajectory is in line with previously conducted projects, aiming at studying lipid identity and dynamic regulation of spatial organisation of membrane organelles.

In a first part the team proposes to decipher deeper the regulation of organelle dynamics by Arf. The team identified Arf-related protein in Asgard archea, thought to be a lineage from which eukaryotes emerged. The team has preliminary data suggesting that Arf-related proteins in archea indeed is a bona fide Arf proteins (manuscript in preparation).

In a second part the team will pursue at understanding the function of RE-organelle membrane contact sites in physiological processes. Based on the identification of post-translational modification of Vapa tether and one of its partner at the membrane contact site, the team proposes to better decipher at the molecular level, i/ the regulation of Vapa-mediated function during cell division, ii/ the dynamic of Vapa localisation and interaction at membrane contact sites with a partner during the process of cell polarity, and iii/ how Vapa-mediated membrane contact sites control mechanobiological properties and the turnover of focal adhesion to delineate regulation of cell motility by Vapa-mediated mechanisms.

Finally, the team proposes to pursue innovative strategies for imaging development.

The project proposed is well-balanced between a highly fundamental evolutionary study and more physiological-related studies, to better understand membrane dynamic and trafficking.

RECOMMENDATIONS TO THE TEAM

The team is recommended to further strengthen the integration of the individual expertise of team members, in order to synergise efforts and skills to obtain articles in the most visible journals, for which the conceptual and technical potential is strong.

Stabilisation and integration of staff scientists is recommended to strengthen the team, especially in a team with researchers with high level of extra duties (teaching and facility responsibility). To secure the team, the transfer of the imaging facility responsibility to a manager would free time for the team project of one of the co-directors already widely involved in teaching.

Recruitment of more PhD students or postdoctoral fellows is also recommended to draw maximal benefit from a very promising project.

Team 16: Comparative developmental neurobiology

Name of the supervisor: Mr. Nikos Konstantinides

THEMES OF THE TEAM

The team studies the evolution of nervous system at cellular, developmental and behavioural levels with the optic lobes of insect brains as a model. They propose to apply genetic approaches and single-cell sequencing to compare in distinct Drosophila species and other insects (1) morphological and transcriptomic diversity within optic lobes, (2) developmental trajectories during temporal patterning of optic lobes, and (3) the co-evolution of neuronal circuitries and specific behaviours.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

There was no recommendation in the previous report, as the team started work in September 2021.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	**1**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	1
Doctorants	1
Sous-total personnels non permanents en activité	**4**
Total personnels	**5**

EVALUATION

Overall assessment of the team

The research performed by this young team active since September 2021 is very promising, designed to providing a global appreciation of the genetic mechanisms that drive the evolution of new behaviours. The team leader is internationally recognised for his work on invertebrate nervous systems, a state-of-the-art dissection of the regulation of cellular identity, connectivity and neuronal diversity. It is too early to assess the team output, but its visibility is outstanding, the team leader having already obtained several major funding grants including an ERC starting grant.

Strengths and possibilities linked to the context

The team has an outstanding visibility and attractiveness. The team leader obtained an ERC Starting Grant in 2021 (BehaEvoDevo), an idex Université de Paris 'Chaires : Nouvelle Equipe', a three-year BioSPC doctoral fellowship. The team is involved as one of the four partners in the Transversal project from labex 'Who Am I?' Université Paris Cité. The team leader has also produced two reviews demonstrating his visibility. Over these

eighteen months, the team leader has given ten seminars and the team has contributed to five abstracts in conferences. Also, the team leader is recognised as a reliable expert in his field with reviews of ten research papers, two research grants as well as edition of five research papers. The connection with biology students is excellent as the team leader is teaching in two Master programs.

This young team has been established in 2021 and is composed of five persons including one postdoctoral fellow , one PhD student and two engineers (3 years IR contract, one year IE contract). The team is applying comparative genetics and single-cell transcriptomics to dissect the evolution of neuronal circuitry and behaviours. To achieve this ambitious and risky goal they use several species of Drosophila as well as other insects like Tribolium they maintain in the lab. As several species are non-model organisms, this implies that they need to adapt genetic tools. The expertise of the team in neurobiology, evo-devo, developmental genetic techniques and bioinformatics is outstanding, primarily developed by the team leader during his PhD and postdoctoral students, well supported by the postdoctoral students and engineers. The publications reported in the document correspond to the work performed by the team leader while he was still a postdoctoral fellow (Nature 2022 as first and corresponding author, Science 2022 as FCA consortium member) or as reviews signed as last co-corresponding author (Frontiers Neuroscience 2022, Developmental Biology 2021). The PI has an extensive network of collaborators and mentors, enabling it to seek expertise, advice and keep abreast of developments in the field before they are published.

The team inclusion in the society is just starting with a two-year participation in the Apprentis-chercheurs program.

Weaknesses and risks linked to the context

The team was set up just two years ago and, like other young groups, was affected by the Covid-19 pandemic.

In terms of IT infrastructures, which are central to the scientific project, the group can rely on its skills in bioinformatics, but will need ongoing support from the Institute.

The team is very international, with several members who do not speak French and who need specific support from the Institutions to help them integrate as quickly as possible.

Analysis of the team's trajectory

The project tackles the fascinating question of the evolutionary mechanisms that lead to neuronal diversity, circuit organisation and the induction of specific behaviours. By comparing closely related species, the project will identify speciation events such as differences in neural identity, neural activity and neural circuitry responsible for specific behaviours. The proposed approaches are state of the art and will enable the team to produce results at a level of cellular and genetic precision never before achieved.

RECOMMENDATIONS TO THE TEAM

Learning French for the PI and team members is certainly not an absolute necessity at the scientific level and is indeed an effort that requires extra energy. Nevertheless, it might be a good investment as it will facilitate integration into the IJM and contribute to the development of activities linking research and society.

The team is encouraged to concentrate its efforts on those parts of the project that will lead to solid research articles in the next few years, before embarking on the riskier parts of the project that may take longer. During this initial period, it is also advisable not to dilute the team's efforts too much in collaborations that do not correspond to its priorities.

Team 17: Cell adhesion and mechanics

Name of the supervisor: Mr. Benoit Ladoux / Mr. René-Marc Mège

THEMES OF THE TEAM

The team studies physical and biological mechanisms controlling cell behaviour and tissue organisation, using an interdisciplinary and multi-scale approach to address mechanisms and functional roles of cellular mechano-sensing, mechanotransduction at adhesion sites and adaptive cell behaviours. The team contributed with fundamental insight into the biomechanics of epithelial tissues, collective cell migration and cell extrusion. Research efforts in these areas will be continued and further strengthened in future.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hcéres evaluation (italics) were:

1- The panel's only recommendation is to maintain the outstanding level of science and continue delivering exciting breakthroughs at the interface of physical and life sciences. The team has maintained an outstanding research productivity and published seminal works in the field of collective cell dynamics and tissue mechanobiology.

2- The committee recommends to keep recruiting students and scientists with diverse backgrounds. The team has been able to maintain its large size and excellent composition with researchers across different disciplines.

3- The panel would recommend to gradually (on a much longer time scale) move even further towards in vivo models, to eventually show physiological relevance of the investigated mechanical interactions. More immediately, the team needs to secure funding to ensure progress of the projects as well as continuity in the lab beyond 2019, which is especially important as there are no permanent technicians or engineers trained at the various techniques employed by the team. We also note that one of the team leaders is taking an important leadership role in the management of the ImagoSeine platform, which will provide an important contribution to the IJM and wider Paris research community. We would therefore strongly recommend to strive to obtain administrative support, which is absolutely required in such a large team, to free up team leader time to focus on research. The team has secured major competitive funding to secure a continuation of high-class research efforts. The use of vivo models is considered in the team's trajectory, for example by extending work to the study of intratumour heterogeneity based on organoids. In addition, the team has continued to engage in a wide range of collaborations to address questions in 3D multicellular and in vivo model systems.

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	3
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**8**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	1
Post-doctorants	5
Doctorants	6
Sous-total personnels non permanents en activité	**13**
Total personnels	**21**

EVALUATION

Overall assessment of the team

The team has an outstanding track record and is highly recognised internationally for its seminal work published in various highly visible journals and focusing on the mechanics and physical biology of epithelial tissues, collective cell migration and mechanotransduction at adhesion sites. An outstanding visibility has been established by the team with invitations to recognised international meetings, the acquisition of competitive funding and different prizes awarded to team members. The team has a multi-disciplinary composition with researchers from diverse backgrounds and is strongly engaged in a wide scientific collaboration network.

Strengths and possibilities linked to the context

The team has an outstanding expertise and international recognition in the field of mechanobiology, particularly in the area of single and collective cell migration and epithelial tissue architecture and dynamics. The team has secured major competitive international and European funds (ERC Adv, ERC PoC, ERC CoG, HFSP) and diverse national grants. The team is very well established and has maintained a large size with seven permanent researchers. It is attractive to international PhD students and postdocs. A major training effort of PhD students is evident (6 previous, 6 current) and the composition of group members (PhD students/postdocs/staff) is very well balanced. Members of the team have been invited to renowned international conferences including Gordon Research Conferences and EMBO meetings. The team received prestigious awards and prizes (for example, EMBO Member and research prize on rare Diseases from the Groupama Foundation).

The team has an outstanding productivity reflected in an extensive publication record in high-class journals (including Nature, Nature Materials, Nature Physics, Science Advances, Nature Communications, PNAS, among others). There is a strong record of first author publications from PhD students in high impact journals. Specific examples of cutting-edge research by the team includes the study of epithelial rotations on curved surfaces (Science Advances 2023), the identification of an adhesion switch regulating contractile versus extensile forces generated by tissues (Nature Materials 2021), and the discovery of cellular migration plasticity controlled by substrate geometry through actomyosin flows (Nature Physics 2019). The publication record reflects the innovative character and modern interdisciplinary perspective of the groups' research and its potential to identify new molecular and physical mechanisms relevant to cell and tissue biology.

The team participated is several public outreach and teaching activities.

Weaknesses and risks linked to the context

The capacity in personnel and established technical expertise of the team could drive further initiatives in public outreach and technology transfer to promote interactions with society and companies.

Analysis of the team's trajectory

The research trajectory of the team will further expand to studies in different 3D model systems to investigate the role of mechanics and collective cell behaviours in tissue development, homeostasis and disease. The team has an ambitious research perspective that aligns with its core focus on mechanobiology. The research trajectory is very well supported by competitive funding available in the team and its established expertise provided through permanent staff members and researchers with diverse training backgrounds. New research lines and tools will further be established and incorporated. In particular, the team will focus on identifying mechanisms regulating tissue homeostasis, collective cell migration and tumour formation, the latter representing a new research line of the team. A diverse set of state-of-the-art methods will be used to address these questions, including opto-genetics, microfabrication and imaging. The team has also established a wide network of collaborators to expand into projects that address various biological processes and involve different model systems as organoids and in vivo model systems. The trajectory of the team reflects a highly ambitious and cutting-edge research program that can be expected to significantly advance our mechanistic understanding of tissue physiology and disease from a multi-disciplinary angle.

RECOMMENDATIONS TO THE TEAM

Given the established competences and outstanding productivity of the team, further courageous steps into new interdisciplinary questions and model systems can be taken.

Efforts to promote in-house and international collaborations can further be continued for the benefit of the team and the IJM research community as a whole.

Team 18: Metabolism and function of RNA in the nucleus

Name of the supervisor: Mr. Domenico Libri

THEMES OF THE TEAM

The team is working on transcription processes in yeast with a new axe of research on human cell line. One main focus is the non-coding transcription but also the integration of transcriptional activities with other DNA-associated activities impacting genome stability. In human cell line the team focuses on the study of the function of the RNA helicase Senataxin, and its role on human diseases contexts.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendation from the previous Hcéres evaluation (italics) was:

Given the approaches pursued it will be critical that there is core expertise in bioinformatics within the team and that the researchers within the group have mixed skill sets covering both experimental and data analysis needs. One expert in bioinformatics is leaving the team and should be replaced by a researcher that can fill this void.
This was not achieved most probably because of the transfer of the team to IGMM in Montpellier in 2022, resulting in a large turnover of team members.

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

EVALUATION

Overall assessment of the team

The scientific production is outstanding with 21 publications (13 research articles as main and 4 reviews) in international journals (including Mol. Cell, Cell report, EMBO J., eLife). The visibility is excellent to outstanding with numerous invitations (including EMBO, Cold Spring Harbor) and organisation of conferences (EMBO and TERM) and excellent fund raising. The non-academic activities were outstanding with the team leader taking administrative duties (DAS-CNRS).

Strengths and possibilities linked to the context

The team has an excellent to outstanding attractiveness and visibility with numerous invitations in conferences (including EMBO 2017; CSH 2017, 2021 for the PI and EMBL 2020; EMBO 2018 and SifrARN 2020 for the coPI) and organisation of conferences (EMBO and TERM). Four PhD students were trained during the period and three postdoctoral students were recruited. The fund raising capacity is excellent (1MillionE including 2 ANR, 1 FRM team, 1 AFM) though only focused on national grants. Four reviews/book chapters were published.

The scientific production is outstanding with 21 publications (13 research articles as main author and 4 reviews) in international journals. Thirteen publications were as main author including in highly visible journals: 1 Mol. Cell, 1 Cell report, 2 EMBOJ., 2 eLife, 1 Sci adv) with some key publications with national (and intra unit) as well as international collaborators (Switzerland, Spain).

The non-academic activities were outstanding with outreach actions but also with the PI taking administrative duties at the CNRS (chargé de mission).

Weaknesses and risks linked to the context

No major weakness has been identified even though the PI and co-PI could apply to international grants to secure long term financial supports especially for human cell research.

The move to the IGMM has also been followed by the loss of three permanent staffs (1 technical staff 1 Assistant professor and 1 researcher CNRS). To regrow the team would need to secure new permanent recruitment.

Analysis of the team's trajectory

The trajectory was not analysed as the team left the unit.

RECOMMENDATIONS TO THE TEAM

The team should continue such outstanding research but could certainly target prestigious funding through European networks to secure mid and long-term novel expertise recruitments as the team size has been reduced.

Outreach activities could also be developed to increase attractiveness after the lab transfer at IGMM.

Team 19: Membrane trafficking, ubiquitin and signalling

Name of the supervisor: Mr. Sébastien Léon

THEMES OF THE TEAM

The team studies the regulation of transporter endocytosis by glucose availability. The team identified regulating pathway for nutrient uptake, protein assembly and function, and glucose resistance, using yeast as a main eukaryotic cell model.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team addressed most of the recommendations provided in the previous report.

It was recommended *to increase visibility by participating to key meeting and working to obtain major grants*. The team was invited to international conferences (Faseb (2021), EMBO workshop (2022 & 2023)), and had one main major grant (ANR 2016-2022). The team increased its visibility by contributing as a guest editor to a special issue for a scientific journal and by giving six seminars in French and foreign laboratories.

The second main recommendation was *to recruit new students (MSc and PhD) through an active recruiting strategy*. The team trained three PhD students during the period (two defended in 2017 & 2021) which is few, but has to be related to the presence of only one HDR in the team (the team leader). The team trained 5 MSc students.

The third recommendation was *to delineate, within the main highly competitive field of nutrient sensing and membrane transport, a specific program which could avoid the team to be less in competition with big labs working in the same field.* The team was able to identify itself as a strong competitor, by publishing in excellent journals their own works (PLoS Genetics, Science Signalling and J. Cell Biol.).

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	1
Sous-total personnels permanents en activité	**3**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**2**
Total personnels	**5**

EVALUATION

Overall assessment of the team

The scientific achievements of the team are excellent. Four articles were published in leading positions in excellent journals (PLoS Genetics, Science Signalling and J. Cell Biol). Relative to the size of the team, visibility and attractiveness is excellent with three PhD students and three postdoctoral fellows trained, the publication of one editorial and one review, and the securing of one major grant. The contribution to society is excellent with contributions to lab/research presentation to young students (middle and high school), two press releases and attempt to get industrial contracts.

Strengths and possibilities linked to the context

Visibility and attractiveness of the team are excellent. Team members were invited to give three talks in international meetings (Faseb and two EMBO). The team was involved in a founded European network of knowledge as a member of the strategic committee and leader of a working group (COST network), and guest edited a special issue of a journal in its field of competence (Biol. of the Cell. The team has been supported by grants for a total of >0.6 M€ in the reporting period on a regular basis. Grants include a national one (1 from ANR as leader (2016-2022), three from ARC, one from FRM (2015-2017)) but no international grant was obtained. They also contributed to three editorial/reviews including two in leading position (EMBO J. and Biochem. Pharmacol). The team has trained three PhD students, two having completed the thesis at the time of the report (2017 and 2021 respectively, with 2 articles each); three postdoctoral students were also enrolled during the reporting period (9 to 36 months in the lab).

The scientific production of the team is excellent. The team was composed of two researchers (one research director and one staff scientist) who worked together on the main projects of the team, while contributing independently to collaborative works, and one emeritus researcher (up to 2022). They identified a novel mechanism that controls the degradation of cell-surface sugar transporters in yeast, that involves a protein of the arrestin family, which is regulated at several levels by glucose availability. They also characterised a mechanism of resistance to the metabolic inhibitor 2-deoxyglucose (2-DG), which involves the expression of enzymes which dephosphorylate 2-DG induced metabolite to detoxify the drug. More recently, they described how 2-DG regulates AMPK activity to modulate nutrient endocytosis and drug toxicity. These findings are associated to thirteen original articles: four with team members in leading position, seven in collaboration with IJM teams and five in the context of international collaborations. Relative to the size of the team, the quality of the main publications was excellent, with articles published in high-profile journals and/or well-established ones (Science Signalling, PLoS Genetics, J. Cell Biol. and Mol. Biol. Cell).

The team pursue important interactions with middle and high school students, initiated by a prior emeritus researcher of the team. The team communicated on two of their discoveries through press release coordinated by CNRS. The team tried also to get industrial funding with two signed confidential agreements obtained during the period, which were however not funded at the end.

Weaknesses and risks linked to the context

The size of the team is small to compete with larger laboratories. The team did not expand during the reporting period and with the two permanent researchers, the team is currently composed of one permanent technical staff (arrived in 2022) and one PhD student.

The absence of postdoctoral fellow and secured important funding for the coming years is a threat to the team trajectory.

Analysis of the team's trajectory

The team is going to pursue as during the previous contract with, as permanent members, two researchers and a technical staff. The trajectory is in line with works previously conducted by the team: glucose-mediated signalling and endocytosis.

A first part proposes to decipher at the molecular level the regulation of the PP1 phosphatase by AMPK under glucose uptake. To achieve this aim, preliminary results were obtained using an unbiased screen-based genetic approach. Candidates will be evaluated at the functional level, and molecular partners (interacting proteins)

will be characterised. Additionally, beyond the above-mentioned question, new potential PP1-related functions are proposed to be evaluated, in regards of organelles signalling.

In a second part, the team will explore ubiquitin-dependent mechanisms involved in endocytic trafficking. To this end, the team will use new synthetic biology tools allowing to interfere with K63-polyubiquitin-dependent signalling, or to force K63-polyubiquitin at a localised site. The team proposes to use these tools for both genetic screening to identify molecular mechanisms regulating endocytosis, and to better decipher actors and biophysical processes necessary for endocytosis.

Due to the expertise of team members, the well-defined organisation of the responsibilities and the originality of the preliminary data proposed, the trajectory described has the potential to generate excellent science, even in a competitive field of research.

RECOMMENDATIONS TO THE TEAM

The committee recommend to increase the team's size, by increase the number of HDR hold in the team, so to increase the PhD recruiting potential.

The team is encouraged to maintain a high level of collaboration with other IJM teams, in order to avoid isolation in its conceptual and technical approaches.

Given that the team's highly fundamental niche is difficult to fund by major agencies, establishing strong collaborations with national/international partners, who develop pathophysiological projects complementary to those of the team, could increase the chances of obtaining major grants including PhD or postdoctoral students' salaries.

Team 20: Cellular spatial organisation

Name of the supervisor: Mr. Nicolas Minc

THEMES OF THE TEAM

The aim of the team is to understand how cells define their morphologies, and how geometric information governs cellular functions, intracellular organisation and the development of tissues and embryos. To do this, the team uses mathematical models and highly interdisciplinary approaches combining molecular biology, genetics and physics. The team is pursuing two main lines of research: 1) the mechanisms that govern cell growth, polarity and morphogenesis using yeast and fungus model systems; 2) cell division and early embryonic development using sea urchins.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The only recommendation to the team was "*to keep continuity in the lab's diverse expertise by generating a constant revenue stream from competitive national and international grant, which will require good strategic planning*". The team has responded perfectly, with outstanding success in national and international calls for projects: four ANR grants, including two as coordinators, one ERC consolidator grant, one ERC Proof of Concept, one Labellisation La Ligue, one CNRS momentum grant, one Inserm ITMO cancer, two ARC Post-doc fellowships, one EMBO Post-doc fellowship and several national and local grants from the Paris-Cité University.

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	0
Sous-total personnels permanents en activité	**2**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	3
Post-doctorants	4
Doctorants	1
Sous-total personnels non permanents en activité	**8**
Total personnels	**10**

EVALUATION

Overall assessment of the team

The team studies the basic principles by which cells define their morphologies, and how geometric information governs cellular functions, intracellular organisation and the development of tissues and embryos. The team's scientific output is outstanding, with 38 articles including 32 research articles and six reviews in prestigious journals such as PNAS, Nat. Commun., Current Biology, Dev. Cell, J. Cell Biol., and Nature Physics for which team members are lead authors. The team's attractiveness and visibility are also outstanding. The team funding is above the standards with one ERC consolidator grant, one ERC Proof of Concept grant, four ANR grants among others. The team's members are frequently invited to international conferences (20-30 invitations) and the team leader was awarded prizes from the French Academy, the CNRS and the Fondation Bettencourt-Schüeller.

Strengths and possibilities linked to the context

The team's attractiveness and visibility are outstanding. The team's level of funding is exceptional. It is important to stress that the two permanent researchers contribute to the team's funding, although the main grants are brought by the team leader. The team has obtained four ANR grants, including two as coordinators, one ERC consolidator grant, one ERC Proof of Concept, one Labellisation La Ligue, one CNRS momentum grant, one Inserm ITMO cancer, two ARC Post-doc fellowships, one EMBO Post-doc fellowship and several national and local grants from the Paris-Cité University. Team members have been highly invited to give talks at international conferences such as EMBO and Gordon Research Conferences and at european and french labs (Crick, ETH, UNIL, UCL, ENS, Pasteur, Curie). The team leader is currently member of CNRS Section 22 and he was also part of ANR, FRM, IST Austria co-fund, Pasteur Group leader call, CBI Toulouse group leader, Hcéres committees (2017 and 2018). The team
leader was awarded the Simone and Cino del Duca award from French academy (2022), the Coup d'élan prize from the Fondation Bettencourt-Schüeller (2020), the National prize CNRS (2019), the Bronze Medal of the CNRS (2018).

The team's scientific output is outstanding, with 38 publications in total, including 32 research articles and six reviews and book chapters. The team has published numerous research articles in highly visible journals for which team members are first author or lead author, such as PNAS (2022), Nat. commun. (2022), Dev. Cell (2021), J. Cell Science (2020), Current Biology (2020), Dev. cell (2020), Nano Letters (2020), European Phys lett (2019), PNAS (2019), J. Cell Biol. (2019), Current Biol (2018), Nature Physics (2018), Dev Cell (2018), Mol Biol Cell (2017). The team also published several review articles in journals such as Semin Cell Dev Biol. (2021) and Methods Mol Biol. (2019). The team has made major achievements. Within the cell growth, morphogenesis and cell surface mechanics research area, the team has been able to measure the mechanics and dynamics of the cell wall in detail, in many different contexts. The team's work has also made it possible to characterise the mechano-sensation modules of the cell wall. Within the research area of division positioning and early embryo development, the team has identified the forces and torques that position asters and spindles in vivo. It has also revealed unexpected contributions from the cytoplasmic medium to the positioning of division in early embryos.

The team has filed a patent on a method for the real-time measurement of a wall thickness and uses thereof.

Weaknesses and risks linked to the context

None identified

Analysis of the team's trajectory

The team will continue to investigate cell wall mechanics during the growth of fungi. In particular, they will study how the architecture of molecular mechanosensors has evolved to support cell wall integrity in fungi. To this end, it will use super-resolution methods to map the size of mechanosensors in cells, and compare wsc homologues from various species in fission yeast with regard to their ability to detect and transduce forces exerted on the cell wall. Another original line of research involves studying the importance of cytoplasmic viscoelasticity. To this end, they will map hydrodynamic flows in the cytoplasm and develop models to estimate forces. This approach will allow for the study of the relationship between cytoplasm hydrodynamics and division positioning in early embryogenesis. Finally, they will study how actin filaments and cytoplasm granules viscoelasticity influence the motion of cytoplasmic elements. How size scaling, determined by cell volume

modification, affects cell fate determination during early embryogenesis is also a promising line of research. Finally, the team is developing numerical simulations of actin networks and collaborating with experimentalists to understand the biological functions associated with these networks.

Overall, the research project has the potential to bring out major concepts in mechanobiology, and the team has the strengths and expertise to address them.

RECOMMENDATIONS TO THE TEAM

The team has acquired international visibility thanks to its scientific output and multiple successes in national and international competitive calls. The team has succeeded in attracting permanent members to ensure the continuity of its multiple interdisciplinary approaches and experimental models. The team leader will have to manage his new position as deputy director of the IJM in such a way that it does not affect his research activities.

Team 21: RNA Biogenesis and Genome Homeostasis

Name of the supervisor: Mr Benoit Palancade

THEMES OF THE TEAM

The team is focused on the mechanisms that control the different stages of mRNA metabolism, from nuclear events to their cytoplasmic fate. By combining genetic, genomic and biochemical approaches in the yeast S. cerevisiae, the team addresses how mRNA biogenesis is synchronised with DNA-metabolism, dealing with DNA:mRNA hybrids (R-loops) interfering with spatial organisation, signalling pathways or gene regulons.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has been created in 2018 so no recommendations were made in the previous report.

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

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

EVALUATION

Overall assessment of the team

The scientific production of the team is excellent to outstanding for a recently created team (2018) with eleven publications, five as main contributors, including in highly visible journals (2 Molecular Cell, Nature Commun., PLoS Genetics). The visibility is excellent to outstanding with regular invitations to conferences (over 20, including chair at EMBO workshop 2018), the writing of reviews, and high fund raising (900k€ incl. 3 ANR and labex calls). Attractiveness is also excellent to outstanding with the recruiting of three PhD, four postdoctoral fellows and one CRCN in 2022.

Strengths and possibilities linked to the context

The visibility is excellent to outstanding with regular invitations to present the team work (20 invitations in conferences with one chair at the EMBO workshop 2018), numerous reviews and editorial activities (Cell Stress and Nucleus editorial board). The attractiveness of the team is outstanding as exemplified by the training of

three PhD students and four postdocs and the arrival of a CRCN in 2022. The fund raising is excellent with more than 900ke over the period including 3 ANR and labex calls.

The scientific production of the team is excellent to outstanding for a recently created team (2018) with thirteen publications (including 2 reviews and 8 as main author) in the best journals with one Science report (2022), one PLoS Genetics (2021), two Molecular Cell (2021, 2017), one Nat Commun (2018) with some ongoing collaborations mostly nationally with leader in their field (transposon, Rloop)

The non-academic activities are excellent with several initiatives in valorisation of the methodologies (patent study) and outreach presentations towards young people (Apprentis chercheurs and Fête de la science).

Weaknesses and risks linked to the context

The team is growing very well with very few weaknesses. However, the lack of international prestigious or collaborative grants such as ERC could slow down the recruitment of high-profile postdocs or engineer.

The end of the labex in 2024 will have direct consequences for the team's financial support putting at risk some projects.

The team has recently recruited a permanent scientist (2022) but is lacking a permanent lab manager or technical staff to maintain expertise on a long-term perspective.

Analysis of the team's trajectory

The team trajectory is mainly the continuity of the current research based on preliminary data, using both hypothesis-driven and screen-based strategies. The project will address three questions.

1- How does genome organisation impact mRNA and R-loop metabolism? This will be approached by looking at transposon regions identifying cis and trans acting factors but also by studying the role of RPA in synchronising DNA and mRNA metabolism. This is supported by current funding (ANR, ARC/LNCC grants) and collaborations (IGMM, Montpellier, IBPS Paris).

2- Which signalling pathways regulate mRNA and R-loop metabolism at a system level? The results of a dosage lethality screen provided evidence for a role of R-loops in transcriptional termination and RNA decay. A second systematic search will aim at identifying writers, erasers and readers of R loops by Rloop chromatin IP proteome sequencing. This is supported by current funding (Funded PhD and ARC/LNCC grants) and collaborations (USA and CRCM, Marseille).

3- Which regulations collectively target functionally-related mRNAs? This will involve exploring NPC-associated translation and its impact on nuclear homeostasis, investigating the role of RNA localisation in stress and development-specific expression programs. This is supported by current funding (labex, ANR RNAFATE, ANR application 2023) and collaborations (Geneva and Gif/Yvette),

In all the strategy is very clear, robust with ongoing funding and key collaborations already set up. Some of the sub questions are high risk in the feasibility but high gain in term of potential results.

RECOMMENDATIONS TO THE TEAM

The team should maintain his excellent/outstanding research and reach the outstanding standards by proposing high gain high risk projects to international prestigious grants. This would attract international and high profile postdoctoral fellow and engineers who might be excellent candidates for securing permanent positions and keep long term expertise within the team.

Team 22: Cell cycle and development

Name of the supervisor: Mr. Lionel Pintard

THEMES OF THE TEAM

The team studies cell cycle control in a developmental context with a focus on the early cell divisions in the *C elegans* embryo. In particular, the team studies regulatory mechanisms for commitment and onset of M phase centred on the activation of CyclinB-Cdk1. Research within this theme is divided into three axes: activation of the mitotic kinase module, mechanism for pronuclei merging during the first zygote division, function and spatio-temporal control of the microtubule-severing protein Katanin.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hcéres evaluation (italics) were:

1- To increase team visibility by attendance to international conferences. Collectively, the team members have contributed to some 45 presentations (e.g. posters, invited talks, workshops, seminars), out of which at least twenty were at international events (ASCB meeting, EMBO workshops, Monod conferences) or invitations to international institutions.

2- To consider applying for an ERC Advanced Grant. The team's funding situation is excellent with several large awards but no ERC grant listed for the period under evaluation.

3- To increase participation in teaching to attract new PhD students. The team reports teaching activities at multiple levels (L3, M1 and M2). PhD recruitment increased relative to the previous period of evaluation. In the last five years, the team has trained five PhD students (3 completed their degree and 2 are expected to carry on until 2025).

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	1
Doctorants	2
Sous-total personnels non permanents en activité	**3**
Total personnels	**7**

EVALUATION

Overall assessment of the team

The team has an excellent to outstanding track record at international level studying cell cycle controls in early embryonic divisions. The team leader has effectively increased international visibility as reflected by invitations to conferences and seminars. Publication output has been excellent to outstanding and both substantial funding and collaborations were secured. Finally, they sustain a presence in outreach/public engagement, by hosting young trainees, contributing to biotech initiatives and participating in open days for science communication.

Strengths and possibilities linked to the context

This is a well-structured team with excellent visibility, possessing expertise in genetics, proteomics and cell biology and an effective set of permanent staff to support an excellent training environment. Furthermore, the team is well connected to a number of national and international collaborators contributing to research in the three axes of the team and also extending the productivity and range of studies beyond the team's prime agenda. The team has been successful in securing major national sources of funding (ANR, Ligue Nationale Contre le Cancer) and sustaining intake of PhD students. Overall, five Master 2, 5 Master 1, two L3, seven BTS, one DUT, five PhD students and three postdoctoral fellows have been trained in the last five years. The team leader has received several invitations to present at international conferences or seminars and holds multiple recognitions or esteem indicators.

The team productivity has been excellent to outstanding. High-quality publications include ten primary research papers (at least 4 first/last author research articles contributed by multiple members of the team published in 2 *eLife, Dev. Cell, Nat. Commun, J Cell Biol*) and four reviews (one of them for the prestigious series Wormbook published in *Genetics*). In relation to the three research axes, the team has made significant progress to reach molecular understanding of particular aspects of cell cycle control using a multidisciplinary approach from the molecular to the organismal scale that includes cutting-edge microscopy, proteomics and biochemistry combined with the powerful *C. elegans* genetics. Briefly, the team dissected components of a hierarchical mitotic kinase cascade, part of a trigger for M phase onset, and its upstream regulation by a cyclin-Cdk module. In addition, a key mitotic kinase has been implicated in the control of pronuclei merging during the first division of the *C. elegans* zygote to ensure that the two parental sets of chromosomes become correctly lined up onto a single mitotic spindle. Finally, a mechanism involving proteolytic control by phosphorylation of the microtubule-severing protein katanin accounts for its differential levels and activity during meiosis versus mitotic cell division.

Although prospects for engaging with non-academic sectors may be limited by the basic nature of the research, the team has collaborated with a biotech company that has also served as destination for a former PhD student. In addition, the team is engaged in other forms of outreach including hosting young trainees in the lab and participating in open days and science communication.

Weaknesses and risks linked to the context

The team recognises that despite successful moves to increase their visibility through teaching and a new website, they continue to struggle to recruit PhD students, perhaps due to the very basic nature of their research. The lack of an international PhD programme adds to these limitations. Also, administrative support to manage work permits to facilitate the intake of international students and postdocs is scarce.

The team could not retain human cell expertise that could otherwise enable validating findings from *C. elegans* in human cells and perhaps open routes to translation of their research. The uncertainty that findings in *C. elegans* could hold true in other systems might be construed as a potential weakness. Yet, the history of cell cycle research has taught us repeatedly the benefits from in-depth exploration in diverse, genetically tractable model systems for uncovering novel paradigms in cell cycle control ultimately proven to be conserved in human cells. Nevertheless, it is of great interest to be in a position to implement such validations.

The team regard itself as newcomers in the nuclear envelope field, which might undermine their impact.

The work of the team relies heavily on access to spinning disk confocal setup which is oversubscribed.

The team has not obtained European grants or secured bids for large instruments that might enable them to purchase a dedicated microscope, in particular.

The basic nature of the research might limit opportunities for outreach, yet it remains important to convey the significance of cell cycle research towards fundamental understanding in cancer. Advocating for the field may also improve recruitment to the lab.

Analysis of the team's trajectory

The team will continue to probe fundamental mechanisms of cell cycle control in relation to developmental context, building on their recent success in reference to the current 3 research axes. Following up from their previous studies on the mitotic kinase control at M phase onset and the control of nuclear envelope dynamics by Plk1, new studies will also bring on board the role of cell cycle protein phosphatases opposing mitotic kinase phosphorylation events.

The team plans to exploit the outstanding fact that unlike other model systems, the stereotypical divisions of the *C. elegans* cleavage embryo, are asynchronous and asymmetric from the start. The team's preliminary genetic data has implicated regulators of the "tug-of-war" between protein kinases and phosphatases in differential timing of mitotic entry between blastomeres and has thus predicted that a Greatwall-like kinase (part of the M-phase regulatory module in other systems only, so far) might exist in *C. elegans*. The team intends to pursue this intriguing possibility by dissecting the regulatory phosphorylation of Bora in detail and its mode of targeting mitotic kinase activity. In addition, they plan to identify targets of Plk1 to achieve an integral view of phosphorylation/dephosphorylation cycles that govern nuclear envelope dynamics along the cell cycle. Finally, the team will characterise two putative novel p80 subunits (MEI-2-like) of Katanin that might contribute to its spectrum of developmental regulation and function.

Taking into account the team's expertise and track record we can anticipate that the proposed studies will yield significant advances and possibly novel molecular paradigms involving evolutionary conserved components of the core cell cycle machinery.

RECOMMENDATIONS TO THE TEAM

The team should continue with their efforts to increase visibility by participation in international conferences to gain recognition in the subfield of cell cycle control of nuclear envelope dynamics, among others.

The team should make every effort to translate their success in research in applying for European funding.

The team should communicate more effectively the significance of basic research in their area and its translational potential to make them more attractive to prospective PhD students.

Team 23: Chromosomal domains and DNA replication

Name of the supervisor: Ms. Marie-Noëlle Prioleau

THEMES OF THE TEAM

The team explores the impact of appropriately regulating the initiation of replication on the integrity of the genome in both bacteria and vertebrates. Additionally, they seek to unravel the significance of a secondary DNA structure known as the G-quadruplex in this biological process. As DNA replication and transcription take place on a shared DNA template, the possibility of mutual interference exists. To investigate the potential disruptions caused by interactions between replication initiation and transcription elongation—recognised as a potential source of genomic instability—they employ genetic and multi-omics methodologies.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hcéres evaluation (italics) were:

1-Tto publish results on a more regular basis and to ensure that all students and postdoctoral students are able to publish a first-author manuscript during their stay in the lab. The team has increased the research output from four to five research articles in high-profile journals. One of these articles is shared between former postdoctoral students and PhD students.

2- To continue to work in a healthy workforce distribution. The size and composition of the team is very similar to that of the previous evaluation period.

3- To continue working fundamental mechanistic questions in DNA replication. The team has continued to address fundamental questions related to genome duplication.

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

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

EVALUATION

Overall assessment of the team

The team has an excellent track record and is internationally recognised in the field of DNA replication, genome organisation and stability, with invitations to present in conferences and seminars. The team has produced high-quality primary research articles, along with review and book chapters, has continued to secure major sources of funding and maintains a network of fruitful collaborations.

Strengths and possibilities linked to the context

This is a well-established team with an excellent visibility. The team leader has received multiple invitations to present at international conferences and seminars, invitations to write review and book chapter. The team was able to secure funding for the period under evaluation from ANR, ARC ("équipe labélisée), labex "Who am I" and Ligue contre le cancer. Three PhD students have obtained very competitive grants from MESRI (ministry of education and research), which testifies the attractiveness of the team. One student has obtained his PhD degree, and in total three PhD students, three Master 2 students, five Master 1 students and four more students have been trained over the period under evaluation. A full professor, expert in the bacterial replication field, has joined the team in September 2022, adding to the visibility of the team. The team leader has been nominated member of CoNRS, section 21.

The team's scientific production has been excellent with 5 research articles, three of them with team members as first and last authors in EMBO J, Nucleic Acids Res (1), Nature Commun. (submitted to BioRxiv and published since in Nature Commun.). The team has made important contributions to the field of genome duplication by high-lightening the essential nature of cis-elements that organise the replication of vertebrate genomes through the establishment of a canonical chromatin structure, and by providing foundations for further studies aimed at understanding the mode of action of dimeric pG4s on the dynamics of vertebrate genomes.

The team interacts with high-school students.

Weaknesses and risks linked to the context

The team suffers from the absence of a home-based bioinformatician, which seems to be a general IJM problem.

Societal interactions are weak.

Analysis of the team's trajectory

The team recently recruited an expert in the bacterial replication field and will thereby be able to combine findings obtained from different model organisms (vertebrates and bacteria) to identify shared pathways and constrains. Based on solid results obtained in the past by the two PIs, the team will pursue three principal projects. Firstly, they will explore whether the transcription machinery has the potential to disrupt pre-RC loading on strong replication origins in vertebrates. Secondly, using human cortical organoids as a model they plan to determine whether Recurrent DNA break Clusters (RDCs) previously mapped in human neural progenitor cells (NPCs) correspond to regions of strong replication delay. Finally, they will try to understand how unidirectional replication fork progression can be established under specific conditions in bacteria and whether this replication mode can be extended to vertebrates. These three research lines are highly original in full compliance with the IJM scientific trajectory.

RECOMMENDATIONS TO THE TEAM

In general terms, scientific productions should be increased. The recruitment of an expert in the bacterial replication field could be an opportunity in this respect.

The PhD students and postdoctoral students should get the opportunity to publish as first author at least one research article during the stay in the laboratory.

Interactions with the socio-economic world should be improved.

Team 24: Intracellular compartmentation

Name of the supervisor: Mr. Ishier Raote

THEMES OF THE TEAM

In the laboratory at the Centre de Regulació Genòmica (CRG) in Barcelona, the PI has previously studied the mechanism of TANGO1-mediated bulky cargo export. The team will build on this to study as a team leader at IJM the fundamental mechanisms of collagen sorting in the early secretory pathway. The team proposes the existence of TANGO1-dependent, inter-organelle tunnels through which larger cargoes including collagen would reach the Golgi apparatus. The team leader has also identified collagen-secretion inhibitors, which will be tested in models of collagenopathies.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has only been founded in 2023 at IJM. It was therefore not mentioned in the previous report.

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

The team has only been founded in 2023 at IJM.

EVALUATION

Analysis of the team's trajectory

Based on prior work of its team leader on mechanism of TANGO1-mediated bulky cargo export through the biosynthetic/secretory pathway, the team proposes to reconstitute collagen 'filtration' at endoplasmic reticulum exit sites (ERES), to understand how unfolded (premature) collagens are prevented from exiting the endoplasmic reticulum. Furthermore, the team plans to explore the sorting of terminally misfolded collagens for degradation at endoplasmic reticulum exit sites. Finally, in collaboration with Dr Neil Rajan (Newcastle, UK), the team will analyse physio-pathological alterations in skin tumours that arise when ERES sorting fails.

This program is fully in line with the scientific and strategic orientations at IJM. It is internationally competitive and addresses a timely research question. For this type of program, funding opportunities exist at the level of fundamental as well as applied research. Initial sustainable funding has already been obtained from Fondation ARC and from FRM (équipe FRM), and the team leader has been granted a CNRS staff scientist position. The proposed research can thereby be initiated in appropriate conditions.

RECOMMENDATIONS TO THE TEAM

The team proposes a highly competitive research program. The presentation during the Hcéres visit was much appreciated by its dynamics, the strength of the proposed arguments, and the depth of the scientific reflection. The team leader is encouraged to put into practice his well thought-through program with corresponding prioritisation, and to strive for additional national and notably international funding. Step-by-step, this should allow him to build up an appropriately sized team and to harvest the full potential of his exciting ideas.

Team 25: Human neurodevelopment and disorders

Name of the supervisor: Ms. Vanessa Ribes

THEMES OF THE TEAM

The team research aims at understanding how signalling molecules and transcription factors (TFs) create and order cellular diversity in the developing spinal cord. The team addresses these question using models of human and mouse development, including organoids derived from human and mouse pluripotent stem cells. It also extends these studies to pathological situations always with a focus on molecular mechanisms.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hcéres evaluation (italics) were:

1 – The team shows great promise for the future and should be encouraged and supported as much as possible to ensure a fruitful and beneficial output. The team indeed produced quality research as predicted. The report did not mention how much it was supported by IJM, though.

2 – The team has already engaged with the public by setting up a programme to introduce high school pupils to laboratory experience. This activity should be encouraged. This was not specifically mentioned in the report, however the interaction of the team with the general public and society in the past reporting period appears excellent.

3 – As with other junior team leaders at IJM, mentoring from senior scientists will help in strategic planning of ongoing work and funding applications. Again, not clear how much mentoring and help was received from senior scientists at IJM, however the team was able to attract significant funds at the national and regional level.

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

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

EVALUATION

Overall assessment of the team

The team strength lies in the experience it has on studying the interactions between BMP signalling and two transcription factors (PAX 3 and 7) in the patterning of the neural cellular diversity within the dorsal spinal cord. The scientific production of the team is very good to excellent with ten publications, four in leading journal in the field of interest (2 PLoS Genetics, eLife and Development). The visibility and attractiveness of the team is very good, a situation prone to improvement with the fusion with the Nedelec team, that promises great synergies and an ambitious research program.

Strengths and possibilities linked to the context

The visibility and attractiveness of the team is very good. It has visibility and attractiveness as well as good support form charity LNCC. The team leader is a member of Inserm CSS1 scientific committee. There are a few meeting/seminar invitations and participation in panels, however this could be strengthened. The group has a reasonable size and has been able to attract permanent researchers (2 with 1 leave), one postdoc, and four PhD students. The performance is reasonable for a young team.

The scientific production of the team is very good to excellent with ten publications, four as lead author in journal highly visible in the field of interest (2 PLoS Genetics, eLife and Development). An important strength is the research topic as spinal cord pathologies are a pervasive and important biomedical area in need of sustained research. The focus of the team is the interactions between BMP signalling and two transcription factors, PAX3 and PAX7 in the patterning of the neural cellular diversity within the dorsal spinal cord. Their work has shown how these transcription factors act, in parallel to the Smad effectors of BMP signalling to transform the signal into discrete cell fates. The dose and duration of the activity of these factors are critical for the specification of cell fates. Having spent a large amount of time mapping the interactions between the signals and the transcription factors, it is now time to address the mechanism behind this. In parallel to these studies, the group has also began to study Rhabdomyosarcoma associated with fusions between the DNA binding domains of PAX3 and PAX7 and the transactivation domain of FOXO1.

Weaknesses and risks linked to the context

The international visibility is still limited.

There is a prominent lack of medium- and long-term funding

The team has not yet developed valorisation products. This is likely to be developed by the fusion with another team that has patents and some commercial links.

Analysis of the team's trajectory

The project for the next term office is presented as a joint project derived by the fusion of the Team 26 at IJM and one team currently at the Institut du Fer à Moulin. The team strength lies in the experience it has on the experimental system and the quality of their molecular work. The fusion with team from the Institut du Fer à Moulin will reinforce these features and add more cellular perspectives and a strong in vitro system that will allow for novel and insightful experiments.

The joint team will be joined by two permanent researchers. Building on previous collaborations and intense interactions (including shared lab meeting) between the two teams, together with the integration of two more permanent researchers, the new joint team promises great synergies to develop an ambitious research program.

The team from the Institut du Fer à Moulin has expertise in the analysis of signalling and cell fate assignments in the developing spinal cord of mammalian embryos using both model organisms and organoids. The fusion is an opportunity to exploit latent synergies on common themes, in particular it will allow to exploit the spinal cord

organoids recently developed by the entering team, providing means for an in-depth analysis of normal development and disease. This will be achieved by the complementary interests of the two teams: the very molecular, mechanistic approaches of the current team with the very cellular and organoid focus of the team from the Institut du Fer à Moulin. The two teams have already collaborated with some joint publications under their belt and, in this day and age of scarce resources, it is a good idea to combine efforts rather than compete for those limited resources on the same area of research. Both researchers are associated with Inserm and this will facilitate the details of the fusion and, in all likelihood, bring new resources. During the interview there was clear evidence that the fusion will lead to a single functional team under real dual leadership.

RECOMMENDATIONS TO THE TEAM

The fusion of the two teams will allow enhancing their international visibility and, importantly to obtain solid, long-term funding. This is a very important task they should engage immediately as, at the moment, they have secured little support for the next few years, individually or jointly.
They might consider applying for an ERC as a joint team.

It also will be good if they develop their Rhabdomyosarcoma work in a manner that brings them closer to the clinic.

Team 26: Regulation of actin assembly and dynamics

Name of the supervisor: Mr. Guillaume Romet-Lemonne / Mr. Antoine Jégou

THEMES OF THE TEAM

The aim of the team is to understand the mechanisms by which the different cellular actin filament networks coexist. To this end, the team quantifies biochemical assays made of purified proteins observed in microscopy to elucidate the molecular mechanisms that govern actin assembly. The team is particularly interested in the biochemical modifications of actin and their consequences for assembly, the interaction of actin with regulatory proteins, the effect of mechanical stress on actin assembly dynamics, the geometry of filament networks, and interaction with other cytoskeletons such as intermediate filaments.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hcéres evaluation (italics) were:

1- In order to extend their repertoire and to be able to answer more complex questions in the future, the team should establish collaborations with experts in cell biology, cell biophysics, modelling. The team has established sustained collaborations with teams in cell biology in Finland and in France), cell biophysics (London) and modelling (Paris-Saclay).

2- A possible risk for the team is that it does not have a staff scientist with a permanent position. The team succeeded in recruiting one researcher through the national CNRS competition and also recruited one researcher who already held a permanent position as CNRS research director.

3- The mid- long-term strategy will need to be further developed. As IJM is a very strong place to study the cytoskeleton, we encourage the team to pursue and expand their collaboration with other IJM teams. The team has established collaborations with several IJM teams.

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	3
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	3
Doctorants	3
Sous-total personnels non permanents en activité	**8**
Total personnels	**13**

EVALUATIO

Overall assessment of the team

The team is studying the molecular basis of actin assembly. The team's scientific output is outstanding, with 39 articles including 31 research articles and eight reviews in prestigious journals such as Current Biology, eLife, PNAS, Nat. Cell Biol., EMBO reports and Sci. Adv. for which team members are lead authors. The team's attractiveness and visibility is also outstanding, with one ERC starting grant, eleven ANR (including 7 as coordinators), and one FRM team among others. The team's members are frequently invited to international conferences (18 invitations).

Strengths and possibilities linked to the context

The team's attractiveness and visibility are outstanding. The team's level of funding is well above normal standards. It is important to stress that the four permanent researchers contribute to the team's funding. The team has obtained eleven ANR grants, including seven as coordinators, one ERC starting grant (StG BundleForce), two labex postdoc grants, one ARC postdoc grant, one FRM team, one FRM project grant, three PhD fellowships. The team's permanent researchers are regularly invited to present their results at international conferences (18 invitations in 2017-22). The team's researchers also participate in scientific committees. One researcher was a member of Section 5 of the CoNRS for five years (until 2021).

The team's scientific output is outstanding, with 39 publications in total, including 31 research articles and eight reviews and book chapters. The team has published numerous research articles in highly visible journals for which team members are first author or lead author, such as Current Biology (2017), eLife (2018), Biochemistry (2019), PNAS (2019), Nano letters (2020), Nat Cell Biol. (2020), Curr Biol (2020), EMBO Rep. (2021), Biol Cell (2021), Sci. Adv (2022), Phys. Rev. (2023), Mol. Biol. Cell (2023), EMBO J. (2023). The team also published review articles in major journals such as Nat Rev Mol Cell Biol (2022). The team has a very coherent project and made major achievements in multiple fields. Within the research area of actin filament nucleation and assembly, the team showed that the protein SPIN90, known to activate the Arp2/3 complex to generate linear actin filaments, localizes the formin mDia1 at the barbed end of the nucleated filament (Nat Cell Biol 2020). They also showed how mechanical tension applied to the formin-bound actin filament modifies formin conformation to enhance its detachment (eLife 2018). In parallel, they showed that the bundling of filaments by the crosslinking protein fascin imposes constraints that control the association and elongation activity of formins (Nano Letters 2020), Finally, in collaboration with Institut Curie, they resolved the first EM structure of formin mDia1 at the barbed end of an actin filament, which refines the mechanism of elongation (Mol. Biol. Cell 2022). Within the research area of actin filaments disassembly, one of the team's major discoveries concerns ADF/cofilin, whose role in the disassembly of actin filaments has been extensively studied. They showed that filaments saturated with ADF/cofilin disassemble at both ends (barbed and pointed). ADF/cofilin-binding induces a mechanical torque on crosslinked filaments that accelerates their severing (PNAS, 2019). Finally, they showed that filaments oxidised by the enzyme MICAL make them more sensitive to the action of ADF/cofilin (EMBO Rep, 2021). The team also made important contribution to the study of vimentin intermediate filaments Dynamics. The arrival of one researcher has opened up a new line of research in the team. The team's ultimate goal is to understand how actin and vimentin intermediate filaments influence each other's assembly dynamics. To this end, initial results have been obtained on vimentin dynamics alone (BIORXIV, 2022). Finally, using a stretching device, they showed that the mechanical extensibility of vimentin results from subunit unfolding (Science Adv, 2022).

Weaknesses and risks linked to the context

None identified

Analysis of the team's trajectory

The team's project can be broken down into three main areas.

The first is to understand how the cell produces actin networks containing actin filaments regulated in completely different ways. To achieve this, the team will pursue several avenues, such as the importance of actin isoforms, nucleation by specific factors, sensitivity to mechanical stress, decoration of filaments by tropomyosin isoforms that select specific regulators, or post-translational modifications of actin. In particular, the team will continue its work on actin filament bundles by including myosin motors to generate tension or transport cargo. The addition of myosin will also enable the study of actin bundle beating phenomena. Finally, the

reconstitution of the cellular actin cortex and the study of its reorganisation under the effect of mechanical constraints will be carried out. The study of the origin of the chirality of bundles observed in the cell constitutes a research direction with strong potential. The final line of research is the study of the coupling between the various actin cytoskeletons, microtubules and intermediate filaments. In particular, they will study the mechanical coupling between vimentin and actin.

The team has all the expertise required to develop these three lines of research, which should undoubtedly lead to major advances in our understanding of the regulation of cytoskeleton assembly and organisation.

RECOMMENDATIONS TO THE TEAM

The team has an exceptional track record in terms of success in competitive calls for projects and scientific output. Areas for improvement include internal collaborations with more teams. The team would also benefit from developing its own cellular approaches to put molecular mechanisms into context.

Team 27: Molecular oncology and ovarian pathologies

Name of the supervisor: Mr. Reiner Veitia

THEMES OF THE TEAM

The team studies the FOXL2 gene, belonging to a large transcription factor protein family. Several Fox protein family members are expressed in the ovarian granulosa cells and the team wants to understand their specificity by looking at their activation of different targets and cofactors. They are especially interested in a FOXL2 variant associated to ovarian cancer. Their research is done on cell cultures and mice employing genomic and proteomic approaches.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hcéres evaluation (italics) were:

1- The team should strive to obtain teaching relief in order to secure more time for research so that they can continue to produce new highlights in the processes regulating the pathogenic mechanisms leading to ovarian pathologies. It is not clear if the team's teaching load has decreased. In any case, the team's research output is outstanding and does not seem to be affected by their teaching activity.

2- The team would benefit from a postdoctoral students researcher or full-time researcher, who would strengthen the team. The team has maintained a very stable number of researchers. Two ATER/postdoctoral students were in the team from 2015-2018 and another from 2019-2021.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	**1**
Total personnels	**6**

EVALUATION

Overall assessment of the team

The team productivity has been very high and the quality of the research assessed as excellent to outstanding. The team makes an excellent use of their access to human patients to analyse premature ovarian insufficiency, where they can isolate genetic variants associated to the condition using genomic approaches. They have also the capacity to confirm the relevance of these variants by analysing mouse models and established cell lines. The visibility of the team is excellent to outstanding, with the team leader being member of the National Academy of Medicine and of Academia Europaea and assuming important editorial and boards activities.

Strengths and possibilities linked to the context

The team visibility is excellent to outstanding. The team leader is editor-in-chief of the Clinical Genetics journal since 2016, and is in the editorial board of BioEssays. He forms part of two international Scientific Advisory Boards at Idipaz and Ciberer, he is a member of the National Academy of Medicine (2017) and of Academia Europaea (2015) as well as member of the board of European Society of Human Genetics. In the period evaluated the team has been well funded with two ANR and a FRM grants totalling over 550k euros. The team also published eighteen reviews/book chapters.

The team productivity has been very high and the quality of the research assessed as excellent to outstanding. The team published 31 research articles, 22 as lead authors, many of which published in journals of the medical fields (Cancer Res., J. Med. Genet., Clin. Genet., Hum. Genet., Hum Mol. Genet.) and a few in general biology research journals (eLife, Cell Death Differ., Mol. Cell Proteomics, Faseb J., Sci. Rep.). The team is expert on how FOXL2 proteins regulate specific targets in the granulosa cells that surround the oocyte. They showed that FOXL2 is required to maintain granulosa cell fate through the activation of a gene network mediating the expression of oestrogen. FoxL2 interacts with oestrogen receptor (ESR2) and the team has showed they co-regulate numerous common targets. The team showed that among other targets, FOXL2 and ESR2 repress Sox9. In the absence of this repression the ovary granulosa cells transform into Sertoli cells (the testis sperm support cells). Using gene editing, the team has made a mouse mutant in the FOXL2 gene equivalent to that present in the adult granulosa human cancer cells and have been able to replicate the formation of tumours with full penetrance. The team has been able to show that no other mutations are required to induce the granulosa tumours, indicating the importance of this single gene in tumour occurrence. The team also demonstrated the involvement of AKT1 mutations in human juvenile granulosa cell tumours and studied the function of AKT1 in mouse established granulosa cell culture lines, analysing how its down regulation impacts their migratory behaviour.

Using comparative exome sequencing of patients affected by premature ovary insufficiency (POI) with their normal family members, the team has also isolated a number of genetic variants responsible for the phenotypes. They have used mouse models to confirm their observations. This allowed them to link POI to gene recombination and DNA repair machinery defects. The team's great strength is the combination of expertise in bioinformatics with molecular and cellular approaches in mice, as well as their access to human patient tissues (through their collaborators).

Weaknesses and risks linked to the context

Societal interactions are limited. The team could exploit their scientific/medical information to engage with the public.

The research results obtained could have a higher impact if more functional studies were provided.

Analysis of the team's trajectory

The team wants to analyse in cell models the effect of different FOXL2 post-translational variants on the protein localisation and the regulation of its targets. They plan to mutate different residues putatively phosphorylated by various kinases to make phospho-mimetic and unphosphorylated protein forms. If the results are promising, the team will aim at reproducing the mutations by gene editing in AGCT cell culture, where they will perform RNA-Seq and Chip-Seq to analyse the modifications of target expression.

The team will also study the interaction of FOXL2 with the TRIM scaffold protein to analyse how the sumoylation of FOXL2 is affected and how this may influence the phosphorylation of the other sites.

The team will continue their analysis of tumours formed in mice of the FOXL2 C134W heterozygous mutants, applying single cell approaches to observe ovary to tumour gene expression changes. The tumour cells will be used in explants to investigate their behaviour in 2D and 3D cultures. Different drugs will be tested to find their effect on the cells in culture and promising ones will be tested in whole animals in the murine model (in the laboratory or by their collaborators).

The team also wants to explore the possible sites the FOXL2 forkhead DNA binding domain uses to bind the RNA of the transcripts of some of its downstream targets.

As a continuation of the JGCT AKT project, the team plans to investigate the mutant AKT forms they identified in patients using Drosophila melanogaster. They will express the mutant forms in the mesodermal cells of the Drosophila ovary using the Gal4 system. (It is not clear if the Drosophila AKT homologous protein is active in the ovary cells.) The phenotype caused in the follicle cells of the different genotypes will be analysed with mass spectrometry and RNA sequencing.

In summary, the team plans to pursue a variety of experiments, some of which are a logical continuation of previous ones, while others explore several new avenues of research that could give rise to interesting and original results. The introduction of *Drosophila* as a model to test human mutant forms of AKT is an excellent idea to reduce work on mice. For most of the planned experiments the team has the expertise to make the proposed experiments.

RECOMMENDATIONS TO THE TEAM

The introduction of in vivo models to find the functional outcome of different mutations may help to increase the team's research impact.

The team has great potential to interact with the public and should participate in such events.

Team 28: Stem cells, development and evolution

Name of the supervisor: Ms. Eve Gazave

THEMES OF THE TEAM

The team is interested in the evolution of the mechanisms of regeneration using as a model the annelid worm *Platynereis* (Lophotrochozoa), which is capable of continuous growth and regeneration of the posterior end thanks to a pool of stem cells. Despite forming a large part of the phylogenetic tree, Lophotrochozoa are under-represented in the field of stem cells and regeneration, therefore the use of the slow-evolving Platynereis as a model has the potential to trace back ancestral as well as taxon-specific mechanisms for stem cell regulation and epimorphic regeneration.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (italics) have been partially addressed:

1- On scientific production and activities, and team organisation:
The *attraction of PhD students via the various teaching activities of the senior team members* has been successfully implemented as the group now includes four PhD students. Concerning *the recruitment of international team members,* three postdoctoral students joined the group, one from abroad supported by a Paris Region Fellowship Program. By contrast, *the funding opportunities* linked to *the trans-disciplinary appeal of stem cells and regeneration that offer an opportunity to compete for large European or international grants,* were not explored yet.

2- On scientific strategy and projects:
The morphological characterisation of regeneration (1) and the transcriptomics projects (3) were proposed as absolute priorities by the previous Hcéres committee. These approaches have been successfully developed for posterior regeneration (two papers 2019, 2023).
Concerning the recommendation *that the team identifies a focus area in which to make the investments necessary to go beyond the current mainstream in the field, rather than doing a little bit of everything*, some efforts were made (abandon of research axis on epigenetic regulation of regeneration is planned).
Concerning *the overlap with one team in the study of stem cells*, it is still present but methodological approaches appear different.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	**3**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**6**
Total personnels	**9**

EVALUATION

Overall assessment of the team

The team performs a very interesting and unique mix of modern omics technologies and classical embryological approaches to understand posterior regeneration in Platynereis. The scientific production of the team has been very good with 8 research papers, 4/8 directed by the team. Visibility has been very good, with insertion in an European COST network on stem cells (Maristem) and the securing of very good amounts of funding from frequent small grants. Attractiveness has been excellent with the recruitment of four PhD students and three postdoctoral students. Interaction with society has been outstanding.

Strengths and possibilities linked to the context

The team developed a very good visibility, highly integrated into collaborative networks at local, national and international levels, in the Annelid-Platynereis field (Ozpolat et al. 2021) and with an active participation in the COST program on Marine Stem Cells (Maristem; Martinez et al. 2022, Rinkevich et al. 2022, Vervoort and Gazave 2022, Gazave & Röttinger 2021). Pierre Kerner received a prize for having developed innovative teaching. Attractivness of the team is excellent. The team was able to attract four PhD students and three postdocs during this period, among them, two postdoctoral students produced 1st-authored research papers (Planques et al., 2019, 2021; Alvarez-Campos et al. 2022). The team has also obtained very good amounts of funding from frequent small grants, financial support for PhD students and fellowship for postdoctoral students.

Given the difficult period with the disease and ultimate death of Michel Vervoort in Dec 2022, the publication production is very good, with eightresearch papers, 4/8 directed by the team plus three coming currently on BioRxiv, and nine reviews or book chapters, 5/9 signed by Eve Gazave as corresponding author. Among the four research papers produced by the team, three are well cited: two about the morphological (Planques et al. 2019; 62 citations) and transcriptomic (Paré et al. 2023) characterisation of Posterior Regeneration (PR) in Platynereis, and one about the mechanisms controlling PR with the brain-produced methylfarnesoate that facilitates PR in brainless animals (Alvarez-Campos et al. 2022). Data about the role of Wnt and Notch signalling remain to be published.
Another main theme is the analysis of origin and behaviours of blastema cells during PR (Bideau et al. 2023), how cytosine methylation (Planques et al. 2021), or Histone modifications and RNA methylation affect development and regeneration (ongoing). The role of epigenetic and epi-transcriptomic regulation will not be pursued after publication of B. Pichard's results. The team is also interested in the phylogenetic relationships between germ cells and pluripotent stem cells. Using data mining, sc RNAseq analyses and Hybridisation Chain Reaction, the team wants to compare their respective genetic signatures. This is a high risk far-fetched but highly interesting project worth pursuing. The team's strengths are undoubtedly technical, with the successful implementation of single-cell RNA-seq and current efforts to develop Crispr-Cas9 in the absence of efficient gene silencing in Platynereis. As with any non-classical model, long-term efforts are required before functional analyses become robust enough to investigate the mechanisms of regeneration.

Interaction with the general public is very active especially through the scientific outreach work of Pierre Kerner, through the « Université Ouverte" Courses and events related to Citizen Science: the City Nature challenge (2022 and 2023).

Weaknesses and risks linked to the context

As main risk, the team has a high level of teaching duties that affect their research capability.

Also, there is a danger to remain superficial when too many questions are tackled at the same time.

Analysis of the team's trajectory

For the next period, to understand the mechanisms controlling the early stages of regeneration, the team plans to compare posterior (PR) to anterior regeneration (AR) that is abortive, i.e. a blastema forms after amputation but never gives rise to a differentiated new head. After characterising AR, the team will study in both contexts ROS signalling and apoptosis as injury-induced signalling, completed with ATAC-seq to identify the regulatory landscape and map putative regeneration enhancers. As a second line of research, they plan to compare via SCRNA-seq the origin and diversity of the blastema cells during abortive and successful regeneration in Platynereis, which is a promising approach. As a third one, they plan to draw an evolutionary history of

regeneration, as deduced from the knowledge of evolution of genomic networks underlying regeneration in metazoans.

The comparative analysis of abortive versus successful regenerative processes in the same animal appears as an excellent strategy to further understand the mechanisms at work in regeneration in Platynereis. Nevertheless, there should be a clearer definition of the biological questions the team wants to address and a strategical evaluation of the value of the expected results and the load to develop methods that were never implemented in Platynereis so far.

Concerning the last integrative approach (the evolutionary history of regeneration), it needs to be a collaborative effort at international level, and the team is well positioned.

RECOMMENDATIONS TO THE TEAM

Although the different axes have been productive in the last period, in regards of the size of the team and the time dedicated to research, the team should consider to focus on fewer axes. The scientific questions that are investigated by the team should be deepen to define a line of research that is original and explores one by one the scenarios that seem plausible regarding each scientific question. In that respect, the committee believes that mentoring by an experienced scientist would be very useful to the team leader, to help her prioritize original questions in ongoing projects and thus retain those that will bring the most significant results. This mentoring would also help to distribute forces on future projects.

In terms of scientific production, the team should concentrate on the production of research papers at the best level, rather than diluting efforts in writing too many reviews and book chapters.

In terms of scientific communication, the committee feels that it would be highly beneficial for the team leader to get advice from senior colleagues or from her mentor.

The teaching load is heavy and the team should try to reallocate to research as much time as possible.

The effort to attract postdocs via fellowships should be continued.

Team 29: Mechanisms of meiosis

Name of the supervisor: Ms. Katja Wassmann

THEMES OF THE TEAM

The team investigate meiotic mechanisms, employing three distinct model systems: budding yeast, Xenopus, and mice oocytes. Their research centre around three core areas: (i) Unraveling the distinct regulation of CDK-cyclin complexes between meiosis I and meiosis II; (ii) Studying chromosomes and chromatin cohesion during meiosis; (iii) Investigating the regulation of kinetochore-to-microtubule attachment and its control by the spindle assembly checkpoint.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No specific recommendations to the team were formulated.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**3**
Total personnels	**8**

EVALUATION

Analysis of the team's trajectory

The team appears to have rapidly adapted to its new environment and is poised to overcome the recent slowdown caused by the pandemic and the transition from another institute. This positive trajectory is attributed to a robust contingent of permanent staff, ensuring stability and continuity in their work.

This established team based at LBD/IBPS -UMR7622 in Paris recently joined IJM in 2022, showing impressive momentum with the recent addition of two permanent researchers to their existing composition, which includes the PI, an assistant professor, and a technician. Their primary aim is to unravel the crucial regulators and signalling pathways that distinguish meiosis I from meiosis II, vital for ensuring the production of healthy gametes, focusing on Cdk-cyclin specificities and threshold levels. Utilising budding yeast, they will scrutinize kinase and phosphatase activities during both meiotic divisions to delineate substrate phosphorylation differences. Meanwhile, a team member, an expert in frog oocyte meiosis, continues her exploration of Cyclin B3's role in ordering the female meiotic cell cycle in Xenopus laevis oocytes. She collaborates with the marine station in Villefranche-sur-mer to understand its conservation across vertebrates and non-vertebrates.

Another research facet delves into step-wise Cohesin Removal in Mammalian Oocytes. This involves a focus on Separase, studying its activation and inactivation in mouse oocytes. They also delve into Rec8, a cohesin subunit, and the structure holding sister chromatids to grasp the mechanisms underlying cohesin removal.

In essence, the team projects are well-defined, aiming to unravel the role of protein phosphorylation in meiotic transitions, understand cohesin removal mechanisms, and decipher kinetochore functionality and checkpoint recognition during both meiosis I and meiosis II in mammalian oocytes. This will be achieved through multifaceted approach leveraging oocytes from both wild-type and genetically modified mice, along with utilising budding yeast and frog oocytes as complementary models. The team employs cutting-edge live imaging techniques and high-resolution confocal microscopy, capitalising on the transparency of mouse oocytes. Recently, they've integrated biochemical and proteomics methodologies to decipher the global mechanisms governing the meiotic cell cycle. Altogether this defines a solid and highly competitive project.

RECOMMENDATIONS TO THE TEAM

Continue the momentum!

Team 30: Molecular Virology

Name of the supervisor: Ms. Isabelle Jupin

This team was closed and did not provide a report for the evaluation.

Team 31: Development, signalling and trafficking

Name of the supervisor: Ms. Anne Plessis

This team was closed and did not provide a report for the evaluation.

CONDUCT OF THE INTERVIEWS

Dates

Start: 12 décembre 2023 à 08h00

End: 14 décembre 2023 à 14h00

Interview conducted: on-site

INTERVIEW SCHEDULE

Day 1, Dec 12th 2023

8:30 - 8:45 **Preliminary meeting of the expert committee (closed hearing)**
Attending: expert committee, (Yacine Graba, Ina Attrée, Scientific Officers (SO))

8:45 - 9:00 Presentation of the Hcéres evaluation to the unit (Yacine Graba, Scientific Officer).
Attending: expert committee, SO, representatives of institutions and all unit members

9:00 - 10:00 Presentation of the research unit by the unit director (including 15 min questions).
Attending: expert committee, SO, representatives of institutions and all unit members

10:00 – 10:30 Platform presentations (20 min presentation, 10 min questions)
Attending: expert committee, SO, representatives of institutions and all unit members

10:30 - 10:45 Break

10:45 - 12:55 Team scientific presentation Session 1
Attending: Team members, expert committee, SO, unit direction, representatives of Institutions

Subcommitee 1- Room 393B

Balavoine	10:45-11:15
Prioleau	11:15-11:50
Grange / Geigl	11:50-12:20
Greenberg	12:20-12:55

Subcommitee 2 -Room F. Jacob

Ribes and Ribes / Nedelec	10:45-11:25
Wassmann	11:25-11:55
Conduit	11:55-12:30

13:05 - 14:00 Lunch

14:00 - 14:45 Parallel meetings (3 subcommittees)
- Meeting with technical and administrative personnel (in French). *Attending: Technicians, Engineers, Administrative staff, sub-committee A of expert committee, SO*
- Meeting with thesis students and postdoctoral students. *Attending: PhD students and postdocs, sub-committee B of expert committee, SO*
- Meeting with researchers and professors. *Attending: Researchers except group leaders, sub-committee C of expert committee, SO*

14:45 - 15:15 Committee debrief (closed hearing)

15:15 - 15:30 Break

15:30 -17:50 Team scientific presentation Session 2

Subcommitee 1- Room 393B.

Koonstantinides	15:30-16:05
Gazave	16:05-16:40
Collignon	16:40-17:15
Veitia	17:15-17:50

Subcommitee 2 -Room F. Jacob

Libri	15:30-16:00
Léon	16:00-16:35
Minc	16:35-17:10

Jackson / Verbavatz	17:10-17:45

Day 2, December 13th 2023

9:00 - 11:10 Team scientific presentation Session 3

Subcommitee 1- Room 393B

Azimzadeh	09:00-9:35
Guichet	9:35-10:10
Raote	10:10-10:40
Cadoret	10-40:11:15

Subcommitee 2-Room F. Jacob

Romet-Lemonne / Jégou	09:00-9:35
Duharcourt	9:35-10:10
Palancade	10:10-10:45
Borghi	10:45-11:20

11:10- 11:30 Break

11:30 – 12:30 Meeting with the representatives of supervising bodies (CNRS, University). *Attending: expert committee, representatives of Institutions, SO*

12:30 – 14:00 Lunch

14:00 - 15:30 Team scientific presentation Session 4

Subcommitee 1- Room 393B

Doye	14:00-14:35
Camadro	14:35-15:05
Courtier	15:05-15:40

Subcommitee 2-Room F. Jacob

Pintard	14:00-14:35
Dumont	14:35-15:10
Ladoux / Mège	15:10-15:45

15:30 – 15:45 Break

15:45- 18:00 Deliberation of the sub-committees (closed hearing)
Attending: expert committee, SO

Day 3, Dec 14th 2023

9:00 - 9:30 Meeting of the Committee with the head of the unit.
Attending: Unit Director, unit direction, expert committee, SO

9:30- 14:00 Deliberation of the committee (closed hearing)
Attending: expert committee, SO

PARTICULAR POINT TO BE MENTIONED

None

GENERAL OBSERVATIONS OF THE SUPERVISORS

Université Paris Cité

Le Président

Paris, le 28 mars 2024

HCERES
2 rue Albert Einstein
75013 Paris

Objet : Rapport d'évaluation de l'unité **DER-PUR250024225 - IJM - Institut Jacques Monod.**

Madame, Monsieur,

L'université Paris Cité (UPCité) a pris connaissance du rapport d'évaluation de l'Unité de Recherche IJM - Institut Jacques Monod.

Ce rapport a été lu avec attention par la direction de l'unité (cf courriers joints de sa part), par la vice-doyenne Recherche et le doyen de la Faculté des Sciences d'UPCité (cf courrier joint de la part du doyen Cazayous), par la vice-présidente Recherche d'UPCité et par moi-même.

Je remercie le comité pour son travail d'évaluation, et vous indique ne pas avoir d'observations d'ordre général supplémentaires à apporter.

Je vous prie d'agréer, Madame, Monsieur, l'expression de ma considération distinguée.

Édouard Kaminski

Présidence

Référence
Pr/DGDRIVE/2023

Affaire suivie par
Christine Debydeal - DGDRIVE

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Référence
MC/NE/EB/2024-023

Faculté des Sciences
Université Paris Cité
5 rue Thomas Mann
75013 Paris

Objet : DER-PUR250024098 - Évaluation HCERES de l'UMR 7592 IJM – Retour Tutelle Université Paris Cité

Chères et Chers Collègues,

Nous souhaitons par ce courrier remercier les membres du comité de visite pour le temps qu'ils ont consacré à l'évaluation de IJM, ainsi que pour leur écoute et le travail considérable qu'ils ont accompli.

La Faculté des Sciences est fière de compter IJM parmi ses unités de recherche et rappelle la grande qualité de la recherche menée par tous les membres du laboratoire.

Après lecture du rapport provisoire d'évaluation de l'UMR 7592 IJM, la Faculté des Sciences souhaite ajouter les remarques suivantes :

– Nous nous étonnons que dans son rapport le comité suggère la construction d'une passerelle entre deux immeubles :"*The Institute has to find a way to bolster the bioinformatics support and, at this, they should find a way to liaise with the EDC; here, acknowledging the lack of space to bring them into the Buffon building, it would be good if the University could build a bridge to communicate the two institutions to facilitate the interactions*."
Une telle proposition nous semble dépasser très largement les compétences du comité et nous demandons à ce qu'elle soit retirée.

- Le bâtiment Buffon abritant l'IMJ date de 2008. Depuis sa construction, il fait l'objet d'un entretien régulier. Seul fait notable, une passerelle du bâtiment rendue inutilisable suite à une utilisation inadéquate va faire l'objet de travaux en 2024. Pour le reste du bâtiment, il n'y a pas de dégradations notables qui pourraient être associées à de la vétusté comme l'indique à tort le rapport.

- Notre dernière remarque porte sur la phrase du rapport: "*One solution that is being considered is that the Institute becomes a private foundation as amidst other things, this would allow the Institute use the funds that it can accrue to solve the infrastructural problem something that is now curbed by its two supervising bodies*."
Une telle proposition dépasse très largement les compétences du comité et nous demandons à ce qu'elle soit retirée.

Pour rappel, l'université possède déjà une fondation qui finance des actions et au travers de laquelle l'unité peut attirer des moyens afin d'assoir sa trajectoire scientifique.

En vous priant, chères et chers collègues, d'accepter nos chaleureuses salutations.

Maximilien CAZAYOUS
Doyen
Faculté des Sciences
Université Paris Cité

Nathalie EISENBAUM
Vice-Doyenne recherche Faculté des Sciences
Université Paris Cité

General Comments regarding the
EVALUATION REPORT OF THE UNIT
IJM - Institut Jacques Monod

We would like to thank the evaluation committee for the in-depth review during the site visit and for the quality of the report. We have only a few minor comments to this report.
Corrections to factual errors have been provided in an independent document.

Page 5: While the Institute is a place of excellent solid science with excellent National visibility, it lacks a figure or an achievement that singles it out internationally.

We kind of dispute this evaluation.
The IJM is a collaborative working environment and we are proud to have several internationally distinguished scientists amongst our group leaders (including for instance four elected EMBO members). It would be against the spirit of the IJM to single out one or two scientists to create an institutional "identity"; we thus rather prefer an identity defined by the excellent science performed by its groups.

Page 6: The main, and perhaps only, weakness of the Institute stems from its being very focused on basic research and knowledge that limits translating their excellent science into commercial and entrepreneurial activities,

The emphasis on basic biology is the foundation of our scientific policy. It was presented to our international scientific board who encouraged us to pursue our efforts into this direction. It has not detracted our ability to increasingly fund our research.

INSTITUT JACQUES MONOD
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et d'Université Paris Cité

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