

EVALUATION REPORT OF THE UNIT
IBDM - Institut de biologie du développement de
Marseille - Luminy

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Aix-Marseille université - AMU, Centre national de
la recherche scientifique - CNRS, Collège de
France

EVALUATION CAMPAIGN 2022-2023
GROUP C

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In the name of the expert committee¹ :

James Hombría Castelli-Gair, Chairman

For the Hcéres² :

Thierry Coulhon, President

Under the decree n° 2021-1536 of 29th November 2021:

¹ The evaluation reports "are signed by the chairperson of the expert committee". (Article 11, paragraph 2);

² The president of the Hcéres "countersigns the evaluation reports established by the expert committee and signed by their chairperson." (Article 8, paragraph 5).

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

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:

Mr James Hombría Castelli-Gair, Consejo Superior de Investigaciones Científicas, Espagne

Ms Jimena Berni, University of Sussex

Ms Susan Chan, Inserm, Illkirch

Mr Damien Devos, Consejo Superior de Investigaciones Científicas-CSIC, Espagne

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Experts:

Ms Alicia Hidalgo, University of Birmingham

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Mr Christophe Le Clainche, CNRS, Gif-sur-Yvette

Ms Anne Pacquelet, Inserm, Rennes (representative of CoNRS)

Mr Didier Stainier, Max Planck Institute for Heart and Lung Research, Allemagne

Mr Lucas Jacques Waltzer, CNRS, Clermont-Ferrand

HCÉRES REPRESENTATIVE

Ms Ina Attrée

CHARACTERISATION OF THE UNIT

- Name: Institut de Biologie du Développement de Marseille
- Acronym: IBDM
- Label and number: UMR 7288
- Number of teams: 21
- Composition of the executive team: Director for the current contract: André Le Bivic (01/2016-01/2019) ; Laurent Kodjabachian (since 02/2019); Deputy Director: Pascale Durbec (since 01/2018)

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 Institute focuses on Developmental Biology but is also strong on Neurobiology and has lines of research focusing on Evolution of Developmental mechanisms and the Physics of Development.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The IBDM is a research Institute created in 2006 by the merger of various existing laboratories located in Marseilles. Initially affiliated to the Université de la Méditerranée is now currently affiliated to the University of Aix-Marseille II that resulted from the merger of the three main regional universities. The IBDM is the CNRS and the Université de Aix-Marseille unit. The Institute occupies the TPR2 building, the largest in campus, which is currently under refurbishment.

RESEARCH ENVIRONMENT OF THE UNIT

The Unit is located in the Luminy campus of Marseilles, which comprises twenty different Research Institutes with which the IBDM has federated since 2018 through the Centuri program. These institutes work on various fields including biology, physics, mathematics, computer science and engineering, and their federation focuses on Research, Education and Engineering with the aim of creating a superstructure studying biology with an interdisciplinary approach.

The Unit belongs to the Aix-Marseille University, which has also created several Thematic Institutes to promote modernisation and interdisciplinarity. The IBDM participates in four of these thematic institutes: NeuroMarseille (dedicated to neurobiology), Imaging (dedicated to Imaging approaches), Marmara (dedicated to rare diseases) and ICI (dedicated to Cancer and Immunology).

IBDM also hosts PICsL, a regional cell imaging platform, which is a node of France Bioimaging infrastructure. The IBDM team leaders are extensively involved with all these institutes/platforms, participating in some cases as their directors.

The Unit was awarded a Labex Inform project that ended in 2018 and acted as the seed of the Centuri program.

UNIT WORKFORCE: in physical persons at 31/12/2021

Permanent personnel in active employment	
Professors and associate professors	3
Lecturer and associate lecturer	13
Senior scientist (Directeur de recherche, DR) and associate	20
Scientist (Chargé de recherche, CR) and associate	28
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	50
Subtotal permanent personnel in active employment	114
Non-permanent teacher-researchers, researchers and associates	13
Non-permanent research supporting personnel (PAR)	84
Post-docs	10
PhD Students	53
Subtotal non-permanent personnel	160
Total	274

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: NON-TUTORSHIP EMPLOYERS ARE GROUPED UNDER THE HEADING 'OTHERS'.

Employer	EC	C	PAR
CNRS	0	43	42
Aix-Marseille Université	15	0	7
Inserm	0	5	0
Collège de France	1	0	0
Inrae	0	0	1
Total	16	48	50

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	7723.0
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	2552.0
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	17,692.0
Own resources obtained from international call for projects (total over 6 years of sums obtained)	10,837.0
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.)	412.0
Total in euros (k €)	29,214.0

GLOBAL ASSESSMENT

The IBDM is one of the best-known centres in France for its work on the genetics and cellular regulation of development and morphogenesis, but the Unit also houses strong teams working on neurobiology and the evolution of developmental mechanisms (Evo-Devo).

The Unit houses several *in vivo* experimental models including *Drosophila*, *C. elegans*, *Xenopus* and a small mammal model. Their research employs a wide palette of approaches including genetic and molecular biology as well as biophysical and computational approaches, directed to understand the mechanisms controlling stem cell biology, morphogenesis, heart formation, evolution of development and relationships between the microbiota and the adult organism making it an attractive institute to develop research programs.

Members of the IBDM have been very successful at obtaining European grants including an Advanced ERC that was renewed for a second term (Dr. Lecuit), four ERC starting/consolidator grants to (Drs. Michelot, Moqrich, Schnorrer and Prud'homme) and an ERC synergy grant (Dr. Schnorrer), as well as contracts from the H2020 program (Fasano) and an ITN among others. Various researchers have participated on the Labex Inform as well as other competitive contracts, each providing over 500 keuros. The teams are also successful at obtaining charity funding, some of these grants providing large amount of funds like *Fondacion Leduq* for nearly 800 keuros (Dr. Kelly).

The institute's publication record is outstanding, having been maintained despite the disruption caused by the ongoing building renewal and the Covid-19 crisis, with around 350 articles most of which appeared in highly respected journals of the field.

The unit has a moderate involvement in research dissemination that could be increased. The unit has a moderate, but reasonable, impact on transfer (mostly thanks to two teams lead by Moqrich and Maina), which would be difficult to increase in the short term due to most teams being focused on basic research activities.

A strong point of IBDM is the ambition and leadership displayed by most of its team leaders as demonstrated by their heading of the interdisciplinary federative centre -Turing Centre for Living Systems- (Centuri), and the thematic institute NeuroMarseille, as well as active participation in national boards (Director of the Biological Sciences Department of CNRS – INSB – ; member of Research Evaluation Department, Hcéres, Vice-president for Biological Sciences at AMU). International visibility is also very well attested by their position as editors in scientific journals, invitations to major international conferences or nomination as EMBO members (one in 2020 and one in 2022).

The participation of IBDM in Centuri, and the thematic institutes like NeuroMarseille, Imaging, Marmara, ICI as well as PICsL has been an efficient way of increasing the Unit's visibility and providing an important source of funds to support the acquisition of state-of-the-art equipment and PhD student and postdoc recruitment.

The Unit as a whole has high international visibility and an outstanding reputation.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous evaluation recommended that the IBDM use its turnover to recruit new team leaders. This has not been possible in this period due to the disruption caused by the building's refurbishment and due to the lack of space available for new groups.

The evaluators also recommended coaching groups that may encounter difficulties.

The support to groups in difficulty has been restricted to the creation of a new Chalk talk and to extend PhD contracts for some students at the end of their grants. Over the review period, 4 teams have received support from the institute's funds for a total amount of over 230 k€, in the form of PhD contract extensions (3 teams), of a fixed contract for an engineer (1 team, 24 months), of help with running costs (2 teams), and of free access to core facilities (2 teams).

The evaluators also pointed out that the building refurbishment would impact negatively on the IBDM's performance. This does not seem to have been the case, with the Unit maintaining its research activity and demonstrating a high level of resilience in during a very difficult period when the building works disruption was compounded by the stress caused by the Covid-19 crisis.

B – EVALUATION AREAS

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

Assessment on the unit's resources

There are four main scientific facilities at IBDM.

Facilities for experimental *in vivo* models: These are especially important for the unit, in particular the facility that is currently being refurbished. The *Drosophila* facility have been already finished.

Optical imaging: The microscopy unit is used by almost all teams, also serving external users. Among its equipment it provides DWM wide field microscopy, SDCM spinning disk ideal for life imaging, CLSM confocal laser scanning microscopy and multiphoton microscopy, Fluorescence microscopy SPIM/dSLSM Light sheet microscopy, Fluorescence Nanoscopy including SMLM Palm, and STED super-resolution microscopy. Functional imaging including FRET, FLIM/FRET, FRAP, FCS and High-speed imaging.

Electron microscopy: A service offering electron tomography (ET), Scanning transmission electron microscopy (STEM) and Correlative light and electron microscopy (CLEM). Overall, the imaging facilities provide access to high end technologies and excellent support.

Software development: An informatics support facility that helps developing and adapting software and workflows for specific research projects. The level of IT support is currently reduced due to limited human resources.

Assessment on the scientific objectives of the unit

The unit has an integrative approach to complex biological processes, focussing mainly on developmental biology and neurobiology systems. The unit aims at studying how molecules control cell behaviours during the generation of tissues and organs, as well as analysing how organism homeostasis is maintained and how these processes evolve. These studies integrate all levels of organic complexity (molecular, cellular and organismal) applying molecular, computational and biophysical approaches. The unit's research is mostly basic with only marginal applications.

Assessment on the functioning of the unit

The Director is assisted by a Vice-Director and an Assistant Director. The unit has a work structure based on a flexible organisation where the different teams decide freely on their research topics. There are no separate departments, but different overlapping areas of research shared by the different teams. The Unit is integrated into higher local structures that promote interdisciplinary projects and allow increasing the Unit's visibility by running joint PhDs and the use of common technical platforms.

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

Strengths and possibilities linked to the context

The unit has excellent advanced microscopy techniques and the IBDM provides state-of-the-art equipment. The unit has facilities for different *in vivo* experimental models. The *Drosophila* and *Xenopus* facilities have been renovated during the current contract, but the other one for small mammals has not yet been finalised. Once all the refurbishment works end, it is expected that the teams will have a better working environment making the Unit more attractive to outside researchers. This linked to the Unit's international visibility may result in attracting additional talented young researchers to the Institute. In the past, the recruitment policy of the Unit resulted in the attraction of successful scientists that have been able to obtain a large amount of European funding.

The integration into higher structures like Centuri and France bioimaging (FBI) attracts visibility and funding.

Weaknesses and risks linked to the context

There may be a weakness on the computational support for the use of sequencing projects associated to modern genomics and single cell technologies. This is currently solved by access to the platform offered by Centuri. However, the software development facility should be reinforced to support, in-house, the biocomputational analyses required for multiomic studies and single cell technologies. It seems that the scientific manager of the informatics facility has made an effort toward creating a Biocomputing facility at IBDM, but this may still be insufficient and requires additional investment.

A major problem is the departure of administration and *in vivo* models' facility personnel, partially solved by a temporal contract and by the opening of two CNRS administration positions. However, the administration situation is still far from perfect, as six people left out of a total administrative and technical personnel force of nine.

2/ The unit has set itself scientific objectives, including the forward-looking aspect of its policy.

Strengths and possibilities linked to the context

The main strength of the institute resides in its team leaders, the Unit's scientific cohesiveness and its use of novel techniques and approaches. The strong leadership of some of its team leaders offers the Unit a great national and international visibility. The capacity of many different team leaders to attract external international funding is remarkable.

Weaknesses and risks linked to the context

The main risk could reside in competition from other institutes with a similar research focus, especially Institute Curie Paris, CBI Toulouse, iBV Nice or IGFL Lyon. However this does not seem to be an immediate problem. As most of the Unit's teams work on basic science projects, a further danger could come in the future if the supporting institutions stepped up their priorities on funding translational research. Although the Unit has benefited from the establishment of alliances with other research units in the region, the sharing of technologies may also become a risk if fundamental technologies/facilities stopped being available in-house.

3/ The functioning of the unit complies with the regulations on human resources management, safety, the environment and the protection of scientific assets.

Strengths and possibilities linked to the context

The Unit provides its researchers with an optimal environment to perform outstanding scientific research. The high international visibility of IBDM has a very positive influence on its students and postdocs future careers. The recent renovation works of the building, although have been disruptive for a couple of years, will provide an excellent work environment.

The institute has a committee dedicated to analyse the Unit's environmental impact, suggesting actions to decrease it.

Weaknesses and risks linked to the context

Despite the unit's good overall internal organisation, the building refurbishment during the evaluation period, the temporary geographical separation of teams and facilities and the concomitant Covid pandemics lockdown raised the new important challenges to its staff and direction board. To help to address them, the unit should reinforce its health and psychosocial risk prevention. The permanent staff in every team should feel there is recognition of their work and have guidance from the IBDM and their team leaders to understand how to progress in their careers. It should not be left to each team leader to decide how to promote their staff, but the Unit should have a unified strategy.

Permanent Senior members on the different teams can apply for research grants, but only the team leader is given access to the administrative information provided online, resulting in some grant holders not being able to administer their own resources.

The authorship/acknowledgement policy guidance should be unified for all teams and core facilities, to avoid disparities and maintain staff motivation. The next foreseen reunification of the unit will probably be a good occasion to revise internal rules, including staff promotion/ranking policies, the priority rules of the access to common facilities and to democratise staff participation in decision-making.

The unit has a bad gender balance among the team leaders. The Unit should analyse if their recruitment policies are inadvertently promoting certain characteristics of team leaders (assertiveness, aggressiveness, mobility etc.) that may be more associated to one gender due to common social uses.

The unit should consider if it is providing sufficient guidance and support to groups that, performing well scientifically, may have just entered a spiral of low financing that reinforces itself, increasing with time until it becomes unsurmountable. Early targeted support can be an investment for the unit as a whole.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The IBDM is an attractive place for researchers because of the concentration of outstanding teams and support platforms that facilitate high-quality research in the fields of developmental biology and neurobiology. The Unit is located in a major city allowing opportunities for interaction with other research institutes. Besides, the city's location in the Mediterranean, well connected to Lyon and Paris and close to a main airport facilitates the organisation of international conferences that attract foreign researchers and increase its visibility.

1/ The unit has an attractive scientific reputation and contributes to the construction of the European research area.

Strengths and possibilities linked to the context

25% of the Unit's personnel are foreigners, 14% of which are of European origin, indicating its international reputation and contribution to European science. The attraction of foreign researchers and their daily life at the unit is facilitated by its bilingual English-French internal communication system. The unit is well funded by the European Union with a total of ten grants in the analysed period. The unit is proactive in hosting national and international meetings acting as a hub for research in the area of basic and applied aspects of neurobiology and developmental biology.

Weaknesses and risks linked to the context

The lack of new laboratory space to recruit new group leaders may delay the expansion and rejuvenation of the centre.

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

Strengths and possibilities linked to the context

In the last six years, the unit has recruited junior and senior researchers who successfully applied for European funding and rejuvenated the IBDM. This serves as a call for other young teams that may see the Unit as an attractive place to develop their research careers. The high quality of research performed by the team leaders and the outstanding record of publications is likely to attract national and international postdoctoral researchers to the IBDM. The recent refurbishment of the laboratory space may contribute to making the centre more attractive to potential group leaders.

Weaknesses and risks linked to the context

The refurbishment of the building and the Covid crises have temporarily stopped the recruitment process. The extreme success of the larger teams may be stifling the smaller ones and prevent further external team recruitment. It is unclear if the laboratory space refurbishment has created new opportunities for the recruitment process or if it will only benefit established existing groups.

The number of PhD students hosted by some teams is rather low, apparently due to difficulties in the recruitment of students interested in developmental biology.

3/ The unit is attractive because of the recognition gained through its success in competitive calls for projects.

Strengths and possibilities linked to the context

The Unit has obtained a large number of research funds from national and European institutions. Some of the members of the Unit have also been leaders of joint programs that include other institutions in the Marseilles Provence area. The interaction with other teams in the Marseilles area through Centuri has provided a large number of collaborative PhD studentships.

Weaknesses and risks linked to the context

Possible shifts in funding policies toward projects with applied outcomes may seriously affect the unit as it is dedicated to basic science.

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

Strengths and possibilities linked to the context

The unit's research has a high reliance on imaging. In this aspect the unit has outstanding microscopy services organised around an Optical imaging department and an Electron microscopy department supervised by Dr Lenne acting as Scientific manager. The Optical imaging section is led by C. Matthews as team leader and assisted by four team members. The Electron microscopy section is led by N. Brouilly (who appears in numerous publications) and is assisted by two team members. The microscopy departments are integrated through PICsL in the national France-Bioimaging national infrastructure.

The unit also has a very useful Software development section supervised by Dr Saurin and led by F. Daian assisted by one technical staff that help integrate computational approaches to the Unit's research.

Weaknesses and risks linked to the context

It is important to know if the funding for the microscopy departments through France-Bioimaging is going to be maintained, and consider how the PICsL platform would be financed in case this funding was discontinued. Access to single-cell genomics is not yet available on site, which may hinder the development of some projects.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

About 350 publications have been reported in the evaluated period. This accounts to two publications annually per team, which is an excellent output especially in view of the disruption caused by Covid and the buildings refurbishment works. These publications result from national and international collaborations in many of which the leadership rests on IBDM team members.

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

Strengths and possibilities linked to the context

The Unit's publications appear in most prestigious journals in the natural sciences as well as in highly respected specialised journals of their field. This is the result of the innovative approaches taken by the teams in their respective areas.

Weaknesses and risks linked to the context

There are no immediate risks. However, as most of the Unit's publications are on basic science, the current trend of funding mostly applied science may affect the productivity of teams focusing in non-vertebrate models.

2/ Scientific production is proportionate to the research potential of the unit and shared out between its personnel.

Strengths and possibilities linked to the context

Although there are clearly some groups that excel in their scientific production over others, all teams produce an excellent rate of publications in prestigious journals according to their financial capabilities, prioritising publication quality over quantity.

Weaknesses and risks linked to the context

There appears to be a two speed IBDM in terms of publication productivity. Some of the less productive teams may get their research funds cut down, entering in a descending spiral from which is difficult to recover.

3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science.

Strengths and possibilities linked to the context

There are no concerns on this aspect. Whenever there is no alternative approach to investigate on new biological knowledge in its domain, the unit relies on work performed on animal models used for scientific purposes. Does this apply, the unit complies strictly to international 3R guide lines for research in order to reduce this activity to the minimum needed and to promote and respect animal wellbeing [A French national reference Centre for 3R is available for advice, training and sharing practices]. However, the experts noticed that the unit remains discrete on this activity. It would be up to the unit to become more involved in advocating the fair and respectful public research conducted on animal models, in accordance to the openness recommended by European professional associations.

Weaknesses and risks linked to the context

In accordance with the policy of their employers, the teams could consider being involved in transmitting to the society the usefulness to work on animal models for scientific purposes and the implementation of measures to avoid animal suffering (all recommendations of the 3R international guidelines).

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The unit's basic research objectives complicate having an immediate impact on the socio-economic world. This results in a modest, although significant, contribution to the socio-economic environment. The unit can in contrast participate in the transference of knowledge to the society.

1/ The unit stands out by the quality of its non-academic interactions.

Strengths and possibilities linked to the context

Despite the unit's basic research objectives, some teams make a significant contribution to the socio-economic environment. Especially relevant are the creation of the start-up company Tafalgie Therapeutics (Moqrish Team), the generation of patents (Maina Team) and the licencing of antibodies (Le Bivic Team).

The unit participates in the transference of knowledge to society with several groups participating in school demonstrations and others imparting general talks, for example, one team member (T. Lecuit) has imparted a series of original lectures at the College de France, which are freely accessible in YouTube. On the other hand, one team (B. Prud'homme) has contributed regular columns in Le Monde presenting emerging research directions.

Weaknesses and risks linked to the context

The pressure exerted on all teams to publish excellent scientific work makes it difficult to employ additional time on science communication to the general public, an area where this unit could excel.

2/ The unit develops products for the socio-economic world.

Strengths and possibilities linked to the context

Working on various models (*C. elegans*, *Drosophila*, *Xenopus* and small mammals) allows the study of genes and cellular processes conserved in humans. This gives the unit the opportunity of testing treatments, or investigating the involvement of certain genes in human diseases. This has led to a very promising research in pain that has already resulted in the creation of a spin-off company. Other groups are finding relationships between autism and renal defects..

Weaknesses and risks linked to the context

The focus on basic research at the frontiers of biological knowledge of most teams hinders the development of economic valuable products.

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

Strengths and possibilities linked to the context

Due to their research in neurobiology and developmental biology which encompasses many different areas of biology, the unit is in a very strong position to educate society in many aspects of the biological sciences that are highly relevant for the day to day of the population. This can range from the use of transgenics in medicine and agriculture, the introduction of gene editing techniques, the evidence of biological evolution or the intricacies of having babies with genetic information from three different parents.

Weaknesses and risks linked to the context

The increased pressure on publication may detract the unit from their enormous capacity to interact with society.

C – RECOMMENDATIONS TO THE UNIT

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

- Aim at having single-cell technology in-house. Reinforce the biocomputational analyses required for multiomic studies and single cell technologies.
- Permanent staff in every team should feel there is recognition of their work and have guidance from the IBDM and their team leaders to understand how to progress in their careers. It should not be left to each team leader to decide how to promote their staff, but have a global Unit guidance.
- Facilitate access to all IBDM personnel (DR, CR etc.) that has applied and received a grant to administer their own resources online, do not make access to this information exclusively restricted to team leaders.
- The authorship/acknowledgement policy should be common for all teams and core facilities, so as to avoid disparities in the unit and maintain staff motivation.
- Aim at equilibrating the gender balance at the team leader level.

Recommendations regarding the Evaluation Area 2: Attractiveness

The Unit currently offers an attractive scientific environment. If anything, it should consider how it can interact with the University to improve support to its personnel with children (Campus nurseries, flexible working times etc.) that could make the Unit parent-friendly.

Recommendations regarding Evaluation Area 3: Scientific Production

The Unit's scientific production is outstanding. However, the teams should ponder if their effort to produce first-rate publications is delaying their students' publication record, affecting their CV negatively.

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

The Unit may consider having a dedicated person in charge of transferring its scientific knowledge to society, increasing the Unit's visibility and societal impact.

TEAM-BY-TEAM ASSESSMENT

Team 1: Polarization and binary cell fate decisions in the nervous system,
Name of the supervisor: Mr Vincent Bertrand

THEMES OF THE TEAM

The team uses *C. elegans* as a model organism to investigate how neurons are generated during nervous system development. They address this question with two main approaches: 1, the role of Wnt ligands in progenitor cell polarisation; 2, the role of gene expression noise. To address the latter, they have developed a novel methodology to visualise gene expression in vivo. As well as these strands, the team also investigate how three bHLH transcription factors function together to maintain stable neuronal fate and prevent cell death and they have a collaboration with the lab of Dr Cremer to investigate the role of Zic factors as repressors of dopaminergic neuron fate.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The 2018 report stated that this group had had very good productivity in its first 5 years since being established. Furthermore, they had invested effort in developing technologies that would pay off in future years. However, they raised some concerns over the publication record. The main weakness they identified then was that the two out of 3 main peer-reviewed publications still had the PI's former supervisor, as an author. The report made the recommendation that the PI should make an effort to make his research distinctive from that of his former supervisor. Since then, the PI has indeed published 4 research articles in *Biology Open*, *Nucleic Acids Research*, *J Neuroscience and Development*, none of which have former supervisor as a contributing author. In two of these articles, the PI is senior author and in a third one, he is co-senior author. He is also senior author in three reviews and book chapters during this period. For a four-year period, this is very good productivity.

The previous recommendation was for the PI to make an effort to increase his international profile. The PI has received 4 invitations to speak at seminars and at conferences since 2018. Considering there was a pandemic in between, this is very good.

The previous report raised as a weakness the reliance of the PI on collaborations. This has now been addressed as at least two of his recent publications originate from his lab.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	3
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	1
Post-docs	0
PhD Students	1
Subtotal non-permanent personnel	3
Total	6

EVALUATION

Overall assessment of the team

The team is formed of five people: two tenured CNRS researchers, one tenured CNRS engineer, one postdoc and one PhD student. In the assessment period, one other postdoc worked with the team, three PhD students completed their theses and one Master student was trained in the lab. Except for the most recent arrivals, all lab members are authors in publications. The team published one article in Development, one in Biology Open, one in Nucleic Acids Research, one in J. of Neuroscience, and three reviews. The PI has been involved in the organisation of one meeting, Chair at another conference and has been invited to speak at six conferences or seminars. The lab is well funded until 2025, accumulating a total of 1,915 k€ for 2018-2025.

Strengths and possibilities linked to the context

Strengths: The team combines a good expertise in development, genetics and imaging, and whilst they maintain collaborations, they have progressed away from their over-reliance on collaborations. The team had a very good publication output during the assessment period, most particularly considering that there was a global pandemic. Funding has been excellent in the assessed period.

Weaknesses and risks linked to the context

The team is relatively small, currently with only one PhD student and one postdoc, on top of the permanent staff. Considering this team belongs to a research institute with no significant teaching duties (i.e. contrary to universities), the team should make an effort to attract more PhD students and postdocs. The PI could raise his profile by organising more conferences or having other initiatives (e.g. summer programmes for undergraduate students). The advert in The Node is a good start. The lab does not have a distinctive, dedicated website and this could also help.

Although the publication output is good, aiming for higher-profile journals would be good. This would help raise further the profile of the team, facilitating future recruitment and funding. The PI hasn't published any more with his past supervisor, which is good, as this helps make his line of research distinctive. However, during the assessment period the team published 4 research articles and only in two of them the PI was primary senior author (in the two other articles the PI was respectively co-senior author and co-corresponding author). Being primary senior author in more publications per cycle would be an improvement.

Funding for the period 2022-2025 is not very high and the PI will have to find complementary sources of funding.

RECOMMENDATIONS TO THE TEAM

Overall, this team is doing very well, with excellent publication outputs and funding. The PI has done well at establishing their independent line of research, reducing the reliance on collaborations. The PI has now published as senior author in multiple articles, including some high profile and has secured a very good level of funding.

The recommendation is to take care to maintain this momentum and sustain a high international profile to secure future funding and attracting postdocs and PhD applicants to the team. The PI should be aiming to increase his leadership initiatives. Some examples include: aiming for high-profile publications, organising international conferences, creating a lab-dedicated website and being active in social media platforms (e.g. LinkedIn, Twitter), and leading in funding applications when collaborative.

Team 2: Molecular control of Neurogenesis
Name of the supervisor: Mr Harold Cremer

THEMES OF THE TEAM

The team has three main lines of research: 1, Neural stem cell determination. This project focuses on post-natal neurogenesis. They showed that postnatally generated neurons maintain lineage-specific gene expression, but also express *Zic1* and *Zic2*, which repress dopaminergic cell fate and promote GABAergic fate. Furthermore, the transcription factor *Vax1* regulates *mir7* expression, which inhibits *Pax6* expression, resulting in the inhibition of dopaminergic neuron cell fate. Interestingly, different neuronal types have different susceptibilities to neuronal stimulation. 2, Non-coding RNAs in the control of neurogenesis. They identified the involvement of *mir200* family in neuronal differentiation. They found that long-non-coding RNAs and microRNAs are co-expressed in post-natal neural stem cells and are required for progenitor cell proliferation. To investigate this, the team developed a tool - Argonaute binding peptide - that allows the isolation of microRNA actively involved in inhibition. 3, Neuronal integration in the olfactory bulb. This involved imaging analysis to test whether newly generated neurons normally replaced dying cells, and they found they do not. Instead, the brain continues to expand and grow over time. The PI gave an excellent presentation on the team's cutting-edge research.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report overall praised the good publication record and the excellent funding of the team. The weaknesses raised included the observation that although the group had published five articles in the last evaluation period, with ten members of staff, this group should be publishing more. A concern was raised about the fact that funding seemed to be going less well and lab size had to be reduced. The PI was urged to find new funding and expand the range of his presentations and conferences and seminars to include Asia and America, to raise his international profile. The panel observed that whereas the industry collaboration with Mylteny Biotech is a good asset, they did not seem to be looking after this relationship with sufficient care. Since 2018, the team has published ten research articles as main PI, including two articles in *eLife*, and others in *J Neuroscience* and *Stem Cell Reports*. These are excellent journals, and this productivity is excellent to outstanding. The team is or has been formed of four permanent members of staff, which also contribute to teaching, two postdocs, six PhD students (some of the PhD students and postdocs have now left the lab). Thus, in response to the previous report, this team has learnt how to increase their attractiveness and attract more students.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	4
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	3
Post-docs	0
PhD Students	2
Subtotal non-permanent personnel	5
Total	9

EVALUATION

Overall assessment of the team

Overall, this is a large team that has published very well during the evaluation period and has secured good funding. The team includes four permanent staff. They carry out teaching and some outreach. The team has a long-standing collaboration with Miltenyi Biotec. The PI has sustained a high profile, by participating in scientific evaluations in multiple countries. He has also been invited to give research seminars or to speak at conferences. Visibility is excellent and attractively is excellent to outstanding.

Strengths and possibilities linked to the context

Strengths: The research topics are all interesting, cutting-edge and within high-profile scientific areas. The team was very well funded in the last assessment period. Productivity is excellent to outstanding, visibility is excellent and attractively excellent to outstanding.

Weaknesses and risks linked to the context

If the collaboration with Miltenyi B is as valued as it seems, the PI should include the participation of Miltenyi to the research environment. The team has very limited participation in outreach activities that can benefit society, and they should consider activities they could embrace (e.g. organising events for the public, etc.). Society participation is good to very good.

RECOMMENDATIONS TO THE TEAM

The team should make an effort to attract and recruit a bioinformatician. The team should sustain the momentum of doing the excellent science they do, and maintain or enhance their current excellent to outstanding productivity, excellent visibility and excellent to outstanding attractively. They must put more effort into how they give back to society, as on this their involvement was very limited, to only good to very good.

Team 3: Stem Cells and Brain repair

Name of the supervisor: Ms Pascale Durbec

THEMES OF THE TEAM

This team investigates neural stem cells and brain repair, focusing on myelin regeneration. They have demonstrated that in demyelinating lesion models, repair can be increased by manipulating endogenous progenitor cells, by stimulating their proliferation, migration and differentiation. They have discovered: 1, the function of *Ndst1* involved in heparin sulphate synthesis, showing that it is expressed in oligodendrocytes to create a belt around lesion that concentrates Shh, which promotes regeneration. This is a very interesting finding, providing a novel perspective in CNS injury repair and regeneration. 2, The contribution of neural progenitor cells and oligodendrocytes to remyelination. This was done using lineage tracing methods after demyelinating lesions. They showed that neural stem cells secrete MGFE8, a ligand of integrin $\beta 3$ expressed by microglia, and together they phagocytose myelin debris enabling repairs. They also demonstrated that neural stem cells can directly convert to oligodendrocytes, through cell state transitions driven by two factors *Olig2* and *Sox10*. 3, They developed a novel method to measure myelin content. The PI gave an excellent, interesting, cutting edge presentation on remyelination.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report said that the team had done very good, relevant research into neural stem cells and myelin repair, that had resulted in very good publications. Further strengths included the expertise of the PI and the very good funding during the assessment period. Some weaknesses were raised, which included: 1, postdoc and PhD students tended not to have 1st author publications, but rather be middle co-authors. 2, The PI had not been invited to give talks in the assessed period; 3, The team had very few PhD students, considering that it had three permanent scientists and one postdoc. The recommendations were for the PI to engage further with the scientific community to raise their profile and to establish a relationship with the pharmaceutical industry - with particular reference to a therapeutic drug that they tested for their impact treating multiple sclerosis. There was also a recommendation to keep the proposal within focus and minimise the risk of high-throughput transcriptomic analyses.

In the current assessment period under evaluation, the team has supervised two PhD students, one postdoc and two permanent scientists. All of them have published.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	2
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	3
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	2
Post-docs	0
PhD Students	2
Subtotal non-permanent personnel	4
Total	7

EVALUATION

Overall assessment of the team

Overall, this is an excellent team that has continued to carry out excellent work, addressing fundamental questions with a potential impact for understanding how to promote CNS regeneration and repair. Productivity and publication record are excellent: the team published eight articles and three book chapters, in high-profile journals such as eLife and Stem Cell Reports, from this period, with four team papers (eLife, 2x Stem Cell Rep, Neuropharmacology). They also engaged in collaborations, from which they also published. The team visibility is excellent, as the PI has been involved in the organisation of conferences, including rather large ones, and they are Deputy-Director of the IBDM. Team attractiveness is excellent, with 3 PhD students and one postdoc, though recruitment decreased after 2018. Team reputation is excellent, with robust funding during this period, bringing in about 800K euros. The team interaction with society is outstanding, given the multiple activities that the PI and some team staff participate in (e.g. committees, organisation of conferences, outreach, deputy director of IBDM).

Strengths and possibilities linked to the context

The group addresses important, excellent scientific questions and their research has resulted in very good funding and a very good publication record. The productivity of the team, visibility and attractiveness are all excellent. Interactions with society are outstanding.

Weaknesses and risks linked to the context

The group is rather small and the PI should make an effort to try to attract and recruit more PhD students and postdocs. This is important because the other permanent researcher in the team left at the end of 2021. Giving international seminars, writing reviews and increasing public engagement would help. The PI ought to secure further funding for the next period, and try to get involved in international consortia.

RECOMMENDATIONS TO THE TEAM

The PI should make an effort to increase their international profile, e.g. by giving seminars in other institutions, participate more pro-actively in public engagement activities, and others, that could increase their visibility to attract more PhD students and postdocs. It will be important to secure further funding for the next period.

Team 4: Transcriptional regulatory networks in development and diseases
 Name of the supervisor: Mr Laurent Fasano

THEMES OF THE TEAM

Team 4 is interested in understanding the transcriptional regulatory networks underlying normal and pathological development. It focuses its research on the Teashirt transcription factor family using a small mammal as a model organism, where it studies the role of Tshz3 in the physio-pathological development of the renal tract and the brain. It aims to establish a link between basic research and clinic for the understanding and treatment of autistic syndrome disorders.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report made 4 main recommendations: (1) focus its research on in renal/smooth muscle development beyond TSHZ3, (2) seek closer collaborations with neuroscience groups and gather more manpower if they wish to continue to work on nervous system development, (3) attract more PhD (as well as post-docs), (4) develop its communication/outreach activities. Team 4 has benefited from a very good internal collaboration to work on brain development and function, a line of research that was productive during this period. The team still remains very much focused on Tshz3 and has not attracted many PhD (2), postdoc (1) nor any additional manpower, which may restrain its ambitions. The communication and outreach activities of the team during this period were strongly improved.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	2
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	4
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	1
PhD Students	0
Subtotal non-permanent personnel	2
Total	6

EVALUATION

Overall assessment of the team

Team 4 has developed a sound project exploring the function of *Tshz3* in brain and renal development/function to unravel the basis of a rare autistic spectrum disorder in humans. Together with a milestone publication (Nat Genet) at the beginning of the contract, the production of the team has been very good to excellent (Biol Psychiatry, Front Genet, Hum Mol Genet). The international reputation of the team is well established. It obtained an excellent level of funding from European and national grants, but has had difficulty in recruiting PhD students and postdocs. Its involvement in training through research and its interaction with the non-academic world are excellent, with a notable emphasis on public outreach activities.

Strengths and possibilities linked to the context

Based on their previous cornerstone finding that *Tshz3* heterozygous deletion is involved in autism spectrum disorders (ASD) and renal tract abnormalities in human (Caubit et al., Nat Genet 2016), the team has developed a sound, well-integrated and multi-scale research program aimed at deciphering 'where, when and how' *Tshz3* controls the proper development of the brain and the renal tract. Thereby, Team 4 contributed to some valuable findings concerning neuronal and renal development that are relevant to ASD. In particular, as part of ANR-funded collaborative project with teams 6 & 9, and using a combination of developmental, transcriptomics, neurophysiological and behavioral approaches, they showed that *Tshz3* is critically required during post-natal life both for the development and function of both cortical projection neuron and striatal cholinergic interneuron. Importantly, their results indicate that these two populations of neurons contribute to distinct ASD-associated behavioral traits. These findings raise interesting prospects concerning ASD aetiology and treatment. In parallel, Team 4 also further explored the impact of *Tshz3* heterozygosity on behaviour and brain ultrastructural organisation as well as on kidney development, obtaining some promising results on both lines of research. Some of these findings were published by team 4 members as main authors in well-established journals (Biol. Psychiatry 2019, Frontiers Genetics 2021, Human Mol Genetics 2021) and in a method paper (Methods Mol. Biol. 2019). In addition, the team is associated with one publication in Behav. Genetics (2021) and one published conference abstract (Magn Reson Mater Phy, 2021).

The team funding is strong: the team coordinated one European grant (H2020 ITN 2015-2019) as well as one ANR (2018-2022). It also benefited from support from the AFM (2013-2017) as well as Marseille University (2 contracts: 2019-2020; 2021).

The members of the team are very well integrated in the local environment and actively take part in different committees as well as in teaching at the university. Notably, the team leader participates in the scientific board of 2 AMU 's institutes (Marmara & NeuroMarseille) and contributed to the organisation of two meetings of the SBCF in Marseille. One of the MdC is member of the CNU. The international visibility of the group leader is attested by its leading role in the H2020 ITN 'Renaltract' (2015-2019) and a good number of invitations to conferences and congresses as well as PhD examinations abroad. Both the PhD and the postdoc hosted in the team obtained respectively two and one first author publication.

Although not yet clearly transferred to the bedside, the clinical and societal potential of the research is very good, with an excellent participation in outreach activities.

Weaknesses and risks linked to the context

While the team hosted a number of undergraduate students, the team only attracted two PhD students and one postdoc for a supervising potential of three HDR. Working on a single gene involved in a rare disease may also limit the clinical translation of the findings of the team. The combination of these factors may hamper the overall ambition of the team.

The team has strong and productive collaborations in Marseille, but its network of international collaboration seems more limited. It is not clear that the team took full advantage of the Renaltract ITN program to extend its international visibility and network.

The neurodevelopmental axis of the research program is in part dependent on collaborations.

RECOMMENDATIONS TO THE TEAM

The team should develop a strategy to attract more PhD students and post-doc. Its current size and manpower may not be sufficient to obtain breakthrough results both in the fields of brain and kidney development.

Two of the team members are strongly involved in teaching. At least one of them could seek a delegation from the CNRS/AMU to be able to devote more time to research.

The team should take further advantage of its expertise in developmental genetic and of its participation in ITN program to increase its network of international collaborations.

The team could strengthen its links with the clinic if it does not overstretch its manpower.

Team 5: Mechanisms of Gene Regulation by Transcription Factors

Name of the supervisor: Yacine Graba and Andrew Saurin

THEMES OF THE TEAM

The team studies how Hox proteins control gene regulation during development applying genetic and transcriptomic approaches in *Drosophila* and in chick.

The team studied the interaction of Ubx, Abd-A and Abd-B with their cofactor PBX finding novel domains of interaction providing paralog specificity. They also found the interaction with AbdB is in some cases is antagonistic and in other synergistic.

Using S2 cells, the team found Hox bound to promoters interact with M1BP releasing RNAPol 2 from transcription pausing and PcG binding to promoter. The group also analyses how Hox specific and common functions are controlled. The chick model has allowed them to explore how Hox proteins suppress the formation of tumors. Their research is original, offering a new perspective to the field.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In the previous report, it was suggested that it was needed a clear subdivision of responsibilities between the members of the team, especially between the team leaders. This seems to have been achieved satisfactorily. The direction of the genomics projects in this period has relied mostly on the skills of Dr. Saurin while those on the chick model have been directed by Dr. Delfini. Although Dr Graba has had an important intellectual contribution to these projects, in some of which he appears as corresponding author, he has focused on projects relating to autophagy and in the molecular strategies shared by the Hox Ubx and AbdA proteins which are still to be published. Dr Graba has also been involved in the writing of various interesting Hox reviews of impact in the field.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	4
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	2
Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	5
Total	9

EVALUATION

Overall assessment of the team

The team produces excellent research on the field of Hox genes. They are opening new original areas of Hox research combining several approaches and models: These include powerful Drosophila genetics, biochemical 'omic' approaches in S2 cells and, more recently, research in chick. This is a modern approach to Hox research. Their capacity to work with a vertebrate model will reinforce their position. The group is highly regarded in the field with international collaborations.

Strengths and possibilities linked to the context

The team has a well-established position in the field of Hox regulation. The group has been reinforced by the establishment of Dr Saurin as co-head as he has been able to push forward the '-omics' technologies. The group has now the capacity to work with vertebrate models through the introduction of chick as a research model in the lab.

Weaknesses and risks linked to the context

Funding for the period was adequate, but it was finalising at the end of the evaluated period. It seems that the levels of funding may have been decreasing in recent years. This may eventually pose a problem if the funding bodies favour more applied research. In addition, the departure in 2021 of the researcher directing the chick-related projects is a big loss for the team.

RECOMMENDATIONS TO THE TEAM

We recommend considering reducing the excessive number of scientific administrative responsibilities carried out by Dr Graba, as these may be affecting the team's output.

Team 6: Team Computational Biology
 Name of the supervisor: Ms Bianca Habermann

THEMES OF THE TEAM

Team six has a long-standing interest in computational biology in general, in genome organisation and in evolution in particular. Projects include genome sequencing, annotation and analyses, tools development for omics data integration and short protein motifs.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team started in 2016. The previous HCÉRES committee recommended that the team makes clear the distinction between research, collaboration and services. Although the team produced several publications as lead authors, most of its production and grants are collaborative ones.

Since the previous evaluation, seven PhD students, as well as four postdocs have been trained by the lab, and one permanent researcher was recruited. So, the team was successful, however, considerable time is spent in teaching (just short of 700 hours).

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	0
Subtotal permanent personnel in active employment	2
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	5
Post-docs	0
PhD Students	4
Subtotal non-permanent personnel	10
Total	12

EVALUATION

Overall assessment of the team

Team Computational Biology has developed interesting computational tools that they have then applied in various analysis. Its scientific production is of excellent level. It has been successful in securing financial support from the main national funding agencies. It attracted several PhD students and its involvement in training through research is excellent. Its reputation is very good, but could be increased at the international level.

Strengths and possibilities linked to the context

Strengths and possibilities linked to the context

This team has interest in computational biology, in particular mitochondria related and evolutionary computational biology, with a strong focus on data integration. They have made contributions to various subfields.

Their contributions include the mitoXplorer pipeline, a user-friendly mining platform for mitochondria gene expression, currently available for four organisms. They successfully kept developing MitoXplorer and are developing ataxiaXplorer for cerebellar Ataxias data. Again in the same line, they have developed a tool for integration of -omics data. They also contributed to the usage of networks for data integration. Eventually, they also contributed to genome sequencing and annotation, as well as to short linear motifs analyses, related to the function of the proteins.

All these projects resulted in many publications, including 12 as lead authors and books, and most were developed with local or national collaborations.

The team was successful in its funding strategy, obtaining major national grants; three ANR (one as coordinator) and one FRM.

The team is also extremely attractive to PhD students with three defended and four ongoing, and it hired four postdoctoral fellows, notably through support from the Centuri program. It recruited one 'maitre de conference' and is actively involved in teaching in bioinformatics at the master level.

Weaknesses and risks linked to the context

Weaknesses and risks linked to the context

Despite good publication record, the majority of the publications are in collaboration with team members in the middle of the authorship, and all but one grant is participated, with only one coordinated.

The team should develop its own independent research program. This will be reflected both in primary publications and in grants coordinated.

In these lines, the team should define more clearly, and may be restrict, its research lines. As it stands, the interests of the team appear as a meltingpot of many unrelated bioinformatics themes. They are interested in mitochondria expression data, integration of -omics data, epigenetics and DNA occupancy, SLIMs, network, genome assembly and annotation... All very interesting but somehow weakly related.

Although the team leader is a member of the editorial board for Gene, its national and international recognition could be improved. The PI is a member of various committees and invited to a few (<1/year) international talks. The other members of the team have similar or lower recognition.

The implication of the team in outreach activities and/or interaction with the socio-economic world is limited.

RECOMMENDATIONS TO THE TEAM

The team can be commended for developing platform and software for general usage and analysis. However, it should try to increase its own research as well as its international exposure by participating to more meetings. Also, it should seek to attract some senior scientist either as a postdoc or permanent staff to uphold its ambition and to better define its specific focus.

Team 7: Development and pathologies of neuromuscular circuits
 Name of the supervisor: Ms Françoise Helmbacher

THEMES OF THE TEAM

The team investigates the development and homeostasis of neuromuscular circuits, focusing on motor circuit assembly, dysfunction in disease and injury, and interactions between motoneurons, muscle and connective tissue. Using cell-type specific conditional knock-out, the principal investigator (PI) discovered that the function of the Fat1 cadherin is required in muscle, motoneuron, connective tissues and neural crest cells for muscle and motoneuron differentiation, and motoneuron axon guidance. In essence, Fat1 is required in all of these interacting cell types to establish and coordinate the morphogenesis and innervation of the neuromuscular circuitry. This was published as a single author article in PLoS Biology in 2018, which is outstanding, and she was invited by The Node to write a blog about it, highlighting the novelty of her findings. It would be interesting to know what is the contribution of glial cells in this context. The PI then investigated a potential involvement of Fat1 in muscle repair. After injury, muscles are regenerated and this process involves non-myogenic cells, including fibro-adipogenic progenitors (FAPs), that derive from connective tissue and express Fat1. Conditional Fat1 knockout in these cells showed no effect in muscle repair, but revealed an excessive differentiation of FAPs leading to fibrosis and excessive adipose tissue. This demonstrated that here Fat1 maintains homeostasis and prevents differentiation. This work is currently being written up for publication, an article with two authors and where the PI is second author. She also discovered a role for Fat1 in planar cell polarity and migration of astrocytes, which they published in Development this year, 2022. This is really excellent, as Development is a journal with a very good and solid reputation.

The PI is and has also been involved in various very productive collaborations over the assessment period: 1, She is currently engaged in a collaboration with Stricker (Berlin) and Schnorrer (IBDM) to investigate the function of a transcription factor called Osr1 in connective tissue interacting with muscle. They have written a review together in 2020 (which is excellent, as this was a pandemic year), where the PI is first author, and they have applied for a joint research project. 2, With Blanpain (Belgium), they investigated the involvement of Fat1 in epithelial-mesenchymal transitions, metastasis and cancer, and this was published in a very impactful article in Nature in 2021. 3, Collaborating with Lallemand (Sweden), the PI characterised the functions of transcription factors identified through single cell RNAseq in the specification of retinal neuron cell fate. This was published in Nature Communications in 2018. 3, With Belluschi (Germany) they investigated these same genes in the context of the lung and published their findings in Frontiers in Genetics in 2019. 4, With Andoniacoudu (UK), the PI investigated the function of Fat2 and Dchs2 in a murin model of PSIS, a pituitary developmental malformation, and this was published in JCI Insight in 2020.

To conclude, during the assessment period the PI has carried out interesting research that has been published in excellent or outstanding journals, some work has been published as single author, some as co-author of two, and some as a member of a collaborating team. This is an excellent output.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In the report from 2018, it was reported that the PI had supervised one PhD student and two postdoctoral researchers in the previous period (2011-16) and had one permanent researcher in the period to 2018. The 2018 report observed was that her group was too small, the PI had not supervised any PhD students in the previous five years and this was limiting research output and international visibility. The recommendation was for them to increase the size of her group, to attract and supervise Master and PhD students and to engage in external and internal collaborations. The funding situation was worrying then, and the PI was recommended to put effort into securing funding, and was advised to engage in collaborations as an additional means to achieve this. Another recommendation was for the PI to associate more closely with the group of N. Levy, of the Institute of Rare Diseases in Marseille.

The PI has addressed some of these recommendations. For example, by establishing various collaborations, both international with Belgium, Germany, Sweden and UK, and internal with Schnorrer team. These collaborations have already been very productive, resulting in high-profile publications in excellent and outstanding journals. This is really excellent. However, the PI has still not increased her group size. In the assessment period she did not have a permanent HDR team member, and the PI did not supervise any PhD students. The PI did host various M1 and M2 students. Regarding the recommendation to put effort into obtaining funding, the PI has indeed put a considerable amount of effort. They applied for a grant in 2018 for renewal to 2020 and a collaborative grant with the US from 2015-2017, and they have submitted two applications, the outcomes of which are still pending, one in which is single PI for 116k euro and one collaboration with Schnorrer and Stricker, from which they would obtain 296 k euro. This is all very good and hopefully they will obtain funding from at least one of these sources. During the interview they declared to have received a small grant. However, in total the PI applied for eighteen

grants during this assessment period, most of which have been rejected. The common argument for rejection is that the team is too small and the size of the team does not guarantee feasibility. There has been no progress or change in this regard since the previous report.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	2
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	0
Subtotal non-permanent personnel	0
Total	2

EVALUATION

Overall assessment of the team

The research team is currently formed of only the principal investigator and one technician. In the assessment period, the team has not supervised any PhD students nor postdocs and does not comprise a permanent researcher either, putting the group in a very difficult situation. The research quality, publication outputs and productivity are excellent (7 papers, several in very high impact journals) and the principal investigator is recognised nationally and internationally as proven by her collaborations and grant application with collaborators. Sadly the lack of attraction of human resources and of substantial funding is hampering the development of the laboratory as such. Also the laboratory visibility is good, but has been affected. The attractiveness of the group is fair to good. The interactions with society are good, although the PI has not been involved in any activities in particular.

Strengths and possibilities linked to the context

Despite the small size of the group, the principal investigator has delivered research outputs of excellent quality, both as a single author or in collaboration with international teams, and published in high-profile, reputable journals. This demonstrates her ability, talent and commitment to scientific research. The principal investigator has established international and internal collaborations, which have resulted in high-profile outputs and new grant proposals. Overall, productivity is excellent.

Weaknesses and risks linked to the context

The team currently has no funding, risking a research stall. In the assessment period, the group leader has applied for multiple grants that have been rejected, and the common argument has been the small size of the team. The fact that the PI works alone is preventing them from acquiring funding, as the lack of a team is seen as lack of guarantees for the feasibility of the project. Consequently, visibility and interactivity are good, and attractively is fair to good.

RECOMMENDATIONS TO THE TEAM

There is no doubt that the principal investigator (PI) has the talent and ability to develop and deliver high profile, international research with impact. However, the fact that she works alone, without a team, is preventing her for developing her research further and even putting this research at risk, if she will to remain unable to guarantee sustained funding. Times have been very tough for the PI in the assessment period, due to the combination of the Covid pandemic and personal issues.

Thus the managers could consider providing a special support to team 7. Among the measures that could be considered are: direct financial support, merging with another research group, advice and support on grant writing. This should be helpful to continue to carry out experiments.

The principal investigator argues that a recurrent reason for having grants rejected is that the lab is too small, this reduces feasibility as seen by funders, and the argument is that she is not able to host PhD students because of her lack of an HDR. The PI says she does not have an HDR because she has been too busy writing papers and grants. Thus, a recommendation ought to be to prioritise obtaining the HDR so that she can supervise PhD students. Overall, given its situation, the group did very well and productivity was excellent.

Team 8: Genetic Control of Heart Development

Name of the supervisor: Mr Robert Kelly

THEMES OF THE TEAM

The Kelly lab studies mammalian heart development to identify biological mechanisms underlying organogenesis, regeneration and congenital disease.

These studies are being conducted in the appropriate in vivo models and are focused on two main areas: 1) the growth of the embryonic heart by progressive addition of myocardium from progenitor cells known as the second heart field (SHF). SHF derived parts of the heart are hotspots for common congenital heart defects. 2) the development of the cardiac conduction system that forms the electrical wiring of the heart and coordinates the heartbeat. The conduction system is derived from common progenitor cells with contractile cardiomyocytes of the heart and studies are focused on the cellular and genetic mechanisms required for the establishment of these specialised myocytes during normal development and under pathological conditions.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

All the recommendations made in the previous evaluation were addressed adequately.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	4
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	6
Post-docs	0
PhD Students	5
Subtotal non-permanent personnel	11
Total	15

EVALUATION

Overall assessment of the team

The Kelly lab has achieved clear international recognition from its many scientific contributions in the field as well as the participation and leadership positions in scientific conferences.

The PI is also well known for his very supportive mentoring style which has facilitated the development of several members of his lab, most prominently L. Miquerol to become an independent scientist within the group.

Strengths and possibilities linked to the context

The strengths of the team include an excellent to outstanding scientific productivity, with 9 papers published in high-ranking journals as main author during the period of evaluation, some of them of broad impact (e.g. Circ Research 2022, Development 2020, Nat Comm 2017 & 2020). In addition, the team has established many outstanding and productive collaborations with a number of teams in France as well as abroad, and many of these collaborations have also led to highly visible publications (e.g. Cell 2017, Cell Stem Cell 2020, Dev Cell 2020, eLife 2018 & 2019, Nature 2018, NCB 2019, Nat Comm 2021...).

The PI himself has very high national and international visibility, as attested by many invitations to give conferences and write reviews/text books, or participations in six editorial boards. He very recently received the Lamonica Grand Prize for Cardiology - Fondation pour la Recherche Biomédicale PCL 2022 from the French Academy of Sciences. This prize acknowledges Kelly's work on heart morphogenesis, in particular the discovery of the second heart field (SHF) of cardiac progenitor cells (published in 2001).

The lab has also been very successful in raising funds including from the ANR on Purkinje system remodeling in Life-threatening ventricular arrhythmias, and on the Mechanisms of boundary formation and septal morphogenesis at the interface between heart fields. The team also obtained grants from the FRM, AFM and other charities as coordinator and was partner on a major international grant from Leducq Foundation.

The team was very attractive for PhD students (6 + 4 ongoing) and postdocs (3). Three of these trainees obtained best presentation awards in international conferences and all the PhD pursued a career in research.

Weaknesses and risks linked to the context

No major weaknesses were identified.

RECOMMENDATIONS TO THE TEAM

The Kelly lab is an international leader in heart development and needs to be supported adequately by the institute (eg, by increasing the number of cages available to the lab).

Team 9: Cellular Interactions, Neurodegeneration and Neuroplasticity
Name of the supervisor: Ms Lydia Kerkerian

THEMES OF THE TEAM

This team research focused on: 1, the portico-basal ganglia circuitry, its function and pathology, with particular attention to dopaminergic neurons and Parkinson's Disease (PD) and Autism Spectrum Disorders (ASD). In the former, they investigated the relationship of dopaminergic and cholinergic neurons, and how inhibition can improve PD symptoms; for the latter, they focused on the function of the transcription factor TSHZ3, which revealed a synaptic basis for ASD. 2, They investigated the function of TP53INP1 and its Drosophila homologue Dor, a positive regulator of autophagy and mitophagy under stress and protective for dopaminergic neurons. This was a novel finding in the molecular contributors to PD. 3, They also provided new perspectives on the involvement of astrocytes on Glu toxicity. 4, And they showed that there are adaptive mechanisms in place between contralateral brain sides, that should be taken into account for therapeutic approaches tot PD. 5, In collaboration with other teams, they investigated the regulation of neural stem cells to produce dopaminergic neurons and the consequences of deep brain stimulation in distinct parts of the dopaminergic circuit (eg. induction of unwanted apathy). Altogether, during the assessment period the team has continued to contribute with their expertise in dopaminergic circuitry and the understanding of PD and ASD, with the aim of helping find or improve therapeutic solutions to these conditions.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report had praised that this is a well-established, large team that carries out international level research and whose high profile gets regularly recognised through the request for reviews, invitations to give talks and award of prizes. The weaknesses included the observation that although productivity is high with a good number of publications, they tended to be incremental rather than transformational or innovative contributions; that funding was modest given the size of the team; and that the impact from the understanding of diseases to the clinic was not materialising at the level it could. The recommendation was that the team ought to focus their research projects in order to produce at a more impactful level, that they should recruit postdocs/staff with a higher diversity of skills and that they should collaborate with industry to bring their findings closer to the clinic. It does not appear that these criticisms have been addressed. However, the lab is closing soon because the PI is retiring and the researchers in permanent positions are moving to other teams.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	3
Senior scientist (Directeur de recherche, DR) and associate	3
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	8
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	3
Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	7
Total	15

EVALUATION

Overall assessment of the team

This is a large team with the PI plus five permanent researchers, one Professor emeritus, one Ai, one EI and seven PhD students. The PI is retiring and closing the lab soon, two of the PhD students are still in progress, and the others have completed their PhDs, and the permanent researchers have already or will soon find other labs to join.

Strengths and possibilities linked to the context

The strength is that this is a well-established lab with a solid reputation in the area of dopaminergic circuits, understanding of the biology of Parkinson's disease and ASD; they publish well and regularly; and their expertise is recognised internationally through the requests for evaluating research outputs, involvement in committees, and prize awards among other forms of recognition.

Weaknesses and risks linked to the context

The main weakness is that a considerable number of their research publications are as not-leading collaborators, rather than being the drivers of the research. Given that this is a very competitive field and that the team is large, they could be producing more innovative research and setting the agenda. A weakness was identified in the lack of recruitment of scientists with diverse skills, which could enhance such innovation. Another weakness was the modest funding of the group given its size, expertise and international recognition. Engagement with external and international collaboration could have helped here. The team did not appear to establish collaborations with industry that could bring their findings to the clinic for the improvement of therapeutic approaches to PD or ASD.

RECOMMENDATIONS TO THE TEAM

The PI is retiring in 2023 and closing down her lab, thus no recommendation has been requested and the case was not discussed at interviews.

There was a discussion with permanent research staff on the opportunities offered to them to either join other groups or to establish their own, independent lines of research.

Team 10: Biology of Ciliated Epithelia
 Name of the supervisor: Mr Laurent Kodjabachian

THEMES OF THE TEAM

The team aims at understanding the molecular and physical mechanisms underlying assembly and function of ciliated epithelia in the embryonic epidermis of *Xenopus laevis*, *Xenopus* multiciliated cell lines and the ependymal walls of the brain. In particular, the team studies the synthesis of centrioles and cilia and their spatial organisation and polarity in cells. They also address tissue-level questions such as the mechanisms of ciliated cell distribution and polarity. Finally, the team also investigate the mechanisms by which cilia generate fluid flows.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous evaluation report in 2018 considered that the excess of collaborative projects in the team's scientific output was a weakness. The present report clearly shows that the team has published major works from its own projects in excellent journals.

It was also not clear whether other team members besides the PI contributed to funding, scientific communication or other synergistic activities. During this evaluation period, at least two staff scientists obtained grants from Canceropole PACA (2), CNRS MITI and Amidex and one of them was invited to give talks at two conferences. Although the team is still dependent on the group leader for funding and communication, the involvement of other team members now seems obvious.

The fact that the team had trained only one PhD student in the previous evaluation was considered insufficient. The training activity has clearly progressed since the team reports 3 PhD thesis defended during this period.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	3
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	3
Post-docs	0
PhD Students	1
Subtotal non-permanent personnel	4
Total	7

EVALUATION

Overall assessment of the team

The team is overall excellent. The team's output is excellent with papers in eLife 2017, Nat. comm. 2018, Development 2018, Dev Cell 2021. The national visibility of the PI is excellent to outstanding since he is the director of a leading institute in France and was the president of the CNRS section 22 (Cell Biology, Development, Evolution).

Strengths and possibilities linked to the context

The team's output is excellent with eleven research papers and three journals/chapters, including papers with lead author(s) from the team in eLife 2017, Nat Ecol Evol 2017, Nat. comm. 2018, Development 2018 and Dev Cell 2021. Important discoveries by the team include the mechanisms by which disordered MCCs adopt a regular distribution prior to their intercalation into the epithelium (Dev Cell 2021) and the mechanisms by which the deuterosome produces centrioles in multiciliated cells (Nat. Comm 2018).

The level of funding of the team is excellent with grants from multiple sources: ANR (4), FRM (2), ARC (2), Cancéropole PACA (2), among others.

The training activity is very good with three PhD theses defended during the period.

The visibility of the PI is excellent to outstanding since he is the director of IBDM and has been the president of section 22 of CNRS until 2021. The team members have been invited to give seven talks in national or international conferences.

Weaknesses and risks linked to the context

The involvement of the PI in the direction of the unit and in section 22 are not weaknesses, on the contrary, but this may have created difficulties for the development and maintenance of the team's excellence. It is regrettable that the team has little or no outreach activity.

RECOMMENDATIONS TO THE TEAM

This team must continue its excellent work and maintain its visibility by ensuring that the PI, who is not very available because of his management activity at IBDM, maintains effective relays in his team, by recruiting more staff scientists and experienced postdocs.

Team 11: Cell polarity and morphogenesis of epithelia

Name of the supervisor: Mr André Le Bivic

THEMES OF THE TEAM

The team aims at deciphering the mechanisms underlying epithelial polarity. It has a long-lasting experience on the role of polarity proteins, especially Crumbs, in epithelial cells. Several studies performed in the team during the reporting period have led to the identification of new roles for Crumbs, in epithelial or migrating cells, both in drosophila and cultured cells. Other ongoing projects aim at deciphering the link between extracellular forces and polarity in 3D culture systems.

More recently, the team has also become interested in using new evo-devo models to understand how epithelial organisation emerged during evolution and how polarity proteins and adhesion complexes control epithelial plasticity.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Considering the heavy administrative duties of the team leader, the previous report recommended that senior scientists in the team share the responsibility of leading projects and supervising research. This recommendation was clearly taken into account. Indeed, a new CR, who is in charge of the project on extracellular forces and polarity, was recruited in the team. Moreover, another CR also joined the team and is leading the new *T. adherens* project. Importantly, these two senior scientists supervise two of the three PhD students currently working in the team.

The previous report also recommended reinforcing lab-driven research in comparison to production emanating from collaborations. During this period, 9 published articles emanate from team-driven projects (5) or from a tight collaboration (4), 4 arose from more technical collaborations. This recommendation has thus well been taken into consideration.

Finally, the previous report recommended to improve international visibility by increasing the participation of team members to important conferences in the field. This aspect is a bit difficult to judge considering the restrictions due to the sanitary crisis; the committee nevertheless reiterates this recommendation.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	3
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	5
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	3
Post-docs	0
PhD Students	4
Subtotal non-permanent personnel	8
Total	13

EVALUATION

Overall assessment of the team

During the reporting period, the scientific productivity of the team was very good with five original articles published on the team projects and four papers linked to a tight collaboration with C. Borchelli and E. Renard (who joined the team during two years). Four additional papers emanate from collaborations of one of the team scientist E. Bazellères. The team attractiveness and visibility were excellent. The team leader has in particular obtained an ANR and an AMIDEX grant as a coordinator as well as two ANR and a labex grant as collaborator. The contribution of the team to society is excellent.

Strengths and possibilities linked to the context

The team has a strong, long-lasting and well-recognised experience in the field of epithelial polarity. The interest of the group leader for new evo-devo models and the presence of two senior researchers working either on sponges (Emmanuelle Renard who was hosted by the team in 2018-2020) or the placozoan *T. adherens* (Andrea Pasini who joined the lab in 2020) give the team a unique opportunity to decipher the basic principles of epithelial organisation. Moreover, the recruitment of a new researcher should also allow the team to develop original approaches to characterise the link between extracellular forces and polarity in 3D culture systems.

The attractiveness of the team appears to be excellent. The team has indeed not only been able to attract two new senior scientists but also many PhD students and postdocs (including one American and one Italian/Austrian). Importantly, one of the postdocs, was then recruited as CNRS researcher. The ability of the team leader to raise funding is also excellent.

Finally, the contribution of the team was excellent, in particular through the participation of A. Le Bivic and A. Pasini to several conferences for students or teachers.

Weaknesses and risks linked to the context

The most obvious risk for this team is the rather limited availability of the team leader. While it is impressive that he still succeeds in managing research in the lab, involvement of the senior scientists of the team in leading projects and supervising students will be instrumental to maintain high productivity. Careful organisation of the team is all the more important as there was a high turnover of senior scientists in the assessed period, which has led to substantial changes in the ongoing projects. Nevertheless, as mentioned above, the arrival of two new senior scientists will be an opportunity for the team to develop new and original projects.

Regarding the ongoing work itself, the *T. adherens* model seems extremely interesting to study epithelial plasticity. It should, however, be mentioned that this model has so far been only poorly characterised. The fine characterisation of epithelial plasticity in this model will thus require the development of numerous new tools and imaging protocols for this very fast moving organism. This can be achieved only if sufficient workforce is dedicated to this project. Collaborations with other teams working on this emerging model will also be crucial. The work on the link between extracellular forces and polarity in 3D culture systems has also the potential to become very interesting. This field of research is, however, very competitive and it was not completely clear how this project is positioned in its international environment.

Finally, although the team has been attractive to students and postdocs, the achievements reached by some of them are rather limited. In particular, it is of concern that one of the PhD students did not publish an article as first author.

RECOMMENDATIONS TO THE TEAM

Considering that most of the group leader's time is now dedicated to its function as a director of Life Sciences at the CNRS, particular attention should be given to ensure that the senior scientists of the team carefully define the projects that they are leading and that sufficient resources are allocated to those projects to ensure their success. The senior scientists should also be further encouraged to apply for funding and to participate in international conferences to increase their independence and visibility.

Team 12: Tissue architecture and plasticity
 Name of the supervisor: Mr Thomas Lecuit

THEMES OF THE TEAM

The team is interested in understanding how shape emerges during morphogenesis, using drosophila as a model. The group's current approaches rely on seminal work from the team, which revealed the crucial role of tensile forces during morphogenesis. Recently, they identified the role GPCR and heterotrimeric G proteins in actomyosin polarization. They also found that acto-myosin can self-organise as a response to physical forces. Moreover, they analysed the importance of tissue geometry on the induction of morphogenetic movements and how tissue growth affects tissue shape. Finally, a new interesting line of research focuses on the mechanisms by which neurons organise their arborisations. The team is strongly interdisciplinary and combines genetic, imaging, biophysics and modelling approaches.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report only had minor recommendations. The team was in particular encouraged to further expose the exceptional quality of its work by organising interventions targeting an even broader audience (undergrads, high school pupils, lay society). This objective has been largely achieved by the series of original lectures the team leader imparted at the College de France, as well as lectures at the computational and mathematical biology master course (University Aix-Marseille). These lectures are freely accessible in YouTube.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	1
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	3
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	5
Non-permanent teacher-researchers, researchers and associates	4
Non-permanent research supporting personnel (PAR)	6
Post-docs	2
PhD Students	5
Subtotal non-permanent personnel	17
Total	22

EVALUATION

Overall assessment of the team

This team is outstanding. In the assessed period, the team published eight excellent papers where members of the team appear as first and last authors and four articles where they appear as collaborators. The team is extremely well funded with over six million euros and major grants including an ERC Advanced grant which Dr Lecuit was awarded twice. The team has an outstanding international visibility and the leadership of Dr Lecuit, who has coordinated a Labex grant and heads the Centuri multidisciplinary federative centre in Marseille, is remarkable.

Strengths and possibilities linked to the context

The team has made pioneering discoveries and, remarkably, continues to provide important new results, thus remaining an international leader in the field of morphogenesis. The success of the team relies in particular on the strong interdisciplinary recruitment of student and postdocs and on collaborations with physicists, creating an extremely fruitful environment.

The recent projects of the team, which try to decipher the link between tissue geometry and morphogenetic movements and the link between tissue growth and tissue shape provide an interesting new angle to the ongoing research in the lab. The expertise of the team in understanding morphogenesis processes will probably also allow them to shed new and original light on the mechanisms underlying neuron arborisation.

The outstanding quality of the work of the team is reflected by the large number of international invitations and grants awarded to the team leader. The attractiveness of the team and its role in student and postdoc formation are also remarkable. During the assessment period, seven students have completed their PhD: all have published outstanding papers and have moved as postdocs to prestigious institutes, four of them obtaining an EMBO or HFSP postdoctoral fellowship. During this time, six postdocs were trained. Five PhD students are currently in the team.

Weaknesses and risks linked to the context

There are no major weaknesses. The only possible risk is that the team leader's busy agenda could affect his lab supervision. The presence of senior scientists in the team could help to delegate some aspects of student and project supervision.

RECOMMENDATIONS TO THE TEAM

Make sure the team leader's many responsibilities do not distract him from a close supervision of the laboratory.

Team 13: Physical approaches to cell dynamics and tissue morphogenesis
 Name of the supervisor: Mr Pierre François Lenne

THEMES OF THE TEAM

Team 13 has a long-standing interest in physical principles underlying animal morphogenesis with a clear track record in quantitative live-cell imaging and biophysical tool development. To this end, they develop and apply novel approaches to observe and perturb various systems and models. They have interest in adhesion in cell shapes in drosophila eyes, minimal in vitro system in gastrulation. They are also involved in various collaborations.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was encouraged to maintain the same level of originality and groundbreaking research, as well as to develop new collaborations.

The team was also encouraged to foster interactions with industrial partners to diversify its fund-raising. Teaching was to be developed.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	5
Non-permanent teacher-researchers, researchers and associates	2
Non-permanent research supporting personnel (PAR)	4
Post-docs	2
PhD Students	3
Subtotal non-permanent personnel	11
Total	16

EVALUATION

Overall assessment of the team

Team 13 has developed various quantitative live-cell imaging and biophysical tools with an outstanding publication record. The national and international visibility is very good and they have been very successful in fund-raising. They have been successful in stabilising researchers and recruiting postdocs and PhD students. They made a strong contribution to the training and research activities of the Turing Center for Living Systems.

Strengths and possibilities linked to the context

The originality of the team is in its interdisciplinary nature. Their own research program is well established and successful, which is nicely complemented with many excellent collaborations, resulting in an impressive publication record.

The team was successful in its funding strategy, obtaining major national grants; three ANR and one FRM, and one Labex 'informmost', as coordinator. The senior PI received a Leverhulme grant as invited professor.

The team is also extremely attractive to PhD students with three defended and one ongoing.

Weaknesses and risks linked to the context

The implication of the team in outreach activities and/or interaction with the socio-economic world are not presented. The actual contribution to training and teaching is very good, including the 'strong contribution to the training and research activities of the Turing Center for Living Systems', the Labex Informa and the Centuri program.

Risk of dispersion due to the numerous collaborations.

RECOMMENDATIONS TO THE TEAM

The team is to be commended for developing novel approaches and tools in biophysics and should follow on their successful trajectory.

Team 14: Signalling networks for stemness and tumorigenesis

Name of the supervisor: Mr Flavio Maina

THEMES OF THE TEAM

The team seeks mostly to identify genes and pathways important for cancer initiation, evolution and response to treatment, by exploiting an in vivo model in which liver and mammary gland cells express increased tyrosine kinase receptor levels, thereby predisposing them to additional, spontaneous mutations. A branch of the team studies how changes in environmental signalling affect cell differentiation by studying *Glypican 4* which is involved in the modulation of cell fate. By using inter/multi-disciplinary approaches, the team highlighted a new signalling pathway related to tumorigenesis and cell differentiation with potential for cancer treatment.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report recommended that the team set clearer priorities in its projects, and possibly reduce the number of projects (ie. those in collaboration) in order to fulfil the objectives specific to the group. It also recommended that the team better develop the career of the most senior scientist and to determine if she might want to establish an independent research group of her own. Lastly it recommended that the team be more involved in teaching at the university, especially at the undergraduate level, in order to share its scientific knowledge.

The first recommendation was mostly taken into account, as the majority of the projects were highly focused, and shared common tools and approaches. This has resulted in a productive publication period for the team that has mostly focused on its cancer model. The last recommendation had limited follow-up and not much has changed since the previous evaluation.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	2
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	4
Non-permanent teacher-researchers, researchers and associates	2
Non-permanent research supporting personnel (PAR)	4
Post-docs	2
PhD Students	2
Subtotal non-permanent personnel	10
Total	14

EVALUATION

Overall assessment of the team

The scientific production was excellent: ten team papers in highly respected journals (Cells, Theranostics, 2x J Hepatol, Advanced Sci, Stem Cells Translational Med, iScience, Nat Commun, Hepatol, Oncotarget), two invited reviews (J Hepatol, Semin Liver Dis), one book chapter, one team collaborative paper (Molecules), one collaborative paper where the PI signed as second to last author (Sci Adv). Team attractiveness was excellent: robust national (ITMO, INCa) and regional funding as coordinators; Six postdocs (majority international) were recruited. Reputation and visibility were very good to excellent: the team has limited but productive collaborations, resulting in the acquisition of new postdocs, collaborative papers, and invitations to speak; 2-3 invitations to speak at national and international (Spain, Italy, Israel) institutes. Societal impact was excellent: two patents, a maturation project, three declarations of inventions. Training is a strength: seven PhD students trained, most of the PhD students who graduated earlier in the period published at least one paper as first author. The overall assessment of the team was therefore excellent.

Strengths and possibilities linked to the context

The team has built a very interesting approach to study tissue homeostasis, cancer initiation and disease progression around the Alb-R26 Met model. This work led to the identification of epigenetic changes and multiple genes acting as tumor suppressors, regulators of tumorigenesis and/or biomarkers in liver and breast cancers. The results were published and discussed in a number of highly respected journals (Cells, Theranostics, 2x J Hepatol, Adv Sci, iScience, Nat Commun, Hepatology, Oncotarget), reviews (J Hepatol, Semin Liver Dis), and a book chapter. These previously understudied alterations have given the team fresh material to study for years to come. The results have already led to the successful applications of national grants and patents. A second branch of the team, led by a senior staff scientist (DR) studied the effects of GPC4 (*Glypican 4*) signalling on cell differentiation during development in vitro and in vivo. Though this project seems detached from the main cancer project, it has nevertheless been successful, giving rise to 1 paper (Stem Cells Translational Med), a second one in bioRxiv, and a CNRS pre-maturation project, grants, and student fellowships. Further, this staff scientist is also co-author on many of the cancer papers, indicating cross-fertilisation.

The team has shown great willingness to bring their research to the preclinical stage, with 2 patents, a maturation project and 3 declarations of inventions.

Training is a strength in this team, and most of the PhD students who graduated earlier in the period published at least one paper as first author. Team members were involved in student training, thesis committees and Master student lectures.

Team members were invited to give seminars at various institutes, especially those where they had collaborations. They have served on national evaluation committees (eg. ATIP-Avenir, Canceropole). Four members of the team reviewed articles in numerous scientific journals including Oncotarget, Adv Sci.

Funding and fellowships from public (ITMO Cancer, INCa) and private (GEFLUC, France Parkinson, ARC) national and regional (Canceropole PACA) sources were and continue to be healthy.

Weaknesses and risks linked to the context

The team does not appear to be part of any international consortiums. Some projects rely on a strong need for bioinformatics and no resources (human and funding) have been described. Several projects are more translational in nature, and the team does not include a medical oncologist staff member. The Team has few responsibilities in teaching at the AMU University from License to Master.

RECOMMENDATIONS TO THE TEAM

The team is now ripe to participate in collaborative EU ITN networks in order to gain more international visibility. The team could also consider applying to international cancer funding agencies. Lastly, the team should consider including medical staff members in their group to help advance their translational projects.

Team 15: Axon plasticity in development and cancer

Name of the supervisor: Ms Fanny Mann

THEMES OF THE TEAM

The team has two main areas of research. The first one deals with axon pathfinding focussing on the role of endocytosis for the correct development of axon tracts. They also study the change in response of contralateral axons after crossing the midline in the Corpus Callosum (CC) discovering novel signalling pathways. They have also developed a new model to study the effect of low alcohol intake during gestation. They have discovered an altered contralateral innervation pattern across the CC that resulted in defects during complex sensory-motor tasks that require inter-hemispheric integration.

The second main area of research, which has recently started, is involved with axon plasticity in cancer. i) Working with murine model of pancreatic ductal adenocarcinoma (PDAC), they have shown that several mechanisms coexist to generate the sympathetic innervation and demonstrated that denervation worsened the outcome of cancer in an immune-related manner. This very novel work revealed new insights into the mechanisms by which the nervous system regulates cancer progression. In addition, they have started two collaborations, a) to develop a mathematical model that simulates the effect of the peripheral nervous system on the development of PDAC and b) to analyse neuronal infiltration in murine models of melanoma.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report was very positive about the achievements of the young research group. They recommended continuing to establish itself in the community by collaborating with colleagues at the international level.

During this period the group leader has led the collaboration with two groups in the USA, one in the Europe and five in France, demonstrating the consolidation of the group both locally and internationally.

They also recommend keeping up the interactions with the science community to maintain their visibility and, thus, attractiveness for students and postdocs. During this period the research group has attracted two postdocs and nine PhDs, (and very recently a Researcher) showing that they have remained on the right track.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	1
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	3
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	5
Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	8
Total	11

EVALUATION

Overall assessment of the team

Overall, the research group is an excellent/outstanding team that address fundamental questions in axon guidance while linking their discoveries to human diseases or disorders increasing the impact and visibility of their work. They have also incorporated an exciting highly novel area of research: axon guidance in tumours. This is very promising and will widen the scope of the laboratory.

The scientific production for a relatively young group was excellent/outstanding, with six research papers, two reviews and one book chapter. In a few of these works, Dr Mann lead the work in collaboration with two groups in the USA, one in the Europe and five in France, demonstrating the consolidation of the group both locally and internationally.

Team attractiveness was excellent: They have been very successful attracting grants for about 2M Euros (11 grants) and have a relatively big group of research with one group leader, one professor, two postdocs and nine PhDs.

The reputation and visibility have been excellent. The team leader has been invited to deliver eleven talks in France and four internationally. The professor and postdoc have delivered five national talks. The team is very well integrated in the neuroscience and cancer research community at national and international levels. They have not contributed to outreach activities but have been strongly involved in teaching (master of integrative Biology and physiology) and S. Chauvet is a full professor of Developmental Biology who is also the director of the undergraduate programme and member of one commission.

Strengths and possibilities linked to the context

The research questions are all timely, interesting and exciting. Many of them have clear links to human diseases, which increases visibility and the chances of attracting funding.

The research group seems to be on the rise, adding new research topics and techniques.

The funding acquisition has been excellent and human resources attraction and training has followed in quality.

Weaknesses and risks linked to the context

They have a good publication record (6 research papers, 2 reviews and 1 book chapter), but considering the number of grants they have received, they could have published more.

To this aim, the group should reach a better PhD students/postdocs or tenured researchers ratio.

A considerable proportion of the funding obtained came from small pockets of money. These does not always represent a good income source due to the effort required when applying for it.

RECOMMENDATIONS TO THE TEAM

The team has done exceedingly well; however they could increase the number of publications maintaining the quality that has been excellent. For this aim they should attract more postdocs/tenured researchers (During the interview we were informed of a new researcher joining the group).

In view of the exceptional quality of the research questions and output, we recommend applying for more substantial funding like, ERC.

It would be advisable to increase the contribution to society by the participation in more outreach events for example.

Team 16: Neural Stem Cell Plasticity
 Name of the supervisor: Mr Cédric Maurange

THEMES OF THE TEAM

The team investigates stem cell proliferation, mostly focusing on the nervous system and on the epithelial cells of the fruit fly *Drosophila*. They are interested in the molecular pathways, focusing on the temporal transcription factors (TFs) that control the correct proliferation of stem cells. This led them directly to investigate the processes by which the proliferation of neuronal stem cells become unregulated producing tumours. In the last 6 years they have shown that the TFs control the self-renewal of neuronal stem cells and that a series of ecdysone regulated TFs (Chimno, Imp) are responsible for the external control of renewal during development. They have shown that these Tfs (working with others) limit regeneration, but that they also determine windows of cancer susceptibility and hierarchies within tumours.

Their work has highlighted in great detail the tight molecular links between early development, regenerative potential and childhood cancers.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report showed concern about the funding situation of the laboratory. This seems to have been sorted and the laboratory is in an excellent position with approx. 900 kEuros grant.

The previous report recommended to see if the tumour model was susceptible to impact research on cancer. The group has continued their work on cancer clarifying the role of molecular pathways for the development of tumours, but the direct link with human tumours is still not clear. To expand to a vertebrate model, the laboratory has recently (2020) attracted a tenured researcher that is developing an avian model, but no results are yet mentioned. This is a very promising addition to the lab.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	4
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	4
Post-docs	0
PhD Students	1
Subtotal non-permanent personnel	5
Total	9

EVALUATION

Overall assessment of the team

Overall, this is an excellent team that is taking advantage of the great genetic malleability of *Drosophila* to understand the molecular pathways that control stem cells proliferation in health and disease.

The scientific production has been excellent producing papers of great quality (5 papers where the group leader is main and corresponding author), and has published one book chapter, but the group has not published any collaborative work.

Team attractiveness was excellent: They are well funded (7 grants for approx. 800K Euros) and have attracted two tenured researchers, one postdoc and have supervised 4 PhD students.

The reputation and visibility have been excellent. The team leader has an excellent national and international reputation, being invited to many conferences (6 international and 4 national), he participates in two national committees and has co-organised four conferences. He has been invited to revise papers and funding for several agencies. The team has participated in several outreach activities receiving students from middle school and giving talks.

Strengths and possibilities linked to the context

The team has generated excellent research that has produced high quality publications.
 They have secured approx. 1M Euros of funding
 They have incorporated new techniques in the lab.
 They have recruited 2 tenured researchers.

Weaknesses and risks linked to the context

The group is performing research that is difficult to translate to other species. This is somehow mitigated by the incorporation of a new researcher working on chick development.

RECOMMENDATIONS TO THE TEAM

Having 2 permanent researchers, they could apply to more funding to expand the work of the laboratory to fundamental questions that are more easily generalised.

We encourage the development of new collaborations at the national and international level.

Team 17: Physical and Molecular Principles of Cytoskeletal Organisation

Name of the supervisor: Ms Alphée Michelot

THEMES OF THE TEAM

The Michelot team studies the mechanisms by which cells control the organisation, dynamics and mechanical properties of their actin cytoskeleton. The team has also recently been interested in the consequences of a cellular parameter, which is the amount of energy available, on the dynamics of the cytoskeleton, which is one of the most energy-consuming mechanisms. To develop these lines of research, the team relies on a solid expertise in biochemistry, which allows it to reconstitute complex actin assembly mechanisms, as well as on cellular models such as yeast.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The accomplishments of this team were not evaluated in the previous report because the team was just created in 2015. The few recommendations on the clarification of the objectives have been completely solved.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	0
Subtotal permanent personnel in active employment	1
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	2
PhD Students	2
Subtotal non-permanent personnel	5
Total	6

EVALUATION

Overall assessment of the team

Overall, this team is excellent to outstanding. The scientific production of this team is outstanding with four papers in which the PI is last/corresponding author (2 Plos Biology 2019, 1 Nature comm 2021, 1 EMBO J 2022). The level of funding is outstanding with an ERC starting grant during the period. The visibility of the PI is excellent through his functions in the committees of the Centuri Convergence Institute.

Strengths and possibilities linked to the context

The scientific production is excellent. The team first showed how the size of distinct actin networks is determined by their relative ability to assemble in a common and competitive environment (Plos Biology 2019). The team was also interested in the relationship between the mechanical properties of the actin cytoskeleton and endocytosis in the framework of a collaboration with ESPCI. They characterised the stiffness of the reconstituted actin networks from cell extracts of different yeast mutants and correlated its properties with the efficiency of endocytosis in the corresponding cells (Plos Biology 2019). The team also determined actin isoform specificity by switching the normally present actin to one of its isoforms in biomimetic assays and in yeast. They showed that the defective interaction of a heterologous actin for key regulators of actin assembly limits some actin assembly mechanisms and enhances others (EMBO J 2022). Thanks to the clever use of fluorescent nucleotides that bind actin and allow microscopic observation, the team has opened the way to understanding the recycling mechanisms of actin and its associated nucleotide (Nature comm 2021).

The level of funding is outstanding with an ERC starting grant (ending in 2021), a Labex funding until 2019 and a FRM labelled team funding from 2021.

The visibility of the PI is excellent since he has been awarded the Young Investigator Prize from the French Society of Cell Biology (SBCF) and he has recently been promoted to research director at the CNRS, testifying to the success of his young team within the unit. He has been invited to give talks at nine national and international conferences. He is a member of the steering committee of the institut convergence Centuri, co-organisation of the EMBO Workshop 'Dynamics of Living Systems', Cargèse, 2017, member of the selection committee of four new group leaders recruited by Centuri in 2019 and since 2020, he is reviewing editor at eLife.

The training activity of the team is excellent with four PhD students trained by the PI during this evaluation period. It is also worth mentioning that the PI is the head of the PhD committee of the institut convergence Centuri.

Weaknesses and risks linked to the context

There are very few weaknesses to mention for this team. The level of funding will necessarily decrease after the ERC, which the team has taken full advantage of to launch itself. One can regret that the contribution of the team to outreach activities is not clearly explained.

RECOMMENDATIONS TO THE TEAM

The team must capitalise on its excellent start. The recruitment of senior researchers would allow the team to consolidate and several additional collaborative grants should be targeted to compensate the end of the ERC starting grant.

Team 18: Chronic Pain: Molecular and Cellular Mechanisms

Name of the supervisor: Mr Aziz Moqrich

THEMES OF THE TEAM

The team studies the mechanisms underlying the transition from acute to chronic pain, using the lab's previously generated *in vivo* models to test the function of particular neurons in pain detection, and combining molecular and cellular analyses to understand how pain may become chronic. This topic is timely and important with high societal implications.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report recommended increasing collaborations with other groups. In the current evaluated period, the team showed a good collaboration rate. In fact, most of their publications were collaborative. In this period, they had 13 collaborative publications where members of the team did not sign as leading authors (either as first or last), complemented with other collaborative publications where the team appeared as leading authors and also included members from other groups. It has to be highlighted that in 12 cases out of a total of 19 publications these were international collaborators. This is a clear indication of the high international visibility of the team.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	5
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	5
Post-docs	0
PhD Students	4
Subtotal non-permanent personnel	9
Total	14

EVALUATION

Overall assessment of the team

The scientific production was very good to excellent: five team papers in very good journals (2x Cell Rep, 1x Sci Rep, 1x J Invest Dermatol, 1x Front Cell Neurosci), one team paper where team members were not senior authors (Sci Rep), five collaborative papers in very good to high-visibility journals (eg. Nature, 2x Pain, Cell Rep) where the PI signed as second to last author, and other collaborative papers. Team attractiveness was excellent: five permanent members recruited in this period (DR, 2x CR, MCU, AI); numerous national grants as coordinator (ANR, Equipe FRM, prematuration and maturation grants) and partner (3x ANR), resulting in a robust financial situation; though surprisingly, no postdoc recruitment for this period. Reputation and visibility were excellent: numerous invitations to speak at institutions (>30) and meetings (6); PI was deputy president of ANR CE16 and associate editor of the journal Pain; PI received two prizes (Fondation Unité -Guerra-Paul-Beaudouin - Lambrecht-Maïano, Meilleur chercheur des Marocains du monde). Societal impact was outstanding: 1 start-up with funding for phase 2 clinical trial; Six patents (not yet licensed); appropriate public outreach. Training seemed appropriate with seven PhD students trained, where four students published as first authors. The overall assessment of the team was therefore excellent.

Strengths and possibilities linked to the context

In this period, the team has studied the roles of: the TFA4 chemokine-like protein in gating neuronal transmission; the bhlha9 transcription factor in modulating pain; the Myo1a myosin protein in suppressing chronic pain, all of which led to publications in very good journals, as well as external collaborations. The team is now well established with four permanent senior staff, a lab manager, and seven PhD students, four of which are currently active. The projects have benefited from a well-rounded expertise that ranges from physiology to molecular mechanisms, and murinmodels previously established in the lab. The team has also established an excellent network of collaborators that should further add to their visibility and production. The group has been well funded, and was able to create a spin-off company *Tafalgie Therapeutics* that aims at applying the group's excellent basic research. Additional publications should be forthcoming.

Weaknesses and risks linked to the context

The lab does not seem to be able to attract postdoctoral researchers, which is both a long-term and attractiveness issue. Its implications in teaching and institute environment are unclear. The team has not obtained international funding or been part of European networks in this period.

RECOMMENDATIONS TO THE TEAM

With its robust financial support and current niche in chronic pain research, the team should strive to further advance its molecular understanding of chronic pain, and maintain a good balance between basic research and the socio-economic world. It should try to attract postdoctoral researchers and consider applying to international funding.

Team 19: Evolution and Development of Morphology and Behavior
Name of the supervisor: Mr Benjamin Prud'homme

THEMES OF THE TEAM

The team analyses evolution and development (Evo-Devo) with a special interest on traits that affect behaviour. For that purpose they study neural networks assembly and their influence on reproductive behaviour. The team has started studying *Drosophila suzukii* and the harlequin ladybird, that are invasive pest species of agronomic interest.

The team is interested in how the insect's variable pigmentation patterns are genetically regulated and change during evolution.

A second objective is the analysis of *D. suzukii*'s egg laying preferences on ripe fruit, which contrasts with other *Drosophila* species that only lay eggs in rotten fruit. They both studied the behaviour and the ovipositor structure where they found how changes at cellular level contribute to shape the female's genitalia.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report commented that it was unclear after the departure of Dr Gompel from IBDM how the team now led by Dr Nicolas PRUD'HOMME will separate his projects from those developed in Dr Nicolas Gompel's team, due to their similarity. In the current evaluated period, the two teams have been publishing in collaboration. This arrangement does not seem to have affected negatively the output of any of the two investigators. Dr Prud'homme has published at least one high-profile paper per year as senior author besides additional papers in collaboration with Dr Gompel.

Another suggestion by the previous evaluators was to become involved in a more active contribution to local and international teaching. Although there has not been an observable increase in the teaching duties of the team leader, this is not of any concern to the current evaluators as the group is able to recruit good PhD students and postdocs.

The evaluators suggested more permanent staff should be recruited; now three tenured researchers are in the team.

Finally, the evaluators suggested taking care for optimising PhD and postdoc training in terms of publication outputs. In the current period, with the exception of one, all postdocs and PhD students have participated in high impact publications as first author. Probably the effort to get high impact papers has resulted in a less than optimal situation for some PhD students that should be taken care of.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	2
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	5
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	2
Post-docs	0
PhD Students	0
Subtotal non-permanent personnel	2
Total	7

EVALUATION

Overall assessment of the team

The team is producing outstanding original research that is published in high impact journals. The leader is invited to international meetings and talks, having a great visibility. The team is well funded. Its collaboration with Dr Gompel has been very successful. Although the team's funding may decrease due to the end of the ERC grant, the group is likely to obtain sufficient funds from national grants to be able to maintain its level of excellence. It is possible that the great visibility of the team leader may lead to obtaining international funds in the future.

Strengths and possibilities linked to the context

The international visibility of the leader will allow the team to recruit international postdocs. The new projects on insect pests may open new funding possibilities, especially those on *D. suzukii* where the team has contributed to generating a high quality genome assembly and annotation and put in place techniques to generate transgenics and induction of Crispr mutations. The group has been reinforced with a total of four scientists including the team leader.

Weaknesses and risks linked to the context

The end of the ERC funding may lead to a reduction of the group's size and output. The research supervision time of 5% seems rather low having three PhD students and three postdocs. The group complains of difficulties recruiting PhD students, the team leader should consider if the low supervision time could be in part the cause.

RECOMMENDATIONS TO THE TEAM

Try to have a less ambitious plan B project for PhD students in case the main project does not work. This will help the student leaving the team with at least a first author publication.

The lack of local collaborations should not be a problem, the team can take advantage of their great visibility to increase the number of international collaborations.

Team 20: Host-pathogen interactions in the Drosophila model
 Name of the supervisor: Mr Julien Royet

THEMES OF THE TEAM

Team 20 has a long-standing interest in the innate immune response to bacterial infection using Drosophila as a model organism. Its projects now encompass the broader physiological and behavioural responses triggered by bacteria, studying the impact of bacterial peptidoglycans on the fly nervous system and of gut-associated bacteria on host metabolism.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous HCÉRES committee recommended that the team places more importance on its primary research objectives in terms of publication strategy (less reviews) and task management (lot of teaching, different projects). These recommendations have been clearly taken into consideration by the team, with a clear shift in its publication policy toward original research articles rather than reviews, and the development of two interconnected and well-focused lines of research. In addition, the teaching load of the PI has been reduced thanks to its promotion as a senior member of the Institut Universitaire de France in 2018.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	1
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	4
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	6
Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	9
Total	13

EVALUATION

Overall assessment of the team

The team has obtained very original and interesting results of fundamental interests. Its scientific production is of excellent to outstanding level. It has been extremely successful in securing strong financial support from the main national funding agencies. It attracted a high number of PhD students and its involvement in training through research is excellent. Its reputation is also excellent but could be increased at the international level.

Strengths and possibilities linked to the context

This very well-established team has developed original lines of research on the interactions between bacteria and their host, which go beyond the innate immune response and trigger a wide range of physiological responses in *Drosophila*. Notably, they showed that bacteria-derived peptidoglycans activate the NF- κ B cascade in octopaminergic neurons in the brain, causing a change in behaviour. They also revealed a molecular mechanism by which flies dampen NF- κ B pathway activation by bacterial peptidoglycans in the gut, establishing a tolerance toward its microbiota, and found that some bacteria induce a systemic metabolic shift. Their exciting findings led to several major publications as main authors (Cell Host Microbe 2018, eLife 2017 & 2019, EMBO Rep. 2018, iScience 2020, J. Innate Immun. 2016 & 2017, J. Insect Physiol. 2017, PLoS Genet. 2017 & 2022, Scientific Rep. 2020). Team members are also associated with two other publications (PloS Genet 2018, BMC Biol 2016). Overall, this is a remarkable scientific production.

The national and international recognition of the team is excellent. The PI was nominated as a senior member of the Institut Universitaire de France and stands as an elected member to the CoNRS as well as to the CNRS INSB scientific council. He is regularly invited or selected as a speaker to highly reputed international meetings in the field of immunity or insect research. The PI was also invited to write a review for Trends in Neurosciences (2020) as well as for Cells (2021) and Dev Comp Immun (2016), and 2 previews for Cell Host Microbe (2018, 2020).

The team was exceptionally successful in its funding strategy: it obtained major national grants very regularly. The team was funded twice as an 'FRM team' (2014-2017, 2019-2022) and the PI coordinated 3 ANR (2018-2022, 2019-2022, 2021-2025) as well as the Inform Labex (2012-2020). It also obtained one AFM grant (2016-2019), support from the Institut Universitaire de France (2018-2023) and was associated with one ANR (2015-2021).

The team is also extremely attractive to PhD students: 4 obtained their PhD during this period (all obtaining at least one very good 1st author research publication) and 3 more are currently hosted in the team. Two permanent scientists obtained their HDR during this period, compensating for the departure of two other team members (see below) in terms of PhD supervision capacity. Co-directions of PhD students between the PI and other permanent scientists were very effective and allowed the more junior staff to present their HDR. Although the team has not attracted any postdoctoral fellow, the training through research is excellent. It is worth noting also that 2 team members are strongly involved in teaching at the AMU and stand as coordinator of Pasteur-AMU portal and the Integrative Biology and Physiology master.

Weaknesses and risks linked to the context

Two senior permanent scientists (one DR CNRS and one MdC AMU) who were very productive left the team during the contract, strongly reducing the manpower and critical mass of the team.

The team did not attract any postdoctoral fellow. In addition, it does not seem to be involved in international collaborations.

Although the team is strongly involved in teaching at the university and clearly benefits from the local platforms, its scientific integration within the unit could be improved.

The implication of the team in outreach activities and/or interaction with the socio-economic world are not presented.

RECOMMENDATIONS TO THE TEAM

The team can be commended for maintaining its original and productive lines of research as well as for its successful shift toward the field of neuro-immunology. Yet it should try to further increase its international standing, for instance, by participating in broader collaborative networks. Also, it should seek to attract some senior scientist either as a postdoc or permanent staff to uphold its ambition.

Team 21: Muscle Dynamics
 Name of the supervisor: Mr Frank Schnorrer

THEMES OF THE TEAM

The team is focused on skeletal morphogenesis and function and uses the advantages of the *Drosophila* genetic toolbox with high resolution *in vivo* imaging for their work. Of particular interest is the question of how contractile myofibrils and sarcomeres are built.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

All recommendations made in the previous evaluation have been addressed successfully.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	5
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	6
Post-docs	1
PhD Students	5
Subtotal non-permanent personnel	13
Total	18

EVALUATION

Overall assessment of the team

The team has achieved outstanding visibility and recognition and is very attractive for students and postdocs. The research being done by the time is clearly pioneering and has led to major discoveries.

Strengths and possibilities linked to the context

The team has achieved very high productivity and published several high visibility papers in the last review period, including three eLife, two PLoS Biology, one Nature Communication and one Development as main authors. It also contributed to nine reviews or method papers. Its contribution to the understanding of muscle development and organisation is outstanding, with seminal contributions in the field.

The team has also been very successful in raising money including an ERC synergy grant and an HFSP program grant at the international level, as well as two ANR (1 as coordinator) and one Bettencourt-Schueller grants at the national level. It also benefited from strong support from the AMIDEX program.

The team was very attractive to young researchers: it hosted nine PhD students as well as seven postdocs, two of them were recruited as CNRS researchers in the team, one was recruited as assistant professor, and one set up her own lab in Germany.

In addition, the PI has recently become elected EMBO member and its visibility is outstanding as attested by its network of collaboration or regular invitations to give seminars (>20) and participation to/organisation of international meetings (European Muscle Society, EMBO workshops, HFSP, Asilomar conference). The PI is also guest editor for eLife and PLoS Genet and member of the European Drosophila Society steering board.

Weaknesses and risks linked to the context

No weaknesses were identified.

RECOMMENDATIONS TO THE TEAM

The only recommendation worth giving is to continue on this outstanding trajectory.

CONDUCT OF THE INTERVIEWS

Dates

Start: 17 novembre 2022 à 8 h 30

End: 18 novembre 2022 à 17 h

Interview conducted: online

UMR 7288

Developmental Biology Institute of Marseille (IBDM)

Director : Laurent KODJABACHIAN, Deputy Director : Pascale DURBEC

Committee Chair : James Castelli-Gair Hombria, Experts : Susan Chan, Christophe Le Clainche, Didier Stainier, Lucas Waltzer, Jimena Berni, Alicia Hidalgo, Damien Devos Ayhan Kocer (expert CNU), Anne Pacquelet (expert CoNRS), Alexei Grichin (expert PAR)
Hcéres scientific advisor (CS): Ina Attrée

November, 17th

8:30 Test Zoom connections

8:35 – 8:45 Committee + CS (if needed)

Scientific sessions

8:45 - 8:55 Introduction / Presentation of the Committee members

9:00 – 9:40 Unit presentation by the DU + common facilities (15'+ 10' discussion/10'+5')

9:40 – 11:00 4 Teams (10' + 10' discussion)

9:40-10:00	Team FASANO
10:00-10:20	Team GRABA/SAURIN
10:20-10:40	Team HABERMANN
10:40-11:00	Team KODJABACHIAN

Break/debriefing committee (20')

11:20-12:20 3 Teams (10' + 10' discussion)

11:20-11:40	Team LECUIT
11:40-12:00	Team LENNE
12:00-12:20	Team MANN

Break/debriefing committee (20')

12:40-13:30 **Lunch break/debriefing committee**, if needed

13:30- 14:30 3 Teams (10'+ 10' discussion)

13:30-13:50	Team BERTRAND
13:50-14:10	Team KELLY
14:10-14:30	Team SCHNORRER

Break/debriefing committee (30')

Interviews

15:00- 15:30 Meeting w/ technical staff 15:45– 16:15 Meeting w/students

16:30 Committee/Report briefing

November, 18th

8:45 – 9:00 Committee + CS (if needed)

Scientific sessions.

9:00 –9:05 Presentation of the day program

9:10 – 11:00 4 Teams (10' + 10' discussion)

9:10-9:30	Team LE BIVIC
9:30-9:50	Team DURBEC
9:50-10:10	Team MAURANGE
10:10-10:30	Team ROYET

Break/debriefing committee (20')

11:00-12:00 3 Teams (10' + 10' discussion)

11:00-11:20	Team MICHELOT
11:20-11:40	Team MAINA
11:40-12:00	Team HELMBACHER

Break/debriefing committee (20')

12:30-13:30 **Lunch break/debriefing committee, if needed**

13:30- 14:30 3 Teams (10'+ 10' discussion)

13:30-13:50	Team PRUD'HOMME
13:50-14:10	Team MOQRICH
14:10-14:30	Team CREMER

Break/debriefing committee (20')

15:00–15:30 Committee-Supervising bodies (CNRS, AMU)

15:45– 16:15 Meeting Researchers (no leaders)

16:30- Discussion Committee – Dir

Committee debriefing

GENERAL OBSERVATIONS OF THE SUPERVISORS

Le Président de l'université

au

Département d'Évaluation de la recherche -
Hcéres

Objet : Observations de l'unité relatives au
rapport d'évaluation des experts Hcéres

N/Réf. : VPR/LS/AMS/CM – 23-07

Dossier suivi par : Cécile Merle

Tél : 04 13 94 95 90

cecile.merle@univ-amu.fr

Vos réf :

DER-PUR230023133 - IBDM - Institut de biologie du développement de Marseille - Luminy

Marseille, le lundi 21 août 2023

Madame, Monsieur,

Je fais suite au mail que vous nous avez adressé le 15/06/2023 dans lequel vous me communiquez le rapport d'évaluation Hcéres de l'Unité IBDM - Institut de biologie du développement de Marseille - Luminy.

Comme demandé dans ledit mail, je vous fais part ci-après des remarques et observations de portée générale émises par la direction du laboratoire :

Je voudrais ici faire certaines remarques de portée générale, et toutes personnelles, concernant le processus d'évaluation conduit par le HCERES et le rapport qui nous a été fourni.

Premièrement, je voudrais réitérer ma totale désapprobation de la décision du HCERES de découpler l'évaluation du bilan et du projet, au cours de cette vague C. Cette décision n'a servi ni les intérêts des laboratoires évalués ni ceux des experts mandatés, dont la mission a perdu une grande partie de son sens. Les aménagements proposés à la hâte pour contourner cette mesure ne m'ont nullement convaincu.

Deuxièmement, je déplore profondément la vision hyper-administrative du HCERES qui collecte des morceaux de données, sans que l'on sache ce qu'il en adviendra, et qui impose un format unique de rapport pour des disciplines aussi différentes que la biologie, la cosmologie ou les lettres. La dictature de la norme devrait trouver ses limites lorsqu'on s'adresse à un domaine, la recherche, dont les fondamentaux sont liberté et créativité.

Concernant le rapport, plusieurs points m'interpellent. Tout d'abord, je n'ai trouvé dans la partie relative à l'unité dans son ensemble, aucune phrase concernant la gouvernance et sa capacité ou non à conduire les destinées du laboratoire. Sans doute est-ce la pratique, mais je trouve cela anormal quand on sait l'énergie mise à cette tâche et à coordonner un rapport pour le HCERES, que beaucoup de collègues considèrent inutile.

Plusieurs collègues m'ont fait part d'incohérences flagrantes dans leur rapport d'équipe que je ne reprendrai pas ici, faute de temps et considérant que d'autres tâches plus importantes m'attendent.

Au final, je ressors de cette très longue et pénible phase d'évaluation avec un sentiment d'amertume extrême, de perte de sens et de dépit. Vous souhaitant bonne réception des présentes.

Je vous prie de croire, Madame, Monsieur, l'expression de mes respectueuses salutations.



Eric BERTON



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