IJM - Institut Jacques Monod

Rapport Hcéres

agence d'évaluation de la recherche
et de l'enseignement supérieur

Research Units Department

AERES report on unit:

Institut Jacques Monod

IJM

Under the supervision of the following institutions and research bodies:

Université Paris 7 - Denis Diderot

Centre National de la Recherche Scientifique

December 2012

agence d'évaluation de la recherche
et de l'enseignement supérieur

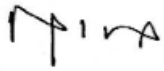
Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head



Pierre Glaudes

The president of AERES "signs[...], the evaluation reports, [...]countersigned for each evaluation department by the relevant head of department (Article 9, paragraph 3, of french decree n°2006-1334 dated 3 november 2006, revised).

Grading

Once the visits for the 2012-2013 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).
This score (A+, A, B, C) concerned each of the six criteria defined by the AERES.
NN (not-scored) attached to a criteria indicate that this one was not applicable to the particular case of this research unit or this team.

Criterion 1 - C1 : Scientific outputs and quality ;
Criterion 2 - C2 : Academic reputation and appeal ;
Criterion 3 - C3 : Interactions with the social, economic and cultural environment ;
Criterion 4 - C4 : Organisation and life of the institution (or of the team) ;
Criterion 5 - C5 : Involvement in training through research ;
Criterion 6 - C6 : Strategy and five-year plan.

With respect to this score, the research unit concerned by this report (and, when necessary, its in-house teams) received the following grades:

- Grading table of the unit: Institut Jacques Monod

C1	C2	C3	C4	C5	C6
A+	A+	A	A+	A+	A+

- Grading table of the team: Evolution and development of metazoan

C1	C2	C3	C4	C5	C6
A+	A+	A+	NN	A+	A+

- Grading table of the team: Pathology of DNA replication

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A+	A+

- Grading table of the team: Mitochondria, metals and oxidative stress

C1	C2	C3	C4	C5	C6
A	A+	A+	NN	A+	A+

- Grading table of the team: Regulation of cell fate specification in the mouse

C1	C2	C3	C4	C5	C6
B	A	NN	NN	A	B

- Grading table of the team: Macromolecular complexes in living cells

C1	C2	C3	C4	C5	C6
A	A+	NN	NN	A+	A

- Grading table of the team: Non-conventional functions of nuclear pores

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A+	A+

- Grading table of the team: Epigenetic regulation of genome organization

C1	C2	C3	C4	C5	C6
NN	A+	NN	NN	A	A+

- Grading table of the team: Cell division and reproduction

C1	C2	C3	C4	C5	C6
NN	NN	NN	NN	NN	A+

- Grading table of the team: Membrane traffic in neuronal and epithelial morphogenesis

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A+	A+

- Grading table of the team: Epigenome and paleogenome

C1	C2	C3	C4	C5	C6
A	A+	A+	NN	A	A

- Grading table of the team: Polarity and morphogenesis

C1	C2	C3	C4	C5	C6
A+	A	NN	NN	A+	A+

- Grading table of the team: Membrane dynamics and intracellular trafficking

C1	C2	C3	C4	C5	C6
A	A+	NN	NN	A	A

- Grading table of the team: Molecular virology

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A+	A+

- Grading table of the team: Regulation and dynamics of cell division

C1	C2	C3	C4	C5	C6
A	A	NN	NN	A	A+

- Grading table of the team: Drosophila evolution

C1	C2	C3	C4	C5	C6
A+	A+	A	NN	A+	A+

- Grading table of the team: Computational modelling and biomethematics

C1	C2	C3	C4	C5	C6
A	A	A+	NN	A+	B

- Grading table of the team: Genetics and development of the cerebral cortex

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A+	A+

- Grading table of the team: Cell cycle and development

C1	C2	C3	C4	C5	C6
A	A+	NN	NN	A+	A+

- Grading table of the team: Development, signalling and trafficking

C1	C2	C3	C4	C5	C6
A	A	NN	NN	A+	A

- Grading table of the team: Morphogenesis, homeostasis and pathologies

C1	C2	C3	C4	C5	C6
A	A	NN	NN	A+	A

- Grading table of the team: Chromosomal domains and DNA replication

C1	C2	C3	C4	C5	C6
A	A	NN	NN	A	A

- Grading table of the team: Biomolecular nanomanipulation

C1	C2	C3	C4	C5	C6
A+	A+	A+	NN	A+	A+

- Grading table of the team: Molecular oncology and ovarian pathologies

C1	C2	C3	C4	C5	C6
A	A+	NN	NN	A+	A

Evaluation report

Unit name:	Institut Jacques Monod
Unit acronym:	IJM
Label requested:	UMR
Present no.:	UMR 7592
Name of Director (2012-2013):	Mr Giuseppe BALDACCI
Name of Project Leader (2014-2018):	Mr Giuseppe BALDACCI

Expert committee members

Chair:	Mr Claude DESPLAN, New Yok University, New York, USA
Experts:	Mr Frédéric BARRAS, Université de Marseille
	Ms Valérie CASTELLANI, Université de Lyon
	Ms Johanna CHLUBA, Université de Bourgogne, Dijon (representative of the CNU)
	Mr Gord FISHELL, Smilow Research Center, New York, USA
	Ms Giuseppina GIGLIA MARI, Université de Toulouse (representative of the CoNRS)
	Mr Acaimo GONZALES REYES, Centro Andaluz de Biología del Desarrollo, Seville, Espagne
	Ms Isabelle LIHRMANN-BISSON, Laboratoire de différenciation et de communication neuronale et neuroendocrine, Mont-Saint-Aignan, (representative of the CSS INSERM)
	Mr Didier MARQUET, Université de Marseille
	Ms Mireille MONTCOUQUIOl, Université de Bordeaux Segalen
	Mr François PAYRE, Université de Toulouse
	Mr Paolo PLEVANI, DIpartimento di scienze biomoleculari e biotecnologie, Milan, Italie
	Mr Ovidiu RADULESCU, Université de Montpellier
	Mr Jordan RAFF, Sir Williams Dunn school of pathology, Oxford, UK

Mr Nic TAPON, London Research Institute, Londres, UK

Mr Marcel TIJSTERLMAN, Department of Toxicogenetics, Leiden , The Netherlands

Mr Olivier VOINNET, Institut fédéral de Technology de Zurich, Suisse

Scientific delegate representing the AERES:

Mr Pierre COUBLE

Representative(s) of the unit's supervising institutions and bodies:

Mr Marc BENEDETTI (Université Paris Diderot)

Ms Brigitte RENÉ (CNRS)

Ms Anne ROCHAT (INSERM)

1 • Introduction

History and geographical location of the unit

The IJM is located in a brand new building within the Université Paris Diderot in the 13th arrondissement of Paris, in a new neighborhood. Although not as centrally located as its former location at Jussieu, it seems that the neighborhood has acquired character and that this remains a 'central Paris' Institution in the heart of a major city.

This new building is entirely dedicated to IJM, although some space is lent for Univ. Paris Diderot's activities. The quality of the new construction which is state of the art, is in very striking contrast with the previous IJM at Jussieu. Because of the imminent move to the new location, Jussieu was left in total disarray and IJM obviously suffered tremendously. Furthermore, absent or temporary leadership had weakened even more IJM that appeared to have lost much of its morale and stamina.

However, thanks to a new permanent leadership that has obviously managed to reunify the Institute, IJM appears to have fully recovered from events that could have been deleterious to its long term survival. It is now a stable place that can focus on improving its scientific impact rather than solving technical issue. Clearly, the scientists are now very proud to work in this institution.

Management team

The IJM director is assisted by a deputy director. A Direction council gathers five group leaders who meet every week, with their term being renewed after two years. There are also an Institute council, a Recruitment Committee and an Equipment Committee with members elected or nominated by the Director.

AERES nomenclature: SVE1

Unit workforce

Unit workforce	**Number as at 30/06/2012**	**Number as at 01/01/2014**	2014-2018 **Number of project producers**
N1: Permanent professors and similar positions	35	31	100%
N2: Permanent researchers from Institutions and similar positions	50	44	100%
N3: Other permanent staff (without research duties)	68 (65,4)	65 (62,4)	
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	2	2	100%
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	29	7	100%
N6: Other contractual staff (without research duties)	23	5	
TOTAL N1 to N6	207	154	

Percentage of producers	***100 %***

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	36	
Theses defended	34	
Postdoctoral students having spent at least 12 months in the unit*	9	
Number of Research Supervisor Qualifications (HDR) taken	20	
Qualified research supervisors (with an HDR) or similar positions	55	49

2 • Assessment of the unit

Strengths and opportunities

- High quality of research.
- Very good publication record with over 100 papers published per year, 15-20 being in journals with impact factors superior to 10.
- Excellent ability to raise grant money (3,5 M€/year).
- Excellent organization of the Institute with a collegial atmosphere and a director who manages to reach a consensus at all levels of the Institute's personnel.
- Collegiality and transparency of decision-making and funding allocation with the director taking the responsibility for final decisions.
- Very strong common core services, including imaging and animal facility.
- Significant effort to contribute to teaching and to be involved in outreach programs.
- Some of the teams have International recognition and manage to publish in the highest profile journals (Cell-Nature-Science).
- Diversity of programs but relative integration and collaboration among teams.
- Excellent success in recruiting new junior/senior teams.

Weaknesses and threats

- Several of the teams are doing good work, but this work often does not reach the top level.
- Few papers in the most prestigious journals (3-4 in the last 4 years).
- No international grant e.g. ERC or prestigious awards (EMBO YIP).
- Some of the teams appear to be isolated and to not receive the feedback necessary to orient their research towards more significant goals.
- Some of the common services only serve one group (e.g. ancient DNA) while receiving technical support.
- Poor initial support for junior teams ("Startup") if those do not come with an ATIP-Avenir.
- Insufficient involvement of CNRS/INSERM scientists of IJM in the administrative structure of the Université Paris Diderot that hosts the Institute.

Recommendations

- Be more ambitious in applying for international grants (ERC).
- Better interactions among teams to orient research towards more significant goals.
- Attract more international scientists at every level, including postdocs and junior group leaders.
- Provide teaching relief for teaching scientists.
- Provide better technical help for teams that have no technicians.
- Dramatically improve mentoring at every level.

3 • Detailed assessments

Assessment of scientific quality and outputs

The "Institut Jacques Monod" (IJM) appears to have recovered very well from a period of changes: A very difficult time in the last years at Jussieu, a very long move from Jussieu, and temporary leadership. It has regained its status as one of the flagships of French science in Molecular and Cellular Biology with international recognition. The current director appears to have gained trust of all levels of the personnel of the Institute and to have greatly succeeded with its 'open door' policy. The reorganization of the institute without tight programs appears to have helped induce more collaboration and to reduce parochial behaviour. The general impression of the Institute is that of a very happy place where people are proud to work. The scientific success that should correlate with this has not yet been fully achieved but there are clear indications that the IJM is on a rising slope and that several of the groups, especially the more junior, are doing very well and contribute to raising the profile of the Institute.

The general focus on the IJM is on basic research, with several themes. The IJM has removed boundaries among teams by cancelling rigid departments. The three themes are:

- Genome and chromosome dynamics

- Cell dynamics and signalling

- Development & evolution

The teams can embark into new directions by taking advantage of existing common core facilities including an imaging facility that serves all teams of the IJM, an animal facility, but also a useful proteomics core facility. The genomics facility is small but it serves to encourage the individual groups to take advantage of novel technology, even if they have to subcontract their sequencing needs to the outside.

The scientific quality of the IJM is demonstrated by its publication output, with over 100 papers published per year, among which 15-20 are in journals with impact factors that are over 10. Several papers have been published in Cell, in Nature and in Science on very different topics, demonstrating the livelihood of the current research. Most of the high profile papers are from younger groups. These teams tend to publish few papers but of high quality. Others have the opposite trend, publishing numerous, sometimes many papers, in lesser journals.

A new strength has appeared with the recruitment of new team leaders who work on evolutionary aspects of biology, development or adaptation (although this was weakened by the departure of a team to the ENS). The teams in this field have managed to attract international attention with high profile papers published, some of them in collaboration, but with great success. Although not historically a strength of IJM, this trend should be encouraged.

Interactions among teams are not yet optimal and this could be improved by inducing better contacts among the groups. The common core facilities serve this purpose to some extent, but more formal induced communication would be granted. More critically, mentoring appears to be lacking, maybe because of the paucity of very successful senior scientists. Although some of the junior groups have established preferential contacts with a senior team leader, this is not formalized and often simply absent. It is highly recommended to implement formal mentoring, making sure that this is not perceived by the young team leaders as interference in their freedom of project.

The common core facilities appear to be one of the strong points of the IJM. Although a majority of the technical personnel is assigned to these 'platforms', there is no resentment and most scientists agree that this should indeed be the priority. The imaging facility (ImagoSeine) is running very well with state of the art equipment. As for personnel, much of the common money spent by the IJM goes towards the purchase of common equipment, microscopes etc. This is also a strategy that seems to be universally accepted at IJM. Although the facility is running well, its current director might have to retire in the next year or two. It is therefore essential to recruit another senior person to run it. Although some of the technical staff is highly competent, it is important to continue the operation under the leadership of a strong director. The Committee understands that a current search committee is in place for this purpose, and this is strongly encouraged.

Other facilities are less significant. The Proteomics core facility is used and the Genomics is just starting. Although the latter runs the risk of becoming obsolete very rapidly since the technology advances so quickly, it is important to have expertise in this field. In this regard, Bioinformatics must be developed: even if DNA or RNA sequencing is outsourced, the scientists do need to process the data and it is often impossible without appropriate expertise in bioinformatics.

The Animal House seems to be functioning well now after very rocky beginnings as it was the last to move from Jussieu and the move encountered many technical difficulties. It employs 6 people and a private company for the management of a pathogen-free facility.

Finally, the purpose of the "Palaeogenomics and Molecular Taphonomy" ancient DNA core facility is not clear since it is extremely specialized ('Taphonomy' is not a term that is widely used or known!) and is only used by one group. It should be folded into this group.

One of the demonstrated strengths of an institute is its ability to attract the brightest available scientists. IJM has been very successful in this regard. A call for new teams received 150 applications from very different backgrounds and origins. A selection committee, with the help of the SAB and external referees led to the selection of 10 candidates who were interviewed. At least four were offered a group leader position, either junior or senior. It appears that most of them have accepted the offer. This reflects the excellent standing of IJM in France as well as the attraction of central Paris and the new lab space at Université Paris Diderot. However, it is commendable that the director assigns a significant portion of the IJM CNRS/University funds to support these young scientists since 25,000€ are automatically attributed to new recruits. However, this is not sufficient to recruit a technician or postdoc and an external source of funding (usually ATIP-Avenir or ANR Jeunes Equipes) is absolutely required to start the lab (which is usually followed by a CR position at the CNRS).

Assessment of the unit's academic reputation and appeal

The IJM is one of the largest Biology lab supported by the CNRS and it is well established and recognized in the scientific world. However, because of the diversity of research themes and the absence of star scientists, it does not appear to be considered as one of the top places in the world for biological research. Although evaluating reputation is not an exact science, there are objective criteria such as publications in top journals or prestigious grants to team leaders or to postdocs. If several postdocs have EMBO or Marie Curie Fellowships (as well as French foundation fellowships), it was very disappointing to the visiting Committee that none of the teams had received a junior or a senior ERC grant. By comparison, ETH in Zurich has 50 of them! It also does not seem that there is an EMBO YIP investigator at the moment at IJM. This might be due to a lack of self-confidence on the part of the team leaders and the Committee encourages the director to strongly push for more applications (it is not even clear whether anyone has ever applied to ERC grants), and to provide technical and intellectual help to the applicants. Several of the younger team leaders are clear and strong candidates. One other cause of this lack of confidence is the absence of very successful senior scientists who can serve as role models for the younger investigators.

On the more positive side, several of the group leaders belong to European networks and many contribute to international conferences and organize them. Several have been the recipients of excellent grants and awards such as Grants from the city of Paris or CNRS medals. Overall, the group leaders are also active on study sections and in reviewing for prestigious journals although few are on editorial boards of high impact journals.

Assessment of the unit's interaction with the social, economic and cultural environment

The incorporation of IJM in the context of the Université Paris Diderot appears to be a success and most of the scientists, even if they are CNRS or INSERM employees, feel that they belong to a teaching institution and that part of their missions includes an outreach to the community. The AERES docket filled by the various groups clearly indicates that most team leaders and their scientists take this outreach very seriously. This is true for those interested in Evolution who see as very important their role in illuminating the public and avoid the flaws of creationism of "intelligent design". Others contribute to science fairs and manage to talk to a larger public audience. It is not clear how these activities are coordinated by the director but the IJM is active in outreach to younger students. One of the labs has organized an EMBO course to teach other scientists their technology. This recurrent course is likely a very intensive ordeal and requires very strong commitment from the scientists involved.

The recommendation for this topic would be to appoint a team leader or a Maître de conference of Professor with the duty of promoting and coordinating outreach activities.

Assessment of the unit's organization and life

The organization of the IJM is one of its strong points and it is extremely rare to have a general consensus from all personnel, team leaders, technicians and engineers, PhD students and postdocs, that they are in an institute where the administration listens to their needs, and the director is always available to solve any potential problem. On the other hand, the director is not perceived as weak but his decisions are considered as strong and fair. The fact that the IJM is concentrated in one tight building is a strong positive, especially after many years of decay at Jussieu where the infrastructure was left in disarray, with the laboratories separated behind close doors (with no elevators!). The sense of happiness and pride of belonging to IJM was extremely well received and even the AERES evaluation was perceived as a positive point for the IJM.

The IJM is organized with collegiality and transparency of decision-making and funding allocation. The director takes the responsibility of final decisions but these decisions are clear and they are in fact posted publicly in the office of the IJM secretary. The director is assisted by a deputy director who is in the process of being officially appointed. There is a Direction council where five group leaders meet every other week, with their term being renewed after two years. The Institute Council, a Recruitment Committee and an Equipment Committee (and more) all appear to function well, democratically and are perceived as fair.

As pointed out by the representative of the University, one point to improve is the more general integration of IJM in the Université Paris Diderot whose Scientific Council does not appear to have enough representation from the scientists at IJM. Their needs might therefore not be well represented for the university that provides very substantial funding to IJM. For instance, teaching discharges or the attribution of technical positions could be better argued by IJM scientists if they were to be present at the Council.

In conclusion, a very nice new building, a very open, strong and popular director and a transparent organization make IJM a happy place to work, thus providing the best conditions to succeed.

The IJM has lively scientific animation with internal seminars once per week, chalk talks twice a month. The prestigious Monod lectures are held every 6 weeks and attract international renowned scientists. An annual meeting is also organized and there are several active discussion clubs (evolution, imaging) that extend beyond IJM. It is clear that the team leaders work well together and with the direction and an illustration was the excellent preparation of the visit of this Committee. The individual dockets were well prepared and the presentation referred to the same charts and diagrams of organization and this coordination helped tremendously in the review process.

The IJM website (http://www.ijm.fr/en/ijm/home-page/) is available in both French and English and appears to contain all required information about the IJM, including some promotional material about recent high profile work from its members. The individual pages for each member of the IJM are homogenized, rendering scrolling through the pages easier.

Assessment of the unit's involvement in training through research

Laboratory members are involved in training via teaching at the Université Paris Diderot, or at Paris 6 (with a past rivalry between the two universities being felt as less important). A good number of scientists at IJM are “enseignants-chercheurs” including team leaders, and even its director. Teaching is indeed an important part of the life of IJM for all scientists, and it is clear that most CNRS employees contribute a significant amount of their time collaborating with their teaching colleagues to classes at various levels, mostly M1 or M2. This is reflected by the number of Masters and PhD students in the labs of IJM, but also of undergraduate students who feel that they can learn Science by working in IJM labs. It is not clear, however, how PhD students are part of a ‘class’ and how they learn foundations of their own field but also become familiar with other fields of research.

Interestingly, the building is not enclosed and separated from the rest of the campus, and during the visit, several University events were held in the lobby of the building. As mentioned above, one of the team leaders has taught twice a laboratory EMBO course for several weeks in his lab that must have required a very important investment in time and preparation. Therefore, teaching is a strong point of IJM.

Assessment of the five-year plan and strategy

The IJM is a relatively young institute when it comes to the age of its team leaders. The move to the new location has allowed clearing out inactive teams. In fact, several of the groups currently at IJM were not evaluated by the visiting Committee, because they were moving to other institutes more appropriate to their themes of research, were closing, or the team leader was retiring. Although this youth creates a very dynamic atmosphere of "start-up" at the IJM, it would be important to have more strong senior groups to serve as role models and to provide political help to the younger teams. The turnover is likely to continue with several groups leaving and four new teams (including senior) joining IJM in the coming months. Although the visiting Committee did not evaluate these groups, the director provided clear information about the group leaders and the research topics. The general appreciation is that IJM has been very successful in its latest recruitment and that the team who will join are extremely strong and will contribute to improving further the scientific life of IJM. New recruitments are still on the way.

The five-year plan is to continue the rejuvenation process, to further develop very strong core facilities, to promote more interactions among the groups. It also offers to recruit into the three main themes of the IJM, Genome and chromosome dynamics, Cell dynamics and signalling, and Development & evolution. The general organization of the IJM is excellent and the current leadership should be maintained in order to keep the stability and further improve the positive atmosphere of the place. However, formal mentoring of young teams must be implemented by favouring interactions with senior investigators. This is necessary to help the young team develop and reach the international level that several groups deserve to attain. The five-year term must see many more grants from ANR but also from European institutions, including ERC, both at the junior level (several groups should be excellent candidates) and senior level.

Another aspect of this plan is to attract international PhD students and postdocs, which requires raising funds from the laboratory, or directly by the postdoc. This will mean to continue the trend to obtain more EMBO and Marie Curie Fellowships. Announcements for team leader positions should also reach internationally: even if the start-up funds that are offered are not to the level of other countries, young teams can be well supported by ATIP-Avenir and by multiple foundations, as well as by the fund attributed by the director.

Finally, the teams will be encouraged to collaborate and to take advantage of the core facilities. One aspect that must be developed is genomics, with DNA and RNA sequencing; even if the cost and efficiency of establishing a sequencing facility in the IJM might not be the optimal situation, there is an important need for helping the teams to utilise bioinformatics and data processing in their research. Therefore, the five-year plan must include the development of a bioinformatics platform built around a strong team working in genomics of systems biology.

Interactions with other institutes at the Université Paris Diderot were rarely if ever mentioned while links should be established with, for instance, the Center for Epigenetics and Cell Fate. In general, a better integration and participation of scientists to the structure of the Université Paris Diderot would allow the building of a culture of a University with its Masters and PhD programs.

4 • Team-by-team analysis

Team 1 : Evolution and development of metazoan

Name of team leader: Mr Guillaume BALAVOINE and Mr Michel VEERVORT

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	2	100 %
N2: Permanent EPST or EPIC researchers and similar positions	1	1	100 %
N3: Other permanent staff (without research duties)			
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	2	100 %
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	6	5	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	3	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the team		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

This excellent team 1 develops experimental and phylogenetic approaches to tackle the question of how animal development has evolved. The team mainly focuses on the annelid P. dumerlilii that provides an attractive model for Lophotrochozoans, the third branch of bilaterians that has remained almost entirely unexplored.

Team 1 has made major contributions to the field, providing, through the study of Platynereis development new insights into the evolution of embryonic segmentation and the development of the nervous system, to a large part through a comparison with insects/worms and vertebrates. For instance, its breakthrough results support the model that the last common ancestor of protostomes was segmented with a metamerism similar to extant insect parasegments, and that the annelid nervous system provides a paradigm to approach the origin of the chordate neural tube. They extended their studies to the sponge Amphimedon, showing that parts of the neurogenic gene network were likely already functional in the very first metazoans.

This small group has published an impressive number (24) of articles over the period, including in the highest profile journals (Science, Curr Biol., Cell), although often in collaboration, in particular with the group of Detlev Arendt.

Assessment of the team's academic reputation and appeal

The team has succeeded in rising major funding (2 grants from the highly competitive ANR-Blanc program) and maintains active collaborations with international experts in the fields they explore.

Team members are well recognized in France and abroad, being solicited for international conferences and societies, editorial and evaluation activities, as well as scientific/academic committees. Team 1 is member of the laboratory of excellence (labex) “Wholam” initiative.

Among distinctions, one of the co-heads was nominated member of Institut Universitaire de France and of the scientific council of the European society for Evolutionary Developmental Biology.

Assessment of the team's interaction with the social, economic and cultural environment

One remarkable feature of this team is an active implication of each member in diffusing scientific knowledge and concepts (notably of evolution theories) to the society through several lay public communications in French media and through conferences.

Assessment of the team's organization and life

Given its small size and its recent achievements, it is clear that the team has coherent and logical scientific goals. In addition to regular lab meetings, Team 1 organizes a joint journal club with Teams 10 and 15, sharing their interest in evolution with other members of the IJM.

The two co-heads actively contribute to the IJM scientific life as current and past member of IJM direction committee and council.

Assessment of the team's involvement in training through research

5 PhD students have being trained in Team 1, and have published two seminal papers including one where a student is first/co-first author. A former student obtained an assistant professor position (MCU) at the Université Paris Diderot.

Two team members are member of the Université Paris Diderot and actively contribute to teaching and organizing the International Master programs. The two current graduate students have significant teaching duties; one of the co-head, a CNRS fellow, is also involved in courses at Paris 7 and other universities.

Assessment of the five-year plan and strategy

The general aims of the project focus on two well-identified and important questions, supported by solid preliminary data and published results. Originality and broad interest are two main features of this research. The team capitalizes on a demonstrated expertise in the analysis of Platinereis development, to address the nature, mechanisms and evolution of segmentation and of neurogenesis. In addition to classical approaches, the scientists aim to embark into novel high risk-high payoff genome-wide assays, as well as more in depth analysis of cell behavior making use of high-resolution imaging. It is not entirely clear how the group is prepared to handle the huge amount of data that will be produced by high throughput sequencing.

The second research direction is, however, more hypothesis-driven. Therefore the proposed program is well balanced between ambition and feasibility. This team has a clear analysis of its activity and proposes strategies to maintain funding and manage the recruitment of additional staff members. All together, the proposed works should produce significant advances in our understanding of the evolution of segmentation and nervous system architecture in animals.

Conclusion

- This team represents a major strength of IJM, developing research at a high international level. In France, it constitutes the link between the past generation of a well-known scientist who died prematurely, and a new school of recently established groups focusing on the evolution of animal development, some of them former students of this group. As proposed in their own analysis, the visiting committee encourages their efforts in further integrating international networks as a way to secure funding in the fast moving landscape of basic research in France, as well as to attract foreign fellows.

- The group has a very successful program, publishing excellent papers in some of the highest profile journals.

- The integration with the international community and the collaboration with a laboratory at EMBL are also very strong points.

- Given the broad interest of the work of the group, its outstanding contribution to the field, its exquisite originality, and the investment in teaching/diffusing modern aspects of evolution, it is important that either one of the supporting organizations provide a position for technical support, which is essential for the future success of this team.

4 • Team-by-team analysis

Team 2 : Pathology of DNA replication

Name of team leader: Mr Giuseppe BALDACCI

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	3	3	100 %
N2: Permanent EPST or EPIC researchers and similar positions	1		100 %
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	6	5	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		1
Theses defended		
Postdoctoral students having spent at least 12 months in the team		1
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The aim of the research is to improve the understanding of molecular mechanisms leading to various types of "DNA replication stress". Work in several laboratories worldwide indicates that replication defects are likely the major cause of genome instability in eukaryotic cells. In recent years two members of Team 2 addressed related issues in the Schizosaccharomyces pombe model system and in human cells. One group also developed in vitro replication systems suitable to analyse in a quantitative way the role of individual proteins and of specific biochemical conditions in replicating DNA regions containing trinucleotide repeats.

The work carried out by Team 2 during the period evaluated is of high quality and led to important theoretical and methodological breakthroughs. In the period 2007-2012, the members of the team have been authors in 31 research articles in peer-reviewed journals (plus four reviews). In 10 of them, team members are in the first or last authorship position.

The journals chosen for publication are quite different from each other since two of the team members are molecular biologists while the third member is a human geneticist. The team includes an emeritus research professor expert in virology with major teaching and scientific editorial responsibilities. In each of the respective fields, some of the publications are on top ranked journals such as Mol Cell, Genes & Dev, PloS Biology, PloS Genetics, PNAS, Nat Genet, Virus Res, etc.

Assessment of the team's academic reputation and appeal

Two members of Team 2 have a long-standing expertise in research and teaching. One of them is an emeritus research director lecturing at the Ecole Normale Supérieure (France) and in South American universities.

Two members recently obtained a position as Assistant Professors at the University Paris-Diderot. The team members collaborate with scientists internal and external to the IJM. One member worked previously in another team within IJM and a fruitful collaboration between the two groups can be envisaged. This collaboration can re-enforce both teams in a synergistic way.

One team's member actively collaborated with well-recognized research groups in Europe and USA especially on projects carried out using the S. pombe model system and such collaborations led to joint publications. Two previous members of the team (1 CNRS CR1 researcher and 1 technician) left the group while two new young assistant professors joined, although they are heavily engaged in teaching. The team should improve its capacity to recruit post-docs and students, particularly from abroad, to reach the ambitious goals presented in the five-year plan. The two senior members of the team act as reviewers for many international journals and public and private organizations and charities in France or abroad and one of them is member of the editorial board of Biochimie. Members of the team have been invited to give seminars and lectures in various institutions in France and Europe.

Assessment of the team's interaction with the social, economic and cultural environment

One member of the team is the Director of the IJM, Chairman of the Scientific Council of the Ligue National contre le Cancer, and acts as a member of the CNRS Scientific Council and Executive Board, playing a significant role in defining the scientific policy of CNRS. As such, this activity impacts on the social, economic and cultural environment.

Outreach activities capable of increasing the socio-economic and cultural environment should be improved.

Assessment of the team's organization and life

The team is presently composed of one emeritus professor, three staff scientists and one graduate student.

They interact with each other, share a common research program and facilities, discuss together the results and program future experiments in weekly lab meetings.

Each team member has unique expertise, as indicated by previous research experience, and they should be able to integrate their competencies in a synergistic way.

Assessment of the team's involvement in training through research

Due to their teaching duties at the University Paris-Diderot the team members have been involved in training through research activities of four students from 2009 to 2012. The capacity to recruit undergraduate and PhD students must be increased in the future to perform the work presented in the five year plan of the team.

Assessment of the five-year plan and strategy

The future 5-year plan is challenging and ambitious. The team proposes to concentrate its effort on human and DT40 cells following three main directions: 1) genome-wide identification of replication pause sites in human and DT40 cells essentially by ChIP on chip analysis; 2) use of DT40 cell lines to characterize cis and trans elements involved in repetitive DNA stability; 3) analysis of the molecular mechanisms linking increased genome instability to specific human diseases using lymphoblastoid cell lines derived from patients. This last aim is linked to the expertise of a human geneticist who recently joined the group.

The project is consistent with previous work and competences of the team members. The proposed experimental strategy combines genome-wide analysis, bioinformatic analyses and more classical molecular biology, cellular biology and biochemical approaches.

The SWOT analysis is appropriate. The project is ambitious but feasible, if the team can recruit scientist in the close future to perform the work.

Conclusion

- Strengths and opportunities:

The team includes experienced as well young investigators with complementary expertise. The 5-year future plan addresses relevant scientific questions with state of the art scientific approaches and cellular models.

- Weaknesses and threats:

The group is quite small with few young scientists working at the bench to carry out an ambitious project. Indeed, the three most active members of the group are overwhelmed with administrative functions and teaching. The group needs to be reinforced by recruiting PhD students, post-docs and new staff members dedicated to the proposed project.

The amount of money is limited, but a new grant has been recently awarded to the team and submission of new grants is under way.

- Recommendations:

The team needs to recruit new students, post-docs and permanent personnel. If possible, the two assistant professors in the team should dedicate more time to research by decreasing their teaching commitment.

4 • Team-by-team analysis

Team 3 : Mitochondria, metals and oxidative stress

Name of team leader: Mr Jean-Michel CAMADRO

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	4	4	100 %
N2: Permanent EPST or EPIC researchers and similar positions	2	2	100 %
N3: Other permanent staff (without research duties)			
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	7	7	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the team	1	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	5	6

• Detailed assessments

Assessment of scientific quality and outputs

Team 3 includes 1 DR2 CNRS, 2 MCU P7, 1 MCU P6, 1 DR1 Emeritus, 2 PhD students. Since 2007, 1 CR1 has left the lab while 2 MCU have joined the group. Team 3 is working on frataxin, a ubiquitous protein associated with Friedreich ataxia pathophysiology. Despite many laboratories throughout the world have studied frataxin for about a decade using different approaches and different models, the actual role of frataxin remains uncertain. Lack of frataxin induces defects in Fe-S biogenesis, iron homeostasis in some organisms but not in bacteria, and oxidative stress but it remains an enigma which comes first.

The group has contributed significantly to our understanding of frataxin and obtained data that might open new avenues and perspectives. In particular, they contributed to rule out a most popular hypothesis, i.e. frataxin is the iron source for Fe-S clusters. Also, Team 3 revealed that the iron form accumulating inside mitochondria of frataxin-deficient yeast cannot be mobilized. Importantly, they suggested a link between frataxin deficiency and mitochondrial protein modification (acetylation, nitrosylation, glutathionylation).

Team 3 has published 35 papers since 2007, 13 of which being contributions to collaborations the group does not lead. Among these 35 papers, publications are in Human Molecular Genetics, Mol Cell Prot, JBC, Biochem J, Free Radicals Biology and Medecine, Advanced in Aging Research, Genetics.

The group has been quite successful in raising external funds (ANR, FP7, ARC) and inside University Paris-Diderot. The group has also been successful in getting funds for training 6 Thesis students.

Assessment of the team's academic reputation and appeal

Team 3 does have a real expertise in frataxin and iron metabolism and is well established in the Fe-S/iron community at the international level. It has a long-standing collaboration with a leader group in Philadelphia (USA) with over 20 joint papers. A new collaboration with another group in Prague (Czech Republic) is beginning on iron metabolism in parasites supported by ANR.

Assessment of the team's interaction with the social, economic and cultural environment

The group participates to Association Française Ataxies Friedreich, including public awareness seminars, discussions with patients and families. The group also participates to various public events such as Maths in Biology, funded by the Paris City.

Assessment of the team's organization and life

Besides traditional group meetings and careful supervision of Thesis students, the Committee appreciated that Team 3 leader allows his colleagues to set up collaborations on their own, as long as they fit in the main scope and objectives of the group. The group benefits from this team spirit and, as a consequence, productivity and fund raising might have significantly increased.

Assessment of the team's involvement in training through research

The team is involved in training students at all levels.

Assessment of the five-year plan and strategy

Team 3 project will remain centred on frataxin but will also branch out towards the general issue of iron metabolism. The project on frataxin will be a follow up of current studies with emphasis on setting up a eukaryotic model amenable to reverse genetics, in order to develop screening of compounds that could “save” frataxin deficient yeasts and Drosophila. Several of the sub-projects will be performed as collaborations such as (i) the protein modification issue will be studied with an expert in the field, working in another Parisian lab, and the two groups will aim at characterizing the in vivo dynamic of nitrosylation and glutathionylation in frataxin-deficient cells; (ii) The study using Drosophila is carried in collaboration with another group from Paris-Diderot and (iii) Another series of projects, all funded, will aim at characterizing iron import and storage in a series of eukaryotes of medical and/or ecological interest. Last, efforts towards modelling iron homeostasis in yeast were developed in the recent years in collaboration with a biomathematic team at IJM.

Team 3 has now reached both critical mass and expertise to engage in all these seemingly different projects, which are actually all tied up to the question of iron homeostasis in living organisms, a key question for many aspects of biology.

Conclusion:

- Strengths and opportunities:

-Importance of the topic of research, namely iron homeostasis control in a series of different organisms with different interest ranging from ecology (microalgae) to medical (frataxin and Friedreich ataxia) via basic research approaches (protein modification in yeast).

-Great expertise and knowledge in iron biology.

-Great capacity to engage in collaborative effort with teams showing complementary expertise.

-Funds secured for most projects.

-Team of good size (6 permanents).

-Excellent publication record.

- Weaknesses and threats:

- Four permanents are also teaching, which takes a lot of time off research.

- No post-doctoral researcher.

- Recommendations:

- Team 3 needs to enhance further its visibility by aiming at publishing in high-profile journals in the next period.

4 • Team-by-team analysis

Team 4 : Regulation of cell fate specification in the mouse

Name of team leader: Mr Jérôme COLLIGNON

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	100 %
N2: Permanent EPST or EPIC researchers and similar positions	3	3	100 %
N3: Other permanent staff (without research duties)			
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	2	100 %
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	7	6	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	1	2
Postdoctoral students having spent at least 12 months in the unit	2	2
Number of Research Supervisor Qualifications (HDR) taken	1	1
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

Nodal signaling has been implicated in numerous roles in developmental patterning for the past decade and has been studied extensively by numerous prominent groups. Team 4 has provided further insights into the role of this signaling pathway at early stages of development, both during, and prior to gastrulation, at stages as early as preimplantation. While the investigators have contributed substantially to our understanding of both these early events and to nodal signaling in particular during previous review cycles, the achievements over the past five years have been significantly more modest. In particular, their contributions have largely come in the form of a series of strategic collaborations whose findings, although relevant and complementary to the interests of this research group, are often not centered precisely on the directions they are most interested in tackling. Examples of such progress are the mapping of movements of the ICM, construction of useful early transgenics for the identification of enhancers and study of an endolytic receptor Cubilin, which are all interesting but somewhat tangential. Team 4 studies of non-neural ectoderm, microelectroporation and work on Notch signaling, while all interesting, represent promising beginnings but rather preliminary findings, all of which have been reported to a greater or lesser extent by others. While by their own narrative, the group has encountered more than its share of misfortunes over the past funding cycle (e.g. with the move of the animal facility), it is difficult to argue from their trajectory that a significant improvement in their productivity will be soon forthcoming. In fairness they have recently published one paper in PLoS One, one in Dev Biol and two in Development. Only two of these represent work primarily centered in this laboratory. The two reviews listed are over five years old and relate to the previous rather than to the present work of Team 4.

Assessment of the team's academic reputation and appeal

The most impressive aspect of Team 4 academic reputation comes from the list of national and international collaborators they have attracted, even though several of these do not seem to have led to publications. The nature of the collaboration should be explicitely stated. International : groups at Sloan-Kettering, New York, USA ; EMBL, Heidelberg, Germany ; KCL, London, UK ; HGU, Edinburgh, UK ; SBC, Coventry, UK ; Gurdon Institute, Cambridge, UK and CHG, Leuwen, Belgium. National : GreD, Clermont-Ferrand ; Institut Pasteur, Paris ; INM, Montpelier ; LPN, Marcoussis ; INRA, Jouy-en-Josas ; IdV, Paris ; CEDC, Paris ; LOB, Palaiseau. Within Institut Jacques Monod Teams 5 and 6.

While the group has continued to attend and present at national and international meetings, the PI has given virtually no high profile talks during this funding period. The PI has however attended a number of meetings without proceedings and hence has remained somewhat active in the scientific community. Invited conferences: international (1); selected conferences: international (9); invited seminars: international (4), national (3).

Assessment of the team's interaction with the social, economic and cultural environment

Not explicitely presented.

Assessment of the team's organization and life:

Team 4 leader has supervised three students during this period, one of which has graduated. In addition three masters and four undergraduate interns were trainees in the laboratory, showing that the team leader has remained active in promoting academic support within his community.

Assessment of the team's involvement in training through research

Team 4 head teaches Master courses in France and European Union (ENS Paris and Lyon, Univ Paris-Diderot, UPMC, Sweden, Italy, Spain). He has mentored the work of three PhD and four undergraduate students, one technician. He was reviewer for only one PhD Thesis, and one HDR, which is surprisingly low.

Assessment of the five-year plan and strategy

The central premise of the present project is that Nodal signaling has profound and unappreciated roles in preimplantation embryos. Towards this end the investigators have set out to examine the function of this signaling pathway in this context. Although a number of the strategic collaborations laid out by the investigators show considerable promise towards exploring this objective, each of the presented pieces of data represents more of a starting point in such exploration than a finishing point. To track fate map and manipulate the early embryos, the investigators uses a variety of methods ranging from the identification of Nodal enhancers and using these elements to target cells in the early embryo, to micro-electroporation methods which allow the introduction of genes in this same context. In addition, the investigators include vignettes aimed at looking at Notch signaling and the endocytic receptor cubilin, but it is never clear how these experiments fall into a larger more coherent plan. Even the most promising of the manipulations, the removal of targeted bits of non-neural ectoderm positioned anterior to the neural plate, while giving tantalizingly interesting preliminary results, is not brought into a larger context. While some enthusiasm is raised by the relatively recent publication of four papers, only two of these are directly relevant to the investigators goals and these papers date back to studies done at the very beginning of this proposal. As such, although one remains sympathetic to the large number of unfortunate set backs encountered by Team 4, it is hard to have much confidence in their ability to overcome these difficulties and moving forward.

Conclusion:

- Strengths and opportunities:

Team 4 has a strong developmental biology background and a solid history of doing work on Nodal signaling. They outlined a promising and ambitious proposal during their previous submission of this work. They have participated in a wide array of collaborations, most of which bring to bear powerful new methods for addressing the questions they hoped to tackle in their previous project. In their favor they clearly continue to be a supporter of education at both the graduate and organizational level within their institute and within France in general.

- Weaknesses and threats:

While the original notion that Nodal signalling has a role in the pre-implantation embryo was good, Team 4 leader has not made a very compelling case that he has devised a strategy to pursue this aim. His work focuses on, and in fact is critically dependent upon the HBE-enhancer he has identified which (i) may or may not mark a subpopulation of epidermal cells in the early embryo (ii) the enhancer itself, may or may not be critical to early development of the embryo. With respect to the later of these experiments, he has made a floxed enhancer allele that should let him address this question (iii) although he proposed genetically fate mapping this population by making a transgenic of the HBE-enhancer with CreER, this approach is technically challenging and may not be feasible. In addition he has proposed a number of approaches such as micro-electroporation or micro-ablation in early embryos, which while technically excellent, are not supported by clear scientific goals to which these approaches will be applied.

- Recommendations:

Taken together, Team 4 leader is clearly at a challenging juncture of his career and should perhaps spend time rethinking his approaches, particularly if the HBE enhancer removal does not provide a robust phenotype that fully supports the role he predicted.

4 • Team-by-team analysis

Team 5 : Macromolecular complexes in living cells

Name of team leader: Ms Maïté COPPEY-MOISAN

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions		1	
N2: Permanent EPST or EPIC researchers and similar positions	3	2	100 %
N3: Other permanent staff (without research duties)	1,5	1,5	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2		
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	6,5	4,5	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

Team 5 is a multidisciplinary group, which uses a large array of methodologies including various microscopy techniques (FRET-FLIM, FCS, two photon…) as well as physical tools such as hydrogels and optical traps. The broad research interest lies in the field of mechanotransduction, and particularly the role of physical forces in adhesion, polarity and signalling.

The publication output of the team has been good: several publications in reputable specialized journals such as the Biophysical Journal and key contributions to high-impact collaborative studies published in high-impact journal such as Dev Cell and PNAS.

There are some interesting ongoing (unpublished) research projects focussed on the role of mechanical forces in focal adhesion dynamics, polarity establishment, and netrin signalling as well as chromatin structure, which should yield high-quality publications.

The research topics are, as expected from a unit with a strong technology development activity, rather diverse as they are influenced by collaborations within and outside the institute. These collaborations have proven very successful, notably with Team 9.

The team has been successful in attracting funds necessary to support their broad technology portfolio. Several of these grants have benefitted the IJM and the research community through the ImagoSeine platform.

Assessment of the team's academic reputation and appeal

Team 5 enjoys a strong reputation in the biophysics field, as witnessed by invitations for the PI to speak at international conferences. Methodologies developed by the team (for example for FRET-FLIM analysis) are widely used in the field. The PI has taken a very important leadership role in the establishment of the France BioImaging program and participates to the preparatory phase of the Euro-BioImaging program. Team 5 leader also participates in a large number of advisory boards, both internal and external. The team has been able to recruit several talented young scientists.

Assessment of the team's interaction with the social, economic and cultural environment

Team 5 participated in the “Fête de la science” at Paris-Diderot.

Assessment of the team's organization and life

The team has a weekly lab meeting and its members participate in Institute seminars. Team 5 leader heads the IJM microscopy core technology platform and several team members play an important role in transferring microscopy technologies from the team to the core platform, making it available to others in the institute and in the surrounding.

Assessment of the team's involvement in training through research

This is a major strength for this group. The team participates in teaching multiple courses, both at the undergrad and postgrad levels. In addition, the Team 5 clearly plays a crucial role in the IJM, maintaining a cutting-edge technology development programme in microscopy, providing access for groups, both at the IJM and outside, to important technologies such as FRET-FLIM, FCS, super-resolution and two-photon through collaborations and by supporting the ImagoSeine platform. The team has also supervised four PhD students, six Master I and five Master II students in the past five years.

Assessment of the five-year plan and strategy

The main challenge for the coming five-year term will be to continue the collaborative and technology development aspects of the work, while maintaining competitiveness in the increasingly crowded field of mechanotransduction. In particular, the upcoming retirement of the PI and the ensuing transition will need to be carefully planned so that the work of the team does not suffer. As the team has successfully recruited two senior scientists, a smooth transition is likely.

The future research proposal is very ambitious, both for basic research and for technology development. The research proposal comprises four long-term aims (netrins in mechanotransductions, mechanics of adherens junctions, nuclear mechanotransduction through nesprins, chromatin states), as well as the continuation/wrapping up of several ongoing projects (focal adhesion dynamics in mesenchymal stem cells, influence of mechanical forces on cell polarisation). On the technology side, several exciting development and technically challenging projects are proposed, in particular further development on optical traps, FLIM (in vivo) and two-photon approaches, as well as combining SPIM with super-resolution (PALM) imaging.

In general, this is a topical, exciting and highly ambitious future proposal. The new recruits in the group will provide strong expertise in the relevant field, and synergies will be possible with new PIs coming to the IJM. One concern is that this proposal may represent too much work for a relatively small group, therefore the PIs (present and future) are encouraged to carefully consider their research focus. Can they stay competitive in their four research areas, one of which, the nesprin work, is new to the lab. The group has plans for further grant applications (ATIP for example), but it will nevertheless take time to build up numbers.

Conclusion:

● Strengths and opportunities:

- Strong expertise in a variety of optical and biophysics techniques.

- Highly valuable support of the IJM microscopy facility and other IFM groups through collaborations.

- Success in attracting highly qualified senior scientists.

- Very relevant and interesting research proposal.

- Leadership position in a national microscopy initiative.

- Many possible synergies between the lab and other IJM groups.

- Continued microscopy development work and new research directions.

● Weaknesses and threats:

- Research project may be too broad for a relatively small group.

- Competitive field, particularly the morphogenesis work. The committee encourages the lab to consider alternative systems on top of the Drosophila embryo, in which several large labs are already operating. Particularly collaboration with Team 11 in the tracheal system might be an interesting avenue.

- The potential retirement of the PI will mean possible loss of expertise.

- It is a possibility that the responsibility of the microscopy facility diverts time of a new facility director away from research program.

● Recommendations:

Overall, Team 5 combines an excellent technology development arm with a competitive multidisciplinary research program, as well as supporting the microscopy needs of the IJM (and external groups) through collaborations and support of the microscopy core facility.

The new research directions proposed by the two recently recruited senior team members are exciting and fit well in the context of the recent recruitments made by the IJM and the mechanobiology/biophysics field. The committee strongly recommends continued support for the Team 5 and the new research projects developed by the group.

4 • Team-by-team analysis

Team 6 : Non-conventional functions of nuclear pores

Name of team leader: Ms Valérie DOYE

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	3	3	100 %
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	1	100 %
N6: Other contractual staff (without research duties)		1	
TOTAL N1 to N6	7	6	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the team		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

Team 6 studies the non-conventional roles of nuclear pore complexes (NPC) in cell cycle progression and nuclear metabolism. Their recent work has led to discoveries in NPC biogenesis, in the interplay between NPCs-kinetochores and NOCs-centrosomes, in the connection between cell differentiation and nuclear metabolism and in the regulation of protein SUMOylation in an NPC-dependent manner. The field of study is central to a wide variety of research areas, such as Cancer, Biomedicine, Cell Biology, Developmental Biology and Genetics. The results obtained by the group are relevant and have been published in high-impact journals, such as EMBO J, J of Cell Biol, Dev Cell and Mol Biol Cell. In the last 5 years, team 6 has published 7 papers and 3 reviews. The PI appears as senior author on 5 of the publications (EMBO J in 2007, Mol Biol Cell in 2007 and 2008, J Cell Biol 2010 [co-senior] and 2011). The PI appears as senior author on the 3 reviews.

Assessment of the team's academic reputation and appeal

Team members are involved in collaborations with national (8 different groups, 3 of them from the IJM) and international (8 from ETH-Switzerland, EMBL-Germany, Japan, Greece, Sloan-Kettering-USA, Emory U. USA, Columbia U. USA, Fox Chase Center USA) groups.

Team 6 shows an excellent record of successful fund raising. It has enjoyed grants from national and international organizations adding up above the 1 M€ mark. The team has also participated in grants for core services at the IJM and in scientific infrastructure grants for network initiatives at national and international levels. Awards include the CNRS silver medal to the PI in 2009 and the Price from the Conseil Général des Yvelines, awarded by the Scientific Council of the Ligue Nationale contre le Cancer, also in 2009.

Team members have participated as invited speakers in 10 international conferences and have imparted 4 seminars abroad and 6 seminars in France. The group leader has co-organised symposia in France and in the US (Stanford, 2008). The group leader acts as reviewer for a number of relevant journals, including Cell, Dev Cell, Nat Cell Biol, PloS Biol and Genes & Dev, for funding bodies in several countries and sits in the advisory boards of a number of national and foreign organisations. The PI was Head of the Cell Biology Programme at the IJM from 2009-2010 and is a member of the IJM Council since 2009.

Assessment of the team's interaction with the social, economic and cultural environment

Members of the team participate in public events such as “Science en fête” (Science day). The PI was a member of the scientific delegation of the U. Paris-Diderot to China in 2011. The team contributed to a general audience book entitled Cellule, étonne-moi! in 2007 and hosted a number of secondary school pupils to provide them with a first experience on active research.

Assessment of the team's organization and life:

Team 6 is composed of 4 permanent staff (1 DR1, 1 CR1, 1 CR2 and 1 AI). Currently, the team is participated by 3 post-docs, 1 PhD student and 1 researcher. It seems solid and sound. The team does not seem to suffer from excessive teaching load, as the group only reports 15 hours/year of teaching and their participation in practical training for 2 days/year. The research-training load, however, is heavier (see below).

All the protocols, reagents, oral presentations, fellowships and grant proposal are registered in a common database. The team seems to implement a schedule of lab meetings and journal clubs. Team members participate in an internal seminar series at the IJM.

Assessment of the team's involvement in training through research

Team members are involved in PhD supervision (4 students, 3 of them have already got their doctorate), Master-2 supervision (5 students, 4 of which did their PhD in the laboratory) and in undergraduate supervision (7 internships, 2 of them from abroad). One of the technicians in the group completed the equivalent to a Masters-2 grade while working in the team.

Assessment of the five-year plan and strategy

Traditionally, nuclear pores complexes (NPCs) have been described to regulate nucleo-cytoplasmic exchange. NPCs are large protein assemblies composed of approximately 30 distinct proteins termed nucleoporins or Nups. The work of Team 6 and others, however, has allowed the identification a number of important roles played by Nups in other cellular processes such as cell division, cell differentiation, genetic stability, and gene regulation.

Team 6 pioneered the analysis of the vertebrate Y-complex, the major subunit of nuclear pores, and uncovered its functions in NPC assembly, its requirement for various aspects of cell division, and its implication in cell differentiation during early embryogenesis. In addition, genetic screens allowed the team to identify previously uncharacterized proteins as well as functional connections between nuclear pores, and sumoylation processes, DNA repair, and messenger ribonucleoparticle (mRNP) metabolism. The current proposal intends to deepen their understanding of some of these processes and to explore novel functions for NPCs. In summary, they propose 1) to characterise the contribution of yeastPom33/Per33 and mammalian TMEM33 to NPC biogenesis and cytoskeleton dynamics; 2) to study the role of the mammalian Y-complex in the coordination of cell division and differentiation mainly in mouse embryonic stem cells (ESCs); 3) to explore the intranuclear dynamics of the Y-complex and Nup98 and its oncogenic fusions; and 4) to investigate the contribution of NPC-dependent sumoylation processes to the assembly, metabolism and trafficking of messenger ribonucleoparticles (mRNPs).

The strategy outlined in the proposal is sound and based on abundant and relevant preliminary data. The host laboratory harbours the necessary experience and has access to the techniques and reagents required to carry out the proposed experiments. In addition, the team is well connected with national and international groups, so in the event of the need of future technical developments (as recognised by the PI in her statement) related to stem cell biology or cell differentiation studies, the group should be able to find advise and help form collaborators. The committee members think that the planned strategy provides enough experimental options to allow the researchers to accomplish the proposed objectives in the event of unexpected drawbacks. Undoubtedly, the past experience of the team, together with the collaborations already established, should guarantee this.

Conclusion:

- Strengths and opportunities:

Some of the proposed objectives can be considered more straightforward than others, but this should not be seen as a negative aspect of the proposal. For instance, the studies on the role of Pom33 and TEMEM33 in NPC assembly and cell proliferation fit very well with the previous work of the host team, and they should yield interesting results in the short term. In contrast, the other 3 objectives imply techniques and biological problems that may not be that familiar to the team members. Considering the tradition of the group, its publication record and the quantity and quality of the preliminary data, there is a strong potential for the proposal.

- Weaknesses and threats:

None of great importance. Perhaps, it is worth mentioning the risk and uncertainties intrinsically connected to the new directions of research proposed in the 5 years plan. Likely, this threat will be overcome by appropriate leadership and funding.

After hearing the presentation of the group leader, it became clear to the visiting committee that the PI has the capacity and skills to lead the project and to be as productive as she has been in recent years.

- Recommendations:

Strong support.

4 • Team-by-team analysis

Team 7 : Epigenetic regulation of genome organization

Name of team leader: Ms Sandra DUHARCOURT

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	100 %
N3: Other permanent staff (without research duties)			
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2	100 %
N6: Other contractual staff (without research duties)	2	2	
TOTAL N1 to N6	5	5	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	2
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		1
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The research aims to unravel the epigenetic mechanism(s) that governs genomic organization and the reorganization thereof in the unicellular organism Paramecium tetraurelia; with the overarching aim to reveal and understand concepts in chromosome structure and stability in eukaryotes. Team 7 project builds upon work previously performed by the PI when employed at IBENS (as part of the team of Prof. E. Meyer). The main question is how the generation of a somatic nucleus (MAC) out of a micronucleus is regulated. What are the genetic determinants? Is there epigenetic regulation of the segments that are to be rearranged? Which mechanisms mark unrelated and non-conserved sequences for processing, and how? These are long-standing questions in the respective field.

Team 7 was very recently established (April 2011) and it is thus difficult to evaluate the progress made at IJM. Recent very relevant contributions of the PI to the field is the implication of two classes of non-coding RNAs, leading to a "subtractive/sequence comparing" model for genome reorganization in Paramecium (Genes Dev. 2008). In a collaborative effort, large collections of fragments that are eliminated in MAC development have been identified (contributor to a PLoS Genetics paper in 2012). Also two reviews have been published (2009, 2012) with the PI as lead author. The group initiated another research line to investigate chromosomal segregation in Paramecium via visualization of the centromeric marker CenH3; key reagents were generated.

Assessment of the team's academic reputation and appeal

Team 7 was very recently established; group members are thus mostly relatively young. The PI, however, has a long track record in this research field; publications on this subject go back to a first author paper in 1995, which allowed her to establish a solid reputation (judged from the steady stream of invitation to speak at and organize meetings) and a strong network of collaborators. The PI and the research seem very well embedded at both national and international level. Especially the community in France working on this particular question is well connected (many joined authorships) but also rather sizable, which can also constitute a threat.

Assessment of the team's interaction with the social, economic and cultural environment

Not developed in the proposal.

Assessment of the team's organization and life:

Good organization for a "starting" team (6 members: PI, one postdoc, one PhD student, one technician and 2 Masters students). Two sizable grants were obtained in 2011, which will allow the group to recruit scientists.

Assessment of the team's involvement in training through research

Seems sufficient and effective. Quite a number of Masters students have been trained (considering the size of the group). It is too early to evaluate other aspects concerning international training networks, etc.

Assessment of the five-year plan and strategy

The future plans/projects are sound and build nicely forward upon previous work: it is consistent, with new lines of research being developed: the strategy is well thought out and reagents and tools are being developed. There will be numerous opportunities to break new ground. The works may answer several conceptual questions: what is the biologic function of IES, e.g. is there a role in centromere establishment? What are the epigenetic marks defining them? How do different putative chromatin marking proteins (e.g. enhancer of zeste homologs) or other proteins acting in small RNA pathways impinge on genome rearrangements in paramecium? Are the determinants evolutionarily conserved?

Mapping the nucleosome positioning and sequencing the MIC genomes of different species are interesting new avenues but heavily rely on bioinformatic analysis as assembling a highly repetitive genome may be a daunting task. It appears that appropriate collaborations have been established.

Conclusion

Some aspects of this team (such as past performance) were not evaluated as the team has only recently been established.

- Strengths and opportunities:

- The work is of high fundamental interest and has great potential.
- Team 7 leader is very well connected at the national and international level; she is a recognized player in the field. This is also illustrated by the fact that she is the coordinator of a multi-lab effort to sequence a range of Paramecium species.
- Upon entry in the IJM, the PI has very quickly established a good-sized team and also has been very successful in securing funds.

- Weaknesses and threats:

- The French community working on this particular question is well connected but also rather sizable, which may lead to competition.

- Recommendations:

- The Committee members felt that the genetic assessment of IES elimination should deserve more attention, as this could constitute a clear competitive advantage over many of the other model systems.

4 • Team-by-team analysis

Team 8 : Cell division and reproduction

Name of team leader: Mr Julien DUMONT

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	100 %
N2: Permanent EPST or EPIC researchers and similar positions	1	1	100 %
N3: Other permanent staff (without research duties)			
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	100 %
N6: Other contractual staff (without research duties)	1	1	
TOTAL N1 to N6	4	4	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		
Theses defended		
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The PI of Team 8 is a young group leader who has only taken his position at IJM at the end of 2011. It is therefore too early to judge the quality of the science coming from his group (as opposed to the work from his post-doctoral studies). Nevertheless, it was clear from his report and presentation that the PI is a very promising young scientist who is highly likely to have a significant impact in the meiosis field. The quality of his work as a post-doctoral fellow was very high.

Assessment of the team's academic reputation and appeal

As above, it is too early to judge the academic reputation of the PI's group, but his reputation as a post-doctoral fellow, and his success in rapidly raising funds, recruiting personnel and obtaining equipment required to establish his own lab should all be highly commended.

Assessment of the team's interaction with the social, economic and cultural environment

It is also too early to assess this at this stage. There are, however, no indications of any problems in this area.

Assessment of the team's organization and life

This seems good, but again it is not possible at judge this properly at this stage.

Assessment of the team's involvement in training through research

This area seems to be strong, but again it is not possible to judge properly at this stage.

Assessment of the five-year plan and strategy

The research proposal is interesting, innovative and clearly explained. The proposal includes a good mix of solid experiments that are very likely to work as well as some more ambitious projects. The PI addresses a fascinating question of the nature of the mechanisms allowing an acentrosomal cell to properly assemble the machinery of segregation of the chromosomal material during division. The project focuses on a particular event — the segregation of the chromosomes. The project follows a direction that follows on from the PI's findings as a post-doctoral fellow, which gave rise to a mechanistic model. The PI will investigate the molecular mechanisms underlying this model to identify the key effectors. The strategy is solid, and the PI already anticipates different possible scenarios, and one is confident that he should be successful in reaching his objectives. It was noted that this project will require strong support in microscopy and proteomics, but this should not be a problem at the IJM.

Conclusion

- Strengths and opportunities:

While it is too early to judge whether the PI will be successful as a group leader, he has made an excellent start and the PI's proposal and presentation were impressive. The PI is aware of the competition in his field and is conscious that the timing of publication might be crucial for the future development of the team. The model is original and offers some specificity, giving him a niche in the field. The PI has available many tools that he developed to address these questions.

- Weaknesses and threats:

The proposal offers to develop an ambitious program; it will be crucial that the PI attracts good scientists to allow him to realize these ambitious goals. It is not always easy for a young PI but being part of the IJM should be a significant advantage. The Institution should be attentive to support the development of the team and to reach his first objectives.

- Recommendations:

The strongest support is recommended for this young PI.

4 • Team-by-team analysis

Team 9 : Membrane traffic in neuronal and epithelial morphogenesis

Name of team leader: Mr Thierry GALLI

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	5	5	100 %
N3: Other permanent staff (without research duties)	1	2	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2	100 %
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	8	9	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	5	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	4	4

• Detailed assessments

Assessment of scientific quality and outputs

Team 9, founded in 1999, is interested in the mechanisms controlling protein trafficking and exocytosis, especially the delivery of transmembrane proteins serving as receptors at the membrane. The studies are conducted in the context of the differentiating neuron and the migrating epithelial cell. The team set up combinations of technical approaches that enable the assessment of the dynamics of vesicular trafficking. The team addresses fundamental questions, concentrating on the v- and t-SNARE proteins, which localize in the donor and acceptor compartments respectively, and mediate membrane fusion. Team 9 obtained several lines of interesting data demonstrating new roles for vesicular trafficking in various processes. The two major publications of the group implicate VAMP2 in the response of axon terminals, the growth cone, to environmental cues guiding axon navigation (J Cell Biol, 2012), and the identification of new binding partners of TI-VAMP which allowed them to delineate a molecular network regulating trafficking (Dev Cell, 2012). A third important publication of the group (J Neuroscience, 2012) reports metabolism modifications as well as behavior defects in mice lacking VAMP7.

The team also contributed to a significant work in their report of a transmembrane protein Vezatin that participates in dendritic spine morphogenesis (J Neuroscience, 2012).

Overall, the quality of the team is excellent.

Assessment of the team's academic reputation and appeal

The PI has a solid reputation and is considered as an expert in his field. He has been invited to give many national and international conferences (20 since 2007). The other team members also have a very good list of invited conferences.

Team 9 PI built over the years a very solid network of collaborations. He attracted several post-docs, and obtained positions for young researchers, which reflects the commitment of the institution to support team development (Three young scientists have been recruited since 2007).

He is also invested in the management of science, being President of the French society of Cell Biology since 2012. He is also fully invested in scientific councils of foundations and scientific journals. He is editor in chief of Biology of the Cell since 2009. He has been also acknowledged by the Grand prix à orientation fondamentale de l'Association Robert Debré pour la Recherche Médicale. The PI has been very successful in obtaining competitive grants. He obtained several ANRs, a FRM label team, and grants from other foundations (AFM, FRC). The team students and post-docs also obtained several fellowships to pursue or complete their projects.

Assessment of the team's interaction with the social, economic and cultural environment

This was not developed in the docket.

Assessment of the team's organization and life:

The team members meet regularly (lab meetings and journal clubs). The team seems to provide scientists with a dynamic and enthusiastic environment to work. The PI encourages young researchers of his team to implicate themselves in the supervision of students, and acquire full autonomy in the management of their research project.

Assessment of the team's involvement in training through research

Team 9 managed three theses during the past period, and received several visitors (both students and researchers). The PI organized or participated in several national meeting organization and two Ateliers de formation of Inserm in 2008. Team 9 is also involved in the Ecole des neurosciences and participates in the training of students. The PI teaches in the Master 2 course on Cellular and Developmental Biology of the University Paris Diderot. Thus overall, the PI invests time in training and teaching.

Assessment of the five-year plan and strategy

Team 9 has a well-defined working hypothesis and clear scientific objectives. The general biological contexts are further delineated towards (i) membrane traffic in cancer and (ii) membrane traffic in brain disorder. Both contexts potentially implicate pathogenic consequences of alterations of vesicular trafficking. The project is very ambitious but includes useful collaborations when needed. The project addresses interesting and yet unsolved questions. These questions are in direct connection with the findings obtained over the past period and integrate multiple approaches (biophysics, mass spectrometry, cell and molecular biology, analysis of metabolic parameters in the whole animal). A series of questions will be asked:

(1) To assess the process of membrane fusion and molecular composition of vesicles; several points will be addressed which concern the role of new binding partners or microdomains for TI-VAMP and the rules governing SNARE dependent and SNARE independent membrane fusion. There is strong enthusiasm for this part.

(2) Membrane trafficking endocytosis and exocytosis in cancer. This question will make use of a transgenic mouse model of breast tumors to investigate the links between adhesion and growth factor signaling and trafficking. Deletion of TI-VAMP in this model (crossing with TI-VAMP KO) will allow at characterizing tumor formation and progression.

(3) Role of exocytosis in neurons. This part will investigate the role of trafficking during synapse formation and function, under normal and pathological conditions. The study will include anatomical and biochemical investigations to characterize alterations of the synapses. It will also consist in screening of metabolic changes, with the help of technical platform.

TI-VAMP and VAMP2 defects to behavioural abnormalities and cancer might provide an immediate disease relevance. Unfortunately, the difficulty in filling in the gap between the cellular function of these SNARE proteins and their cumulative affects at the whole animal level raises the question of how the PI expects to fill in this divide. Having made these broader connections, the investigator might be better advised to focusing on specific cell types and determining on a cell biological, anatomical and physiological basis what particular aspects of development and function are impaired by the loss of these proteins.

This last part seems somehow divergent from the rest of the project. Very general insights will be obtained from such analysis, making an appropriate link with the specifically affected molecular mechanisms extremely difficult.

Conclusion

- Strengths and opportunities:

Team 9 has strong productivity with publications in high impact factor journals and seems to be on a very healthy path. The PI took into account the recommendations made in the past to concentrate onto the most important questions and this has proven to be a good decision. The PI put together a team of scientists having complementary expertise and built a very solid scientific environment to address questions at molecular, cellular and more integrative levels. This allows the team to be fully competitive at international level. The PI has established strong collaborations that have allowed an understanding of the consequences of impairing secretory pathways as a whole animal level.

- Weaknesses and threats:

In an attempt to provide an understanding of VAMPs at the broadest possible context, the PI has created a gap between the direct and indirect actions of these proteins. It is not clear from his proposal how he plans to unite these two highly divergent aspects of his research.

- Recommendations:

To continue to concentrate on a limited amount of central questions, consolidating and keeping the scientific excellence.

4 • Team-by-team analysis

Team 10 : Epigenome and paleogenome

Name of team leader: Mr Thierry GRANGE and Ms Eva-Maria GEIGL

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	3	3	100 %
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	3	100 %
N6: Other contractual staff (without research duties)	2		
TOTAL N1 to N6	10	7	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	3	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

One of the co-PIs of team 10 has a good recognition in the field of transcriptional regulation, noticeably for glucocorticoid receptors, including epigenomics. He had chosen to reorient his research towards analysis of ancient DNA aiming at reaching genome-wide assays. The projects of team 10 are based on the collaboration of researchers with rare complementary expertise in bioinformatics and paleogenetics, mainly focusing on using ancient/extant DNA to explore the influence of human activity, such as domestication on the recent evolution (10-100 000 years) of animal genomes. For a while, the group has been working at developing better experimental conditions to minimize sample contamination by modern DNA. They have shown that standard procedures for fossil excavation and handling are indeed prone to significant alterations and took the opportunity of moving to the new building to set-up an experimental lab well suited for rigorous analyses of ancient DNA. Recent achievements include using these approaches to study the evolution of wild equids.

Primary articles with team members as leading authorship have been published in PNAS (1), NAR (1) Plos One (1) Mol Ecol (1) Paleogeography (1) Annals of Anatomy (1). Review/methodological articles (3) and additional collaborative papers (5) were also published.

Assessment of the team's academic reputation and appeal

The team members have a good individual international recognition. Both team leaders are members of scientific committees and participate to national networks (one of them is member of the Editorial Board of NAR since 2010). They have been involved in organizing several national and international workshops and conference sessions, and are invited in international conferences. Team 10 collaborates with many palaeontologists, archaeozoologists, palaeoanthropologists from throughout the world and the group regularly hosts scientists for short stays within collaborating projects. The team has also recruited a young CNRS researcher in 2012.

Assessment of the team's interaction with the social, economic and cultural environment

The two PI are strongly involved into popularization and promotion of science and research in various media (articles in the written press, advice to journalists, radio and TV broadcasts, invited conferences for the public). They collaborate with museums such as the Louvre, the National History Museums in London, Brussels, Madrid, Vienna and Edinburgh (including collaboration on exhibition on mummies). This is highly commendable.

Assessment of the team's organization and life

Regular meetings of the palaeogenome team are organized with Internal seminar series (entire institute), journal club “Evo-Devo” (Teams 1 and 15) and Bioinformatics club. Team 10 seems also capable of making the right strategic choices to adapt and improve their homogeneity and synergy.

Assessment of the team's involvement in training through research

The PIs teach classes at master level in French and American Universities. They have supervised or are supervising 3 PhD students.

Assessment of the five-year plan and strategy

This interdisciplinary project results from blending together two research directions, namely the study of the epigenome and the palaeogenetics. Team 10 has already produced original research and has the potential to lead to major achievements. The team seems capable of making good strategic choices to reach these goals. The project, based on blending two research directions, is on good tracks.

However, proofs of principles in all aims of the project are yet to come. A major challenge will be to establish protocols for using genome-wide analysis of ancient DNA, with known problems of accessibility/quantity, degradation and contamination. If methylation patterns of such samples are worth exploring, it is not yet clear how their study could extend beyond chemical modifications of DNA, which are a limited part of epigenetic marks. If methodological advances are always important in biology, the theoretical hypotheses behind the choice of the different parts of the project the PIs propose are more difficult to appreciate. The team has to clarify its main questions and the possible collaborative insights into other projects.

Conclusion:

● Strengths and opportunities:

- Good funding, new lab with state of the art equipment devoted for ancient DNA analyses.

- Analyses of ancient DNA is certainly complementary to genetics/genomics of extant races to tackle the question of human impact on the recent evolution of animals.

- Recruitment of permanent fellows should impact future achievements.

● Weaknesses and threats:

- Although the fusion between the two teams is by now complete, frontline papers on paleogenetics are still to come.

- Although graduate students appear to represent most of the scientists in the lab, they should be more involved in the papers.

● Recommendations:

The team is developing research in an appealing field with potential interest in several disciplines. This work is also very attractive to a broad audience. However, the team leaders have to better define their goals and the questions they wish to address in the light of their demonstrated expertise and relative to international competitors. In the two major aspects of the project, proof of principles should be expected to be coming soon.

4 • Team-by-team analysis

Team 11 : Polarity and morphogenesis

Name of team leader: Mr Antoine GUICHET

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	2	2	100 %
N2: Permanent EPST or EPIC researchers and similar positions	3	3	100 %
N3: Other permanent staff (without research duties)	1,5	1,5	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1		
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	7,5	6,5	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	2
Theses defended	2	3
Postdoctoral students having spent at least 12 months in the unit		1
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

Team 11 is focused on the role of the Microtubule (MT) cytoskeleton in cell polarity and morphogenesis, using oogenesis and tracheal development in Drosophila as model systems. In particular, the lab has investigated MT organisation in oocytes, probed the function of phospholipids in polarity protein organisation and examined the nature and function of MT structures in developing tracheal cells.

The publication output over the past five years has been strong: one publication in Dev Cell a top tier journal, five publications in highly respected middle-tier journals (Development, Mol Biol Cell, J Cell Sci) and several collaborative contributions to other studies. The polarity/morphogenesis field is crowded but Team 11 has maintained competitiveness. In particular, the phospholipid work and the establishment of the tracheal system to study the function of the MT cytoskeleton in morphogenesis have had a strong impact on the field.

Several projects are ongoing and not yet published, but appear to be mature and either close to publication or under consideration in good journals. Overall, for this relatively small research team, this is an excellent, coherent research program. All team members appear to have produced work that has led/will lead to publications.

Funding has been very good, with several grants with the PI as coordinator (ARC, ANR) and three postdoctoral fellowships.

Assessment of the team's academic reputation and appeal

The PI has developed a strong international reputation in his field for high-quality work. He has been invited at international conferences and regularly reviews for major journals. He has also participated in two AERES reviews, as well as several recruitment committees/research habilitation, showing that he is a respected member of the French research community. The group collaborates with strong groups abroad and in France, and is well integrated in the IJM through internal collaborations (Teams 5, 15 and 16).

Assessment of the team's interaction with the social, economic and cultural environment

Team 11 has participated in several scientific outreach activities, including science exhibitions.

Assessment of the team's organization and life

The group has a weekly lab meeting and participates in institute-wide seminars, as well as national and international conferences. In addition, team members organise a scientific club (worm-fly) and the PI is involved in the management of the institute. The team has a highly coherent research strategy.

Assessment of the team's involvement in training through research

Several members of Team 11 participate in teaching numerous courses at the Masters and Bachelor levels. The lab has trained three PhD students in the past five years.

Assessment of the five-year plan and strategy

The research proposal is divided into three parts: (i) continuation of the oocyte polarity/oocyte nuclear positioning work, in particular a detailed study of molecular players (NumA, Ketel, Skt, Moe) in this process. Genetic and proteomic screens are also proposed; (ii) continuation of the work on MTs in tracheal development, with an analysis of the relationship between MTs and actin/AJ components, and clonal inhibition of MT polymerisation in a subset of cells; (iii) new research direction on the role of MT post-translational modifications (PTMs) in both systems.

Overall the approaches are well thought through and constitute a cohesive research proposal, which is likely to yield substantial new insights in polarity and morphogenesis. The oocyte polarity part of the project in particular is highly competitive, and Team 11 will have to recruit scientists in order to maintain a critical mass and momentum in this area. However, the group is well established in the oocyte polarity field and the committee feels confident that the scientists will continue to produce important work in this area. The tracheal development work offers some exciting new opportunities (mechanics of collective cell migration) and both model systems will feed very nicely into the new research direction on MT PTMs, which will be strengthened by a new collaboration with an expert in the field. Although the committee noted that the MT/PTM field is a risky one (functions for PTMs have been extremely difficult to address), it should rapidly become apparent whether this direction will yield new insights and the PI will be able to adjust his strategy accordingly.

All the approaches are feasible as the relevant techniques have been established in the lab (long-term imaging, tracheal work) or will be available through appropriate collaborations (modelling, PTM work…).

Conclusion:

- Strengths and opportunities:

- Excellent level of productivity.

- Experienced permanent staff.

- Coherent, well thought-out research proposal in an exciting field.

- Important collaborations in the IJM.

- Very promising research direction on tracheal development.

- Important move into quantitative imaging/modeling.

- Weaknesses and threats:

- Difficulty in recruiting/funding postdocs and students.

- Renewal of funding needs to be secured in the next two years.

- Competitiveness of the oocyte field.

- Recommendations:

Overall, the leader of team 11 has maintained an excellent level of scientific productivity over the past five years, and has some exciting future research directions. As mentioned in the SWOT analysis, the external funding is up for renewal in the next two years and will have to be secured in order for the three research directions to be properly funded. One issue is the lack of postdoctoral fellows. Fortunately, the lab has several experienced permanent staff members. The PI also mentions the difficulty in recruiting students, which may be circumvented by increased involvement of the team in teaching at the Masters level. The committee strongly recommends continued support for Team 11.

4 • Team-by-team analysis

Team 12 : Membrane dynamics and intracellular trafficking

Name of team leader: Ms Cathy L. JACKSON

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	100 %
N2: Permanent EPST or EPIC researchers and similar positions	2	2	100 %
N3: Other permanent staff (without research duties)			
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	2	
N6: Other contractual staff (without research duties)	1		
TOTAL N1 to N6	7	5	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	2

• Detailed assessments

Assessment of scientific quality and outputs

Team 12's research is focused on deciphering the mechanisms mediating membrane trafficking. The works done have contributed to identifying interactors that revealed new mechanisms by which Arf and Rab small G proteins cooperate in the membrane trafficking pathways. More recently, the team has found a novel class of amphipathic membrane curvature sensors that might be involved in the process.

The experimental approach is mainly based on regular biochemistry and cell biology methods applied to yeast and mammalian biological systems. The team has produced a total of 16 publications (13 research articles and 3 reviews) in the last five years, some of them in collaboration. Their own production (4 research articles and 3 reviews) is published in journals of high quality (J Cell Biol, Embo R, J Cell Sci & NRMCB) as well as the work in collaboration (Nat Cell Biol, Plos Pathog, J Virol).

Assessment of the team's academic reputation and appeal

Team 12 has published three reviews, one in a high-profile journal (Nat Rev Mol Biol Cell). It has established a network of national and international collaborations, most of which have been productive as assessed by joint publications.

The PI has obtained funding as main investigator or coordinator: ANR-Chaire d'Excellence (2007), FRM-Subvention Nouvelle Equipe (2007); ANR-Blanc (2010). Moreover, the PI is also a partner of a ERC-Senior Grant.

The PI is member of the editorial board of J Cell Sci, Cellular Logistics and a member of the reviewing editors for Mol Biol Cell, and is an academic editor for PLoS One. The PI serves also as ad-hoc reviewer for excellent scientific journals. She has been invited to one national and five international meetings. Team 12 has also attracted one teaching scientist.

Assessment of the team's interaction with the social, economic and cultural environment

The team described its participation to French national TV news (03/2007), which suggests that the work is of general interest.

Assessment of the team's organization and life:

There is a good balance between permanent staff (1 DR, 1 CR & 1MCU) and more temporary scientists (1 post-doc, 2 PhD, 1 engineer). Regular by-weekly lab meetings are organized with two other teams at IJM. Team 12 is also implicated in different IJM clubs.

Assessment of the team's involvement in training through research

Staff members contributed to training 8 students for 2-6 month internship, 2 M2 and 3 PhD (two of them have left the lab after their PhD with publications; the third one will defend his PhD next year). The PI reports minor teaching activity, but the new teaching scientist in the group will significantly reinforce this point.

Assessment of the five-year plan and strategy

The team will focus on the Arf1 GTPase exchange factor GBF1. Three mains goals will be pursued:

(1) the dual role of GBF1 in trafficking and lipid droplet metabolism. Research will focus on interacting partners common to the two interactomes. Experimental approaches will be based on super-resolution and CLEM microscopy on using RPE1 and HeLacell lines;

(2) the role of two curvature sensors, alpha-synuclein and synapsin. Experiments will be performed in yeast and neuronal systems by lipidomics, biochemical purification of synaptic vesicles and in silico modeling;

(3) the role of GBF1 in hepatitis C virus replication by analysing the localization of GBF1 during HCV replication in Huh-7 cells. Standard cell biology, molecular biology will be combined with yeast two-hybrid screening of GBF1-HCV interactors.

The project that will use very different biological models (yeast, different cell lines, virus) is mainly based on classical experimental approaches using molecular and cell biology, imaging techniques but also more specific methods such as CLEM or lipidomic analysis. The level of funding should be appropriate to support the research plan for the next two years.

Conclusion:

- Strengths and opportunities:

A topic of research of general interest in cell biology.

- Weaknesses and threats:

The team has a good publication record but there is a need to publish more papers centred to their own work. This will help increase their visibility in order to attract good applicants for PhD students, postdocs and permanent position applicants.

- Recommendations:

The translation of the mechanistic of membrane curvature sensors within living cells is very challenging and will benefit from deeper conceptual spatio-temporal understanding by developing original biological tools to analyse this aspect.

4 • Team-by-team analysis

Team 13 : Molecular virology

Name of team leader: Ms Isabelle JUPIN

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	100 %
N2: Permanent EPST or EPIC researchers and similar positions	1	1	100 %
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2	
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	5	5	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		1
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

Using contemporary methods of biochemistry, cell biology, structural biology and genetics, the global aim of the research is to improve our global understanding of the biology of plus-stranded RNA viruses. Team 13 uses plants as model systems (mostly Arabidopsis), but the work they have achieved can be placed into the much broader context of our understanding of host-RNA virus interactions, to which the team has contributed and still contributes in a significant manner. Over the past five years, a clear emphasis has been made on two key, albeit very poorly understood, aspects of RNA virus biology: (i) how is viral replication regulated and (ii) where, when and how are viral replication complexes formed into the host cell? These key questions are not only studied from the viral standpoint, but also from the host perspective, with a novel emphasis on membrane biology. Therefore, both the originality and scope of the research are of high standards.

Regulation of a viral RNA-dependent RNA polymerase via the dual action of host-mediated ubiquitylation and virus-directed deubiquitination (DUB) is a completely new concept in virology at large, and deserves the full attention of the team, because this topic clearly has the potential to bring the laboratory to the forefront of the field. The setting of an Arabidopsis cell line stably infected by TYMV is also a significant step forward, as this tool has already shown its enabling potential by granting the isolation of replication complexes and identification of host and viral factors associated to such complexes. This strategy has already generated a wealth of new data onto which the team can now safely capitalize.

In spite of the relocation of the IJM and, more critically, the simultaneous departure of all other team members (!) within a single year, the scientific output of the team over the past five years has remained not only constant but also of high quality, with several papers published in the best plant science journals (Plant Journal, Plant Cell) and also in more general journals such as EMBOJ or J Virol. A paper in PLoS Pathogens is currently under review as well. Invited reviews, including in Plant Physiology, as well as several book chapters were also part of the scientific output of the group. These factual data demonstrate that, against all odds, the team leader has managed to maintain a critical level of scientific activity at the highest level.

Assessment of the team's academic reputation and appeal

The team leader received two consecutive grants form the ANR over the last 5 year period, which is a significant achievement given that fundamental plant science, and more specifically plant virology, is not particularly high on the list of ANR funding, and also taking into account the current financial situation. Through the two ANR, the PI has established a set of collaborations within the IJM, but also in Grenoble and Gif. Interactional collaborations also exist with high profile institutions such as The Rockefeller University and MIT.

Team 13 has contributed to the setting of the cell imaging facility at IJM (GIS IBiSA), and has strong interactions with the 2D electrophoresis/tandem mass spectrometry platform of the CEA Grenoble.

The team rebuilding exercise shows some real attraction potential, since a new permanent researcher of high calibre has recently joined the group, alongside a new engineer allocated by the CNRS and an ATER supported by the University. Efforts should now be deployed to attract at least one post doc (potentially foreigner) and a PhD student to reach a critical mass.

The PI has been regularly invited to give talks at international and national meetings. She is very actively engaged in the organization of scientific meetings of high standards (e.g. international EMBO workshop, international congress of Virology).

Assessment of the team's interaction with the social, economic and cultural environment

The team leader is an editorial board member of the journal Virologie while a member of the group is actively involved in public outreach activities including the Fête de la science and the setting of student information web forum since 2010. The group has also been involved in raising the awareness of the public and consolidating the field at the national levels (Rencontres de Virologie Végétale, Journées Francophones de Virologie).

Assessment of the team's organization and life

Taking into account its entire rebuilding process, the team has done very well in reorganizing the group, although it would greatly benefit from the addition of at least one Post-doc and/or one PhD student. There is a good combination of bi-monthly group-based lab meetings and scientific clubs involving other groups at the IJM. Regular meetings are also organized with Team 12, which is a particular asset in the context of the second main research project.

Assessment of the team's involvement in training through research

Throughout the years 2007-2012, Team 13 has trained 3 postdocs, one PhD student, six M2 students and three M1 students, demonstrating a very good capacity to mentoring. Non-mandatory teaching has also been taken into account adequately. Being linked directly to the University, a team member seems to be actively involved in organizing student information/educational tools. It is anticipated that this will significantly attract young researchers to the team and reinforce existing links to the university.

Assessment of the five-year plan and strategy

The proposed plan of work was presented in the clearest way, with very focused, pragmatic and completely credible objectives. The team will elaborate on the wealth of data generated during the period of evaluation to take advantage of the simplicity and somewhat reductionist nature of the plant virus-interaction described, which is without doubt one of the most competitive systems currently available to decipher the molecular underpinning of viral RNA replication complexes and their association to membranes, two of the most mysterious aspects of RNA virus biology at large. The enabling tools built over the past years will undoubtedly help expedite some of the underlying questions; the timeliness and clearly ambitious nature of the proposed experiments may well put the team at the forefront of its field within a few years. Also noted was a very good capacity to team up with specialists in various fields of investigation and to initiate a novel research line in the context of innate immunity. A link to RNA silencing, conducted perhaps in collaboration, was also a clear prospect of the work, given the amount and quality of the virology tools available. Therefore, Team 13 provides a very tangible example of how plants can be used as excellent model systems to tackle some of the very fundamental issues of plant-pathogen interactions, with experimental outputs and concepts directly applicable to the broader community (invertebrates, vertebrates).

Conclusion:

The team leader has demonstrated a remarkable ability to tackle and solve some of the most adverse circumstances in a laboratory life while simultaneously maintaining a very solid and constant track record. The proposed line of research for the next five years is very concrete, well designed and original, leaving very little doubt on its success given also the fact that a new, dynamic team has been rebuilt in record times.

- Strengths and opportunities:

A very dynamic and ambitious research program.

Good publication record in spite of problems with the move and the team.

Excellent projects for the future and an excellent recognition in the field with collaborations.

Good spirit and fast recovery from the almost complete dismantle of the team.

New original and ambitious projects for the future.

- Weaknesses and threats:

The team is still small and needs to have young personnel join at the PhD or postdoc level.

- Recommendations:

The assessment of the team is very positive and the recommendation is to continue the successful line of research and to pursue the development of the original projects.

4 • Team-by-team analysis

Team 14 : Regulation and dynamics of cell division

Name of team leader: Mr Roger KARESS

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	4	4	100 %
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2		
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	7	5	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	4	4

• Detailed assessments

Assessment of scientific quality and outputs

The leader of team 14 largely focuses on an analysis of spindle assembly checkpoint (SAC) proteins in flies. Over the last decade or so, he has made two very important contributions to this field:

(1) His group identified and played a major role in characterizing the RZZ complex, now widely recognized as an essential element of the SAC in metazoans (but not yeast);

(2) His group demonstrated that the SAC is not essential for viability in flies and he has been at the forefront in showing that the lethal phenotypes associated with most SAC mutations in flies are not due to SAC defects, but rather due to these proteins playing additional roles in mitosis. That SAC proteins have important additional roles is now widely accepted in the field. This work has led to several excellent publications in top quality journals such as Nature Cell Biology and The Journal of Cell Biology.

The PI's group has also made important contributions to several collaborative projects, most notably with the Team 6 and a group at UCSC, again resulting in high quality publications in Mol. Biol. Cell. A Cell paper had its first author who was a student in the PI's lab before going to do a post-doc in the UCSC lab. She has now established her own group in France. Thus, the publication record of the PI is strong, particularly when one takes into account that the group had to move to new buildings twice in one year, and that the group has historically been relatively small.

Assessment of the team's academic reputation and appeal

Team 14 PI is very well respected in the spindle assembly checkpoint field. The reserach of this small team is considered of high quality rather than of high quantity, nevertheless providing deep thinking and ultimately, highly respected work. The PI has perhaps not taken up as many "leadership" roles as might be expected for someone of his standing in the community.

Assessment of the team's interaction with the social, economic and cultural environment

The visiting committee found it hard during the short visit to make meaningful comparative judgements in this area.

Assessment of the team's organization and life

The team seems very well organised. The committee noted that the PI has been asked to act as deputy director of the Institute, a sign of his standing within the Institution.

Assessment of the team's involvement in training through research

The PI has trained several PhD students who have gone onto establishing their own research groups in France.

Assessment of the five-year plan and strategy

The PI's research plan and strategy are strong and play to the existing strengths of the lab. He is taking a sensible approach to address some very interesting questions. Although this is a competitive area, the PI has successfully carved a niche for the lab. A real strength is that the lab uses Drosophila as a truly "in vivo" system, although the PI intends to make more use of cultured cells in the future. This seems reasonable, and the group will benefit if they can successfully combine the strengths of both systems. We are confident that the PI will continue to produce high quality data that will be of considerable interest to the field over the coming years.

As noted above, Team 14 leader has historically run a relatively small group, but this has changed over the last few years with the addition of several core positions. It was noted that the PI has made these changes largely in response to the criticism from successive external assessments that his group was too small. While there is every chance that overall output will increase, this will crucially depend on the quality of the extra people recruited

Conclusion:

- Strengths and opportunities:

The SWOT analysis produced in the report seems well thought through. The focus of the team on in vivo analyses is a real strength, and the research plan is very solid. Team 14 is well positioned to continue making important contributions to the understanding of how SAC proteins function at the molecular and cellular level, even though the field is competitive.

- Weaknesses and threats:

The key to success will be the PI's ability to assemble a talented team of scientists to perform the work described in his research plan. His move to the IJM should help in this respect, and his lab has expanded in size quite dramatically recently – it does not always follow, however, that this will lead to an increase in productivity. The PI has previously delivered excellent results with a much smaller team.

- Recommendations:

The committee recommends the strongest continuing support for this group.

4 • Team-by-team analysis

Team 15 : Drosophila evolution

Name of team leader: Ms Virginie ORGOGOZO

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	100 %
N2: Permanent EPST or EPIC researchers and similar positions	1	1	100 %
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1		
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	4	3	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

Team 15 is a young group led by a very creative scientist who moved from University Paris 6 to IJM less than two years ago (April 2010). The main focus on the team is to understand the molecular basis of morphological and metabolic evolutionary changes, using different species of Drosophila as model systems. The PI has developed two very creative lines of research, both centred around the ability to genetically and molecularly manipulate divergent species of Drosophila. The small team has recently completed a beautiful study on a species of flies that has become an obligatory feeder on a species of cactus. D. pachea appears to have become cholesterol auxotroph because of a mutation in a cholesterol synthetic enzyme that seriously hampers the ability of this enzyme to use the usual cholesterol precursor. The cactus, which contains a different cholesterol precursor, is thus necessary for this fly to grow.

The publication record of Team 15 is limited in number but the work on D. pachea was recently published in a Science paper that represents a major achievement for a young and small team. Two other excellent papers, one in collaboration, have also been published.

Assessment of the team's academic reputation and appeal

The PI appears to be considered as one of the young stars in the field of eco-evo-devo. She has published a major paper, but is also collaborating with the more senior leaders in the field. She is also often invited at international conferences in the field and has herself organized a (small) international conference on a specialized field (Drosophila genitalia). She is the recipient of an ATIP-Avenir grant that supports work on Drosophila genitalia that is still at an early stage. It is therefore essential that other sources of funding be obtained in the near future and the early success of the team should help.

Team 15 PI is giving lectures at meeting and in prestigious departments, which again confirms international recognition. She has reviewed for prestigious journals, including Science, PNAS and PLoS Genetics, again an achievement for an early career investigator. She has also published an entire specialized book in collaboration with another young bright evolutionary biologist.

All of the above indicate a very strong start for a young team and international recognition that will be extremely useful in this small but very competitive field.

Assessment of the team's interaction with the social, economic and cultural environment

The PI has a strong interest in evolution and has given lay lectures on this topic.

Assessment of the team's organization and life

Team 15 appears well organized with rigorous training of younger members and regular and intensive interactions among members of the group. In particular, the PI in several occasions in her report emphasizes the conceptual contributions of other members. The group also participates to a joint 'evolution' journal club with the teams 1 and 10. The PI organizes the BioInfo Club, presumably because of the heavy reliance on processing of sequencing data.

Assessment of the team's involvement in training through research

One member of the lab appears to be deeply involved in teaching at Paris 7 and a course at the Pasteur Institute. The PI is participating fairly extensively to teaching related to evolution, from Paris 7 to the various ENS' and to the Museum of Natural History, which indicates that she is taken very seriously by hard-core evolutionary scientists. She is involved in the recruitment of students to the ENS, which is presumably a huge amount of work (in a very short time).

Assessment of the five-year plan and strategy

The aims of the future projects are significantly different from the published work on the adaptation of D. pachea to its cactus, although the techniques and expertise used will be similar. Illustrating again the originality of the PI, the future projects focus on the genitalia of species of Drosophila, along three major lines. Identifying an interesting question is absolutely critical in the field of evo devo where tools are often very limited and the questions must be framed precisely to allow insights into molecular mechanisms of morphologic evolution.

The most advanced project still concerns D. pachea, but not its metabolic requirements. It is based on the function of asymmetry in the male genitalia that leads to asymmetric positioning of the male during mating. Careful genetic and behavior experiments have shown that the asymmetry is important if not absolutely necessary for mating success. This project also addresses exciting questions of the genetic basis of left-right asymmetry, analyzed from a very original point of view. One important feature of the work is its connection to real field biology with the analysis of wild variations in populations.

Another project that takes advantage of the technology developed by the PI is the (very rapid) evolution of genitalia between two species, Drosophila simulans and sechellia that are cross fertile, hence allowing rapid introgression of pieces of DNA from one species into another, and the identification of the genes responsible for QTLs. The importance of reproductive organs for speciation is obvious and this allows rapid and extensive divergences in the structures.

Hybrids between two other species (D. yakuba and santomea) will also be investigated because of differences in bristles in the genitalia. The biological meaning of these bristles, the molecular mechanism of their evolution and the dissection of promoters responsible for the evolution of the traits will be analyzed, in part relying on the expertize accumulated as a postdoc in the Stern lab.

Although ambitious, it is clear that the PI knows how to prioritize her projects, and to move on when a project has been completed, or has reached a roadblock (which must both be true for the D. pachea cactus project).

Conclusion

- Strengths and opportunities:

Team 15, along with the two other teams involved in evolution, might be able to contribute to shaping the future of IJM and it is likely that evolutionary biology will represent one of the future strengths of the institute. The PI has already acquired international stature through high profile publications, a book (as well as a landmark review published before joining IJM) and invitations to contribute to meetings.

The main feature of the team is the originality and creativity of the projects offered. Although these projects might appear very focused on some strange aspects of the biology of these non-model organisms, it is clear that they in fact represent very clever paradigmatic models to study how evolution shapes organisms.

- Weaknesses:

None obvious at this stage, besides a need to focus on a few problems.

- Recommendations:

The recommendation is to take advantage of the early success to secure more ‘senior’ funding, ANR or ERC and to continue developing the sequencing technology that will allow the team to rapidly define the molecular nature of the evolutionary changes.

4 • Team-by-team analysis

Team 16 : Computational modelling and biomethematics

Name of team leader: Mr Khashayar PAKDAMAN

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	3	3	
N2: Permanent EPST or EPIC researchers and similar positions			
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	4	4	

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	6	2
Theses defended	3	2
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	1
Qualified research supervisors (with an HDR) or similar positions	2	3

• Detailed assessments

Assessment of scientific quality and outputs

Team 16 has important contributions in mathematical biology. The main focus of the research is the study of models of neuron and neuron networks activity, with emphasis on the generation of biological rhythms. In order to study these complex phenomena the team develops various modeling approaches that use nontrivial mathematics. More recently, the team became involved in data analysis and computational biology. They have developed a classification tool that can be used for data analysis (AutoClass@IJM) and modeled the regulatory networks involved in the metabolism of iron. These developments are in collaboration with Team 3 from IJM.

The team has a good publication record (18 papers in the period 2009-2012). Normalized to mathematical journals impact factors, the chosen journals are of first rank (SIAM Journal of Mathematical Analysis, Mathematical Models and Methods in Applied Sciences). Some papers are published in good bioinformatics and computational biology journals (J. Theoretical Biol (1), Plos Comp Biol (1), BMC Systems Biol (1), NAR (1)).

Assessment of the team's academic reputation and appeal

The PI of team 16 has a good international recognition in mathematical biology. He is regularly invited to national and European workshops and conferences in mathematical biology. He is serving as reviewer for good quality mathematical and computational biology journals. One has a good recognition in the field of computational biology and another is a good expert in partial differential equations.

The modeling team regularly hosts foreign scholars and has developed an international network of multidisciplinary collaborations.

The PI won the Grammaticakis-Neuman prize of the French Academy of Sciences in 2007. Another member was awarded, for her doctoral thesis work, the prize Marie-Louise Arconati Visconti of the Chancellerie des Universités de Paris in 2006.

Assessment of the team's interaction with the social, economic and cultural environment

Team 16 is involved in several actions to promote science and education (Journées de la science, Science sur Seine, etc.). They also contribute to educational research aiming to improve student success, including for those originating from poor families. The team develops partnership relations based on research and education with the company NVIDIA. They won two prizes from NVIDIA (in 2011 and 2010).

Assessment of the team's organization and life

The team has 4 permanent staff members. They have recently recruited a young mathematician specialist of partial differential equations. Technical support is provided by one research technician, who is supported by University Paris-Diderot. The members of the team are involved in different IJM clubs. Unclear positioning on its future activity within IJM can be a considerable handicap.

Assessment of the team's involvement in training through research

All Team 16 permanent staff are faculty members, strongly involved in interdisciplinary training at all levels. The PI is the French representative of the ERASMUS MUNDUS Complex Systems Sciences masters program. Seven PhD students were or are supervised, two in co-direction with Team 3 PI, three in co-direction with external collaborators. Graduate students co-authored papers of the team.

Assessment of the five-year plan and strategy

Attracted to IJM by the former director to develop new quantitative approaches to biology, this team was struggling to find its position, between the mathematical community with whom it has strong collaboration and the experimental groups in the host institute.

Successful on the mathematical level, the team is now searching for new goals and organization. However, the committee found very difficult to understand the project and its articulation with IJM. For the next five years, they propose the continuation of the themes in mathematical biology that are already developed. The novelty of the project is in the computational biology platform. Inspired by a collaboration with Team 3 at IJM on the modeling of iron metabolism, the team wants to generalize this service and find other applications. This initiative will consolidate internal collaboration with experimental teams. In order to be successful with respect to the general community in computational biology, the platform has to be based on new algorithmic developments. Yet, the algorithmic and methodological novelty of the approaches is not obvious in the project. The Probabilistic Boolean Networks used for modeling iron metabolism are used by several other teams worldwide as a solution to parameter uncertainty. The classification tool (AutoClass@IJM) though useful web-service, is based on an algorithm developed at NASA. In conclusion, a better balance between service providing and original developments has to be achieved.

Conclusion

- Strengths and opportunities:

The members of the team bring very good scientific value in a field that is not sufficiently developed in France. There is a great potential into applying ideas coming from the mathematics of dynamical systems to biology and IJM should profit from the expertise of the members of this team.

- Weaknesses and threats:

The team lacks a major project, involving all its members, and leading them to research breakthrough.

The presentation of the work was extremely difficult to follow, reflective an unclear definition of projects

- Recommendations:

In order to consolidate their positions, this team has to work at several levels, both internally and with the other teams. They have to define a set of specificities and develop them to be a reference in the field. Developing computational biology approaches and tools could be a good solution for interacting with other teams at IJM. However, the team should avoid the danger of trading original algorithmic developments for service providing.

4 • Team-by-team analysis

Team 17 : Genetics and development of the cerebral cortex

Name of team leader: Ms Alessandra PIERANI

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions		1	
N2: Permanent EPST or EPIC researchers and similar positions	2	2	100 %
N3: Other permanent staff (without research duties)	1	2	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	2	100 %
N6: Other contractual staff (without research duties)	1	1	
TOTAL N1 to N6	7	8	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		2
Theses defended	3	
Postdoctoral students having spent at least 12 months in the team	1	1
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

Growing evidence supports the notion that the aetiology of numerous neurological and psychiatric illnesses is due to alterations of developmental processes. The aim of the project is to understand the molecular mechanisms that coordinate growth and spatial patterning in the developing cerebral cortex. Team 17 has made major contributions in the field of cortical development by identifying novel populations of migrating transient neurons and their crucial role in the extrinsic control of forebrain survival and cortical patterning. In particular, Team 17 has focused on the role of progenitors expressing the Dbx1 transcription factor at the border of the pallium. Using a multidisciplinary approach in mice and primates (cell tracing and ablation, gene knock out, pharmacological and genetic manipulations of cell cycle parameters, transcriptome profiling and videomicroscopy, in vitro embryonic stem cells for corticogenesis and rescue experiments using transplants in vitro, electroporation in ovo in chick and in utero in mouse, behavioral tests), they have identified restricted subtypes of glutamatergic neurons derived from Dbx1 expressing progenitors at the borders of the developing pallium which have the unique properties of migrating long distances from their generation site and to only being transiently present during development. Indeed, only GABAergic interneurons were known to undergo tangential migration, and Team 17 was the first to show that some glutamatergic neurons also have such mode of migration in the cerebral cortex. Moreover, the team tackles the physiological significance of transient neuronal populations in the evolution of the cerebral structures. Their work introduced the novel concept that long-range cortical patterning and the fine tuning of neuron numbers is mediated by these populations, suggesting that the formation of functional areas depends on the migration of Dbx1-derived transient neurons that serves as mobile signaling units, in addition to passive diffusion of morphogens. Team 17 completed several studies, which were published in good and excellent journals. Since 2007, they have published 7 research articles in peer reviewed journals of high quality (4<IF<15), 3 in 2010 (comprising 1 in Nature Neurosci), 3 in 2011 and 1 in 2012. In addition, they have also produced 1 review in Current Opinion in Genetics and Development IF 8 (2010), 1 in Development, Growth and Differentiation (2009), 1 book chapter (2012). Three manuscripts are in preparation.

Assessment of the team's academic reputation and appeal

Team 17 attracts many applicants a year for both post-doctoral and student positions from European Union and US: 3 Post docs in total (1 Japanese/Korean, 1 British, 1 Italian), 1 has now left the team) and 2 just recruited (02/2010 and 04/2011). It also attracts EU PhD student (Spanish) and undergraduate Portuguese/Brazilian, Italian, NYU students (Erasmus exchanges, staff lecturer etc..). The team's projects have constantly been funded by French (ANR 2005, 2007, 2011, FRM, ARC, NeRF, Ville de Paris, FRC) and European grants (STREP). Team 17 PI has successfully coordinated two ANR grants (5 and 6 publications, respectively) and obtained a third ANR grant in 2011. Team members are involved in national and international collaborations as shown by 6 publications in just 2010. Since 2009, the PI has published 14 original articles in journals of high impact (PLoS Biol, J Neuro, Cereb Cortex, Nat Neurosci) (of which 6 as corresponding author), 2 review articles, and a book chapter (in press). She is a frequently invited speaker to international meetings (3/year) and seminars (3/year) as well as national meetings. She is a reviewer for more than 10 scientific prestigious journals (among which Science, Neuron, Nat Neurosci, J Neurosci, Development, EMBO J) and national and international (EU, HFSP, MRC-UK, AFM, FRM, ICS, CINECA-Italy, ALW-The Netherlands) granting agencies. A team member is a reviewer for MRC.

The PI has been external examiner/reviewer (PhD, HDR, M1, EPHE, INSERM tutoring). She has been awarded a CNRS-ATIPE grant (1999), a City of Paris prize (2006) and the Foulon Price of the Academy of Science (France) (2012).

Team members are selected or invited speakers (2 conferences/year). A Post doc fellow (Contrat Junior INSERM) since 10/2007) has obtained a permanent researcher position (CR2) at INSERM since 01/2012. Overall, the PI has an excellent academic reputation and appeal, and is fully successful in obtaining important grants to conduct the team research.

Assessment of the team's interaction with the social, economic and cultural environment

Not clearly addressed in the docket.

Assessment of the team's organization and life

The PI leads the “Genetics and Development of the Cerebral Cortex” Team at IJM since 2006. The team has made major contributions in the field of cortical development by identifying novel populations of migrating transient neurons and their crucial role in the extrinsic control of forebrain survival and cortical patterning. Since 2006 the team is consistently composed by 7 to 8 scientists (2-3 post-doctoral fellows (most non-French), two students (PhD and M2), two technicians and two undergraduate students from the European Union and the United States for internship (3-4 months). It continues to attract many applicants a year for both post-doctoral and student positions. In the evaluated period, the PI has mentored the work of 2 PhD and 10 undergraduate students, 3 post doctoral fellows and 3 technicians. Two PhD students have graduated since 2008, each with 6-7 publications (of which 3 first authors). Weekly progress report meetings (joint Teams 9 and 17), journal clubs; internal seminar series (entire IJM) and Team Retreat are organized. Team 17 leader is Scientific head of the Animal Core Facility IJM/University Paris-Diderot since March 2010 and is elected member of the Recruitment Committee for IJM Team in 2012. A team member is IJM seminar co-organizer since 2011

Assessment of the team's involvement in training through research

Team 17 leader teaches Master courses in France and European Union (ENS Paris and Lyon, Univ Paris-Diderot, UPMC, Sweden, Italy, Spain). She has mentored the work of two PhD (now in post-doc training) and ten undergraduate students, three postdoctoral fellows and three technicians. Two PhD students have graduated since 2008 each with 6-7 publications (of which 3 first authors). The PI was Reviewer for seven PhD Thesis, one EPHE Master Degree, two HDR and Tutor for four Master 1 students, four Mid-Thesis Committees and one INSERM Researcher. Team members also participate in training of students.

Assessment of the five-year plan and strategy

Previous data have shown that cohorts of transient migrating neurons at the pallial-subpallial boundary (PSB) regulate progenitor divisions in the developing cortex for a restricted period of 24 hrs before their switch to neurogenic divisions. Small variations in the kinetics of generation and arrival of migrating signaling neurons might have profound consequences on the construction of a precise cortical map. The project aims 1) at deciphering the molecular mechanism mediating the signaling function of the transient migratotry neurons (gene expression profiling, ISH, IHC, in utero electroporation, in vitro whole embryo culture) and whether contact inhibition between CR subtypes results in invasion of specific cortical territories (video imaging, explants cultures); 2) characterize the molecular interactions between transient migratory neurons, neural precursor and vascularization (in vitro co-cultures, development of Dbx1 ES cell line which develop in cortical neurons 3) study the role of the Dbx1 gene in the specification of the transient migratory neurons through cell cycle control (Dbx1 KO embryo, ES manipulation of cell cycle parameters, RNA-Seq, Chip; 4) study the role Of Dbx1 in the complexification of the neocortex during evolution (bioinformatics, in ovo and in utero electroporation, transgenic marmosets, humanized Dbx1 BAC transgenic mice); 5) study the consequence on cortex development of the persistence of transient signaling neurons (targeted expression of anti-apoptotic regulators in Dbx-1 cells, behavior). A multidisciplinary approach from mouse and primate animal models to single cell resolution by live imaging will be used.

Conclusion

- Strengths and opportunities:

Team 17 is extremely dynamic. They develop a new concept on the role of transient migratory neurons on cortical patterning. Their research are very relevant both in the field of cortex development and neurological disease; they have been constantly funded (ANR, ARC, European grants). Their results are published in journals with high impact factors. Their team attracts many post-doctoral and doctoral students, many of them from abroad. All team members are involved in student training (PhD students, master training). The project is very ambitious and a number of data have been already obtained. They currently developed many approaches to decipher the molecular mechanisms involved in this new signaling pathway. For that, they benefit of the IJM core facilities. Many collaborations have been established. Team 17 comprises now 4 persons holding permanent positions including a person just recruited at INSERM.

The PI has pursued a novel and original hypothesis in her model that early born DBX populations are critical to patterning various aspects of cortical development. Her efforts have in the present proposal consolidated into a set of specific and testable hypotheses. Her central premise is that early born cortical neurons derived from three diverse Dbx-1 expressing regions act by secreting morphogens in accordance with their distinct sites of origin that affect: 1) areal patterning; 2) corticogenesis; 3) vascularization. Impressively, she has devised approaches to test each of these ideas. 1) With team 9 PI, she will genetically impair secretion of morphogens from these populations to see how each of these processes is affected; 2) She has done whole genome analysis to see what candidate molecules are produced from the Cajal Retzius populations (which is how she came up with the idea that these cells affect vascularization; 3) She has begun to look across species to see how conserved this mechanism might be and to look for species specific changes that might help explain differences seen in cortex in lower versus higher mammals. In total these are an exciting and original set of experiments that show every sign of being ground breaking.

- Weaknesses and threats:

Team 17 PI has done an admirable job crafting a forward looking proposal. It is the hope of the committee that she can turn this into high profile papers that are concomitant with the quality of her work, which perhaps has to date been underappreciated. The project is ambitious. However, the team has shown previously, that with less permanent persons than today, it could be highly productive. Indeed, this weakness reflects the fact that the obligatory high rate of turn-over and limited support for replacement personal hampers a group that could clearly benefit and utilize additional resources were they made available.

- Recommendations:

Strong support from the IJM the since the project is feasible and the team beneficiates of adequate critical mass and of all core facilities.

Grants from ANR, FRC and ARC have been obtained so that running costs and salaries will be covered up to 2015. However, due to the high costs of mouse housing, the ANR grants cannot cover full post-doctoral salaries. Team 17 leader should re-submit a grant proposal to the SFARI Foundation (USA) for the generation of conditional mouse mutants preventing death of transient neurons. FRM team application, if not succeeded this year, should be re-conducted as well as other grants proposal HSF, EU.

Develop collaborations which have already been established with people to obtain human fetus tissues, marmoset tissues and transgenic marmosets, with expertise in angiogenesis, comparative genomics, and in secretion of morphogens (Team 9).

4 • Team-by-team analysis

Team 18 : Cell cycle and development

Name of team leader: Mr Lionel PINTARD

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	100 %
N3: Other permanent staff (without research duties)	0,5	0,5	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4		
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	5,5	1,5	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended		
Postdoctoral students having spent at least 12 months in the team		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

Team 18 research aims to discover and unravel possible regulatory roles of protein degradation in three developmental cell fate transitions: (i) mitotically active germ cells that switch to a meiotic program; (ii) fertilized embryos that finish meiosis and initiate a mitotic program, and (iii) asymmetric cell division in the early embryo. The nematode C. elegans is used as a model system. Relevant contributions were made to the field by assigning in vivo functions of well-studied UPS components, such as CRL2. To study the ubiquitin-proteolytic system (UPS) in a developmental model is appealing but also very challenging. The E3-ligases have multiple target proteins and the biological effects of genetic manipulations can thus be very pleiotrophic. There has been a steady flow of articles in good journals over the past years (J Cell Sci, Development, PLoS Genetics).

Assessment of the team's academic reputation and appeal

The PI has been invited to write review articles, book chapters and a meeting review hence he is recognized in his research field. The PI was the main organizer of the 2010 and 2011 VER Midi meeting, a meeting for French labs that use C. elegans as a model system. The team leader received prestigious medals from the City of Paris and from the CNRS, and performed exceptionally well in grant applications. Also several members of the team received fellowships.

Assessment of the team's interaction with the social, economic and cultural environment

Not directly addressed in the docket

Assessment of the team's organization and life

The size and constitution of the group: 7 members including the Pi, two postdocs, two PhD students, a technician and a master student is a good/solid. There is one centralized theme. Individual team members contribute to national and international meetings.

Assessment of the team's involvement in training through research

This involvement is sufficient and effective. A high number of rotation students have been educated/supervised (>10). Lab retreats are organized, together with a nematode group in Geneva. Management of supervision is sound.

Assessment of the five-year plan and strategy

The work describes builds upon previous work and has the potential to lead to new discovery. For instance, testing the involvement of CUL-2 in GLD-1 degradation seems straightforward. Also, more in depth analysis of the biology upon knockdown of the genes identified in the RNAi based screens (such as HTP-3) in wild type and mutant background is logical and promising. It is recognized that the proposed identification of CUL-2-dependent ubiquitylation sites via proteomic approaches is challenging, especially in the nematode system. Relevant collaborations are however setup.

Conclusion:

● Strengths and opportunities:

- Strong background of the applicant.

- Recognized contributor to the field.

- Great record in attracting funds; good publication output.

- Dedicated and focused towards elucidation of UPS biology and its potential regulatory capacity.

- Unique reagents.

- Possibility to combine genetics, cell biology and biochemistry in one system.

● Weaknesses and threats:

Some of the projects might be technically challenging and alternate approaches should be investigated as well.

● Recommendations:

The future plans section contains a good mix of achievable goals, following up on previous work, and more challenging approaches, which also includes some technological high-risk part. It will be of interest to see whether the biochemical identification of novel interactants and substrates will succeed, given the notion that the phenotypes of interest are the consequences of the proteins acting at specific cellular fate transitions.

4 • Team-by-team analysis

Team 19 : Development, signalling and trafficking

Name of team leader: Ms Anne PLESSIS

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	2	100 %
N2: Permanent EPST or EPIC researchers and similar positions			
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)	1	1	100 %
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1	
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	5	5	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		
Theses defended	1	
Postdoctoral students having spent at least 12 months in the team		
Number of Research Supervisor Qualifications (HDR) taken		1
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

Team 19 focuses its efforts on the molecular a cell biological events behind Hedgehog (Hh) signalling. This includes the definition of the Hh transducing complex, the identification of novel players in the Hh pathway (such as MLF), the cellular mechanisms required for the transmission on the Hh signal (Patched ubiquitination, Smoothened phosphorylation by Fused, the association of the Costal2 kinesin to microtubules, etc). The field of research is competitive and trendy but of great importance in Developmental Biology and in Biomedicine. The results obtained by the group are relevant and have been published in journals with a wide impact such as Current Biology and PNAS.

2 publications as senior author, one of them with all authors from the team (Current Biol 2007) and another one in collaboration (PNAS 2012), two publications from collaborative work (Current Biol 2008; PLoS One 2012), 2 manuscripts planed to be submitted before the end of 2012 and several others in preparation. The PI had a 3-year gap without publications.

Assessment of the team's academic reputation and appeal

Team members are involved in collaborations with national (Gif sur Yvette, Uni. ST Quentin en Yveline, Toulouse, Curie Institute) and international (US, Canada and Japan) groups.

Grants from ARC were obtained in 2008 (50 K€/two years) and 2010 (50 K€/two years). 3 postdoctoral fellowships were funded by ARC (2010, 2011) and by the Ligue contre le cancer (2012). The team attracted two post-docs with previous experience in France and Spain. Both seem to have a strong publication record. Team 19 also benefited for a visiting scholar from NorthWestern University. This professor is yearly invited by University of Paris-Diderot and has visited the host laboratory three times in recent years, each visit lasting between 2-3 months.

Awards include Prime d'Excellence Scientifique (PES) from University Paris Diderot in 2010, and a delegation to the CNRS in years 2010 and 2011, time during which she has her teaching duties waived.

Team members have participated as invited speakers in international conferences (Nice, St Jean Cap Ferrat EMBO workshop, US 2008, Singapore 2012) and have imparted 1 seminar at Heidelberg (Germany) and 7 seminars in France. The group leader has co-organised symposia in France and in the US (Stanford, 2008).

The group leader acts as reviewer for a number of relevant journals, including (Dev Cell, Current Biol, Development, PNAS, PLoS Genetics), for international funding bodies from several countries (UK, US, Netherlands, India, etc.). Team members participate too in recruitment committees (Assistant Professor, Technical staff). A Maître de conference position will join the lab in 2013 (University Paris 7-Denis Diderot).

Assessment of the team's interaction with the social, economic and cultural environment

Members of the team are in charge of the EMBL (Heidelberg)-Université Paris-Diderot "joint thesis" program. They also act as scientific co-organizers of a meeting intended to disseminate Science among high-school teachers. The group participates in public events such as "Science en fête" (Science day).

Assessment of the team's organization and life

Team 19 was constituted in January 2010. The PI obtained a delegation to the CNRS without teaching duties (from Sept-2010 to Aug 2012), which allowed her a full time dedication to research. Before and after these dates, the PI taught around 200 hours/year.

Two post-docs (arriving on 09/2009 and 02/2011) and an Assistant Ingénieur (09/2010 to 12/2011) joined the team. A Maître de conference position will join the group in 2013 (associated to University Paris-Diderot). Every year since 2010, a Professor from North-Western University has visited the team. Undergraduate students are often involved in the team, including Master II students, one of which is now pursuing her thesis in the team.

All the protocols, reagents, oral presentations, fellowships and grant proposal are registered in a common database. The team seems to implement a schedule of lab meetings and journal clubs. Team members participate in an internal seminar series at the IJM. They also present their work at the monthly Drosophile Ile de France meeting. PhD student present their work each year to PhD committee and they participate to one national and international meeting. They participate in the IJM life scheme through speaker invitation.

Assessment of the team's involvement in training through research

Team members are involved in school committees for student selection (PhD school Paris-Diderot and University Paris Sud-Orsay), in Thesis defence committees (8) and HDR (1) as reviewers or president. They are members of PhD thesis advisory committees for the international schemes run between University Paris-Diderot-EMBL or Paris-Diderot-New York University, and for national schemes as well (IJM, Institut Pasteur, Institut Curie). Team members participate in the training and supervision of Master II, Master I, L3, and L2/BTS students.

Overall, Team 19 contributes to about 300h teaching/year (subjects: Development, Genetics, Molecular Biology) at University of Paris 7 (master 1 and master 2, L1, L3, PCEM1). Given the delegation to the CNRS in 2010-2012, Team 19 PI teaching duties were limited those years to a few Master II seminars and to the supervision of a Masters project.

Assessment of the five-year plan and strategy

The project aims at using Drosophila as model to study the mechanisms of HH transduction. In the long run, the project aims at bringing some insight into the HH-related pathologies and providing potentially novel drugable targets. The proposal contains two main themes. The first one intends to study the trafficking and ubiquitination in HH signaling. In an RNAi based genetic screen, they found a number of candidate deubiquitinases (DUBS) potentially involved in HH signalling. Because 2 publications from other groups on the effects of DUBS on SMO were published recently, this theme will be extended to the analysis of the bone morphogenetic (BMP) pathway in collaboration with R. Warrior (US). The work is meant to be finished by the end of 2013, so it is not detailed in depth in the proposal.

The second theme aims at studying the post-translational RNA regulation in HH signalling. Previous high throughput two-hybrid screens (2005) followed by an RNAi screen (manuscript in preparation) have shown that the mRNA-binding protein SMAUG, involved in the regulation of mRNA fate during development, appears to bind SMO. In addition, SMAUG also controls Hh signalling via the regulation of one or several mRNAs. The aim of the study is to characterize the mechanism involved, in particular the mRNA target(s) of SMAUG, the interaction between SMO and SMAUG and how HH signalling controls SMAUG. The theme will be carried out in the host laboratory and in collaboration with teams in the US, Canada and France.

The strategy outlined in the proposal is sound and based on relevant preliminary data. It is the opinion of the committee that there is room for manoeuvre in case some of the experiments planned do not yield the expected results. The past experience of the team, together with the collaborations already established or in the process of, should guarantee the accomplishment of the objectives. In fact, the SWOT analysis presented by the PI takes into account the previous experience of the team, the volume and quality of preliminary data and the fact that the team has access to most of the reagents needed for the development of the planned experiments. Finally, it is unclear how the proposal will integrate into the research themes at the IJM as the PI fails to discuss this information

After the presentation for the visiting committee, it became clear that the PI has a number of ongoing projects that she intends to follow up but that were not mentioned in the proposal. This includes the interaction between the Fused kinase and the known Smoothened interactors CK1 and PKA, kinases in charge of phosphorylating Smo upon pathway activation. In addition, the PI described in detail recent evidence regarding the role of SMAUG in Hh signalling, in particular the seemingly essential mRNA-binding capacity of SMAUG to perform its function in Hh signalling. In all, the PI left a very positive impression on her capacity to lead the project and the viability and interest of the proposed objectives.

Conclusion

● Strengths and opportunities:

The project is ambitious and with a high relevance on the molecular and cellular mechanisms behind the Hh pathway. It harnesses the potential to provide novel targets for cancer therapy in the long term, notwithstanding its potential to uncover novel players and processes involved in Hh signaling (they have developed a privileged relationship with a French biotech company but this aspect, however, was not mentioned in the PIs presentation). The PI and her collaborators are internationally recognized authorities in the field and the publication record so far is solid and of high impact for a group of this size. It was noted however that the PI had a gap of 3 years without publications. The research of the team has provided them with a large amount of new data, essential for the outlining of this proposal and to allow the submission of several manuscripts in the near future. The team is well connected with international teams and has established fruitful collaborations with some of them.

● Weaknesses and threats:

The team is small in size and the PI has a very heavy teaching load. The development of the project requires a new postdoctoral researcher to be hired once the current post-doc leaves the team. Similarly, a PhD student is needed to carry out the proposed experiments. The PI mentions difficulties in obtaining studentships and ANR grants. It is expected that a number of reports will be published soon, thus helping the team to obtain external funding and fellowships for new recruits. The technician did not get recent promotion and there is a risk that he leaves the team.

● Recommendations:

- Support from the IJM and help with teaching.

- Considering the very extensive research duties, it is recommended that the PI's teaching hours are reduced to a more reasonable figure, similar to those due for a full Professorship position.

4 • Team-by-team analysis

Team 20 : Morphogenesis, homeostasis and pathologies

Name of team leader: Ms Françoise POIRIER

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	2	2	100 %
N2: Permanent EPST or EPIC researchers and similar positions	2	2	100 %
N3: Other permanent staff (without research duties)	2	2	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	100 %
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	7	7	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		1
Qualified research supervisors (with an HDR) or similar positions	3	4

• Detailed assessments

Assessment of scientific quality and outputs

Team 20 research focuses on the study of Galectins, a conserved family of glycan (N-acetyllactosamine) binding proteins, with a wide spectrum of potential partners. Galectins are linked to a broad range of processes, such as immunity, inflammation, cancers and recently heart failure, and thus constitute a very active field (>4,000 papers published thus far). The team had generated several galectin KO mice that, unexpectedly, display discrete developmental defects, prompting a shift towards tissue repair and homeostasis in adults. Major contributions concern involvement of galectin3 in ciliogenesis and galectin7 in skin repair associated with adhesion defects.

9 original papers (ave-IF 5) have been published over the period, plus a large number of collaborative works (30) including very good journals (e.g. Nat Immunol, Nat Neurosc, Nat Medecine, etc). Works from the team leader are well cited (>250/y), again with a strong contribution of punctual collaborations (distribution of KO lines).

Assessment of the team's academic reputation and appeal

Research costs seem increasing and are supported by many grants, yet of limited amounts (average: 25L€). Although very active in setting up collaborations (nationally and internationally) with recognized researchers, team members remain participants in major funded networks. The Team 20 leader was invited in a workshop on Galectins (Boston).

During the last five years, the team has attracted new members bringing additional expertise in EM (1 tech), tighter links with the University (1 Professor, 1 Assistant Professor), and recruited a very active CNRS fellow. 3 PhD and 7 undergrads have been trained. A short sabbatical of an outstanding expert of galectins is planned next year.

Assessment of the team's interaction with the social, economic and cultural environment

Not specifically addressed.

Assessment of the team's organization and life

Team 20 has engaged a profound reorganization of its staff (1 researcher has left, 4 new members have joined). Given its small size it is unclear why this team needs two subgroups. Attracting additional colleagues, they would gain in favoring younger experimentalists rather than more senior scientists who are in sufficient number.

Cost of mice facilities appears a major issue with the current levels of funding.

Assessment of the team's involvement in training through research

A former graduate student is 1st/2nd author on two main papers.

Two recent team members are from Université Paris-Diderot and have heavy teaching duties. In addition, other colleagues also contribute to teaching. One team member holds numerous (too many) responsibilities in Masters and Doctorate school programs.

Assessment of the five-year plan and strategy

The proposed research program aims at investigating the influence of galectin3/7 on various aspects of cytoskeletal organization in epithelial cells and exploring their relevance to some human pathologies. The team will address roles of galectins either in epidermal cell migration or in “centrosome biology”, in each case engaging collaboration with clinical groups. The two projects are well supported by preliminary evidence. One difficulty is the multiplicity of cell types to be analyzed (epidermal –mice & human-, enterocytes, intestinal epithelium, cultured cells), as well as of that of the cellular processes (migration, division, morphogenesis…). How these different investigations will synergize remains hard to predict.

Moving from developmental biology to tissue repair/homeostasis in adults, Team 20 has shown good adaptation to the observed in vivo phenotypes, hard to predict from cell based results.

Self-analysis has identified significant difficulties (post-docs, mice facility), a precise strategy to overcome these problems remains to be specified.

Conclusion

● Strengths and opportunities:

- During the last five years, Team 20 has successfully faced difficulties, including moving their mice models to a new building, novels directions to explore and reorganization of its staff.

- The group has an impressive publication record, including many collaborative works.

- Recent collaborations with medical labs may also help assessing relevance of findings to human diseases and diversifying funding sources.

- New skill in EM analysis is also strength for the next period.

● Weaknesses and threats:

- Reaching a funding level suitable for mice in vivo work is a challenge in France by now. This will be determining for future success.

- Reverse genetics is also a demanding approach, embarking on various questions that can exceed available expertise and current recognition.

- How the team will be able to compete successfully on the full spectrum of questions it have chosen to address is an issue to evaluate carefully.

● Recommendations:

- Addition of new staff members (experimentalists) is a decisive step for this active small team, addressing attractive questions in the moving field of galectins.

- Researchers from Université Paris-Diderot would help identifying motivated students and attracting them in the lab.

- Given the broad range of projects and model systems they are interested in, a better prioritization of the most appealing aspects should help. A possible guideline would be to focus on projects with respects of the observed defects in vivo (skin repair, ciliogenesis) and in which the team has advantages over international competitors. As mentioned in their document, the visiting committee encourages this team in their efforts to publish more accomplished studies, favouring mechanistic insights over phenotypic descriptions. Reaching a few numbers of focused publications in front-line journal is an important challenge for the next period. The team has a potential to gain a stronger international visibility: eg through an increased coverage of international conferences and seeking to reinforce networking. This seems a reachable goal with new permanent fellows who appear self-motivated and ambitious. All together, it should help rising larger grants and/or attracting Post-docs.

Team 21 : Chromosomal domains and DNA replication

Name of team leader: Ms Marie-Noëlle PRIOLEAU

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	3	3	100 %
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	1	100 %
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	7	5	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

Team 21 studies the molecular mechanisms governing the spatio-temporal regulation of DNA replication in vertebrates. The team uses two model systems: DT40 chicken cells and the K562 leukemia cell line. The team masters a technique that allows the purification of short nascent DNA strands and combine this technique with high throughput sequencing and bio-informatics analysis (both by collaborations set outside the team) to disclose different aspects of the location and the timing of firing of replication origins. This technical breakthrough is outstanding. The production in terms of scientific publications is limited but of excellent quality. Although similar work was done in simpler model systems, the work of this team expands to vertebrates in important ways. In the period 2007-2012, the team has produced 3 papers of high quality. Two of them have been published in excellent journals (PLoS Biology and PNAS) with team members as first or last authors. The team has also published 5 review articles. A third paper was a collaborative article published in Mol Evol Biol.

The plan for the future 5 years is very challenging, offering to study many different aspects and questions.

Assessment of the team's academic reputation and appeal

Team 21 has had 3 sources of financing from the French National Research Agency. However, the PI is not the coordinator of these projects and the nature of the contribution of the team is difficult to assess. Nationally, the team has managed to set up fruitful collaborations with the Génopole of Evry to perform high throughput sequencing and with a group in Lyon to help with the bio-informatics analysis.

The team does not have students from abroad, working with students from Université Paris-Diderot and Université Pierre et Marie Curie. A researcher joined the team from a closing team in another Parisian Institution.

Nevertheless, the team leader was invited in 4 conferences, 3 abroad (2 in UK and 1 in Russia, one was a FEBS congress) and 2 at international meetings in Paris. The team leader is reviewer of a number of specialized journals.

Assessment of the team's interaction with the social, economic and cultural environment

The technical advances made by the team should interest the DNA replication community. Nevertheless, they are specialized tools, which might be difficult to transfer to teams working on different topics.

The team produced a review articles and members participated to specialized symposia and conferences, with either oral communications or posters.

Assessment of the team's organization and life

The team is composed of one director of research and group leader, 2 researchers, 1 technician, 1 PhD and 1 Post-Doc. The team’s meetings take place once per week. The team appears to benefit from the high quality resources provided by the institute. It seems to have reached a stable number of scientists.

Assessment of the team's involvement in training through research

Team 21 had 5 PhD students since 2007. Two finished their PhD, one with 2 publications (one first author) and the second with only one publication as second author.

The team does not have ITN’s and seems not to participate to international training networks. Its researchers do not appear to be involved in the coordination of master’s training programs.

Assessment of the five-year plan and strategy

The future 5-year plan is very challenging. The team proposes to address the spatio-temporal pattern of DNA replication and to analyse the molecular mechanisms that govern this process by studying 6 different aspects:

- Identifying the consensus cis-regulatory elements involved in origin replication firing.

- Identify new origins of replication during replicative stress.

- Investigate the molecular mechanism involved in the establishment of the Timing Decision Point.

- Imaging DNA replication in space and time within the cell nucleus in fixed cells.

- Imaging DNA replication in single living cells with lac O GFP technology.

- Studying the impact of a chromosomal translocation (found in mantle cell lymphoma) on DNA replication.

These topics are ambitious and, although all related to the same general these of research, they might be too dispersed. The first three aims are the continuation of previous work and within the technical expertise of the team members. The experimental strategies proposed are coherent and feasible and the team has demonstrated experience and knowledge, and has been successful is addressing similar questions. Aims 4, 5 and 6 are newer and rely on technology and expertise that the team needs to develop. Contingency plans were not clearly presented, which might be an issue when developing new technologies.

The team is urged to publish the ongoing work to increase its productivity.

Conclusion

● Strengths and opportunities:

- The team has an outstanding expertise in cutting edge techniques that it has developed during the years and has very efficient collaborations with the platforms and the bio-informatics center.

- The productivity has not been high but the papers published are excellent and the team leader clearly favour quality over quantity.

- The projects for the future are ambitious but should lead to important outcomes.

● Weaknesses and threats:

Although the team is now stabilized by the arrival of 3 permanent members and has very good financing, it needs to improve its productivity further and to demonstrate international recognition.

● Recommendations:

- The team should focus on the aims of its ambitious proposal that are within its real of expertise.

- It should develop alternate strategies to those that require technical development.

4 • Team-by-team analysis

Team 22 : Biomolecular nanomanipulation

Name of team leader: Mr Terence STRICK

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	100 %
N2: Permanent EPST or EPIC researchers and similar positions	2	2	100 %
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	1	100 %
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	7	5	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

Team 22 research focuses on deciphering at single-molecule resolution, the mechanistic of molecular motor involved in DNA transcription, replication and repair. The works done have contributed to significant advance in this field mainly due to single-molecule nano-manipulation or single-molecule fluorescence visualization techniques developed at the state of the art.

These approaches allow monitoring individual molecules in real time and in the same time tracking and tracking their interactions and reactions.

The team has produced a total of 11 publications (3 research articles, 5 reviews, 2 book chapters & 1 book co-edited) in the last five years. 3 research articles from the group were published in excellent or outstanding journals, with in particular a high profile paper in Nature, which placed the investigator among the leaders of the field. Reviews have been published in highly respected journals [Gene&Dev, Trends Biochem Sci).

Assessment of the team's academic reputation and appeal

The PI who is well recognized in this research field has established international collaborations: USA (2), UK (2), NL (2), DE (1) and PL (1) which most of them have resulted in joint publications (3 of them involved joint grants). He organized EMBO practical course for 3 years.

The PI of Team 22 raised research funding at European level with one EURYI (He obtained an ERC-starting grant obtained that could not be combined with EURYI) and one EU-FP7 grant as partner. 3 fellowships were also awarded to lab members. The PI serves as ad-doc reviewer for excellent scientific journals, and for national and international funding agencies. He has been invited to 14 international meetings and to give 8 invited seminars at international and national levels.

One teaching scientist and one CR1-CNRS were recruited by Team 22.

Assessment of the team's interaction with the social, economic and cultural environment

Team 22 has one licensed patent with exclusive license to PicoTwist SA. It is involved in the Fête de la Science, to radio shows and exhibitions for general audience.

Assessment of the team's organisation and life

Team 22 organizes regular lab meetings. The PI is the head of the Genomes and epigenomes IJM program.

Assessment of the team's involvement in training through research

Staff members contributed to train 6 students for 2-6 month internship, 2 M2 and 2 PhD (two of them have left the lab after their PhD defence with publications; the third one will defend his PhD next year). Team 22 contributes very significantly to teaching (the PI as well as the teaching scientist).

Assessment of the five-year plan and strategy

The team aims at providing quantitative data on multicomponent machineries regarding major DNA metabolic processes which occur in bacteria. The objectives are:

(1) to understand the complete DNA repair pathway in order to explore if downstream steps might influence upstream reactions;

(2) to perform such measurements into eukaryotic context or at least in Archaea; (3) to move these measurements into living cells.

Altogether, these projects are very ambitious with methodological challenge both at the biological and technological levels. The translation of these approaches into eukaryotic context would be certainly dependent of the identification of biochemical collaborators already involved into the dissection of DNA multicomponent machineries.

Team 22 provided a clear and realistic SWOT analysis.

Conclusion

● Strengths and opportunities:

- A very dynamic and enthusiastic PI who is clearly among the leaders in his field.

- A unique interdisciplinary team mastering broad expertise from biological methods to physics to analyse the behaviour of single molecules.

- Very original research program with technically challenging experiments.

- Development of new imaging tools.

- Collaboration throughout a network of world-class collaborators. Excellence integration of technological development to serve general biological questions.

- Very successful in obtaining very competitive European grants.

- Very productive after a period of less activity with a paper in Nature.

● Weaknesses and threats:

- Very challenging projects where each step needs to be mastered from biological to technological aspects.

- There is a need to renew the sources of funding.

● Recommendations:

The project is very strong although very challenging in its translation in an in vivo environment. This team has a significant role to play by providing a driving force for the imaging platform not only at the level of instrument development but also on data analysis.

4 • Team-by-team analysis

Team 23 : Molecular oncology and ovarian pathologies

Name of team leader: Mr Reiner A. VEITIA

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	4	5	100 %
N2: Permanent EPST or EPIC researchers and similar positions	1	1	100 %
N3: Other permanent staff (without research duties)	1	2	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3		
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	9	8	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

Team 23's research project is focused on the FOXL2 transcription factor. The group has found that FOXL2 point mutations lead to intracellular aggregations of the protein. Furthermore they identified ten novel interacting protein partners. FOX2L has been shown by others to be mutated in ovarian ganulosa cell tumours. The work of team 23 led to development of the first predictive tools for ovarian dysfunction associated with FOXL2 mutations. They also showed that proliferation of cancer cells bearing FOXL2 mutations may be limited by SIRT1.

The team has produced a total of 63 publications (including reviews) in the last five years. 35 of the 63 publications are research articles with major contributions of the team. The journals are of good quality: PNAS, Human Molecular Genetics or Oncogene. The field of FOXL2 research is quite small, 430 publications can be found in Web of Science.

Assessment of the team's academic reputation and appeal

Team 23 members have published several reviews and opinions in high-profile journals such as Trends in Genetics, Trends in Cell biology, PNAS, J Pathology.

The team has established a network of national and international collaborations. The PI was invited for conferences to national or international meetings. He organized -or co-organized- two national and one international meeting. He is elected junior member of the Institut Universitaire de France (2008-2013) and received the Jacques Salat Baroux Prize of the Académie Nationale de Médecine in 2010. He is member of the Editorial Board of PLoS One and was Communicating Editor of the Journal of Biosciences from 2008-2012.

Research funding was obtained from ICEBERG (ANR-Investissements AVENIR (2011-2016), ARC, Ligue, FRM, IUF, BQR.

The laboratory has attracted one professor and one MCU who will join the team with the next contract.

Assessment of the team's interaction with the social, economic and cultural environment

This aspect was not specifically discussed by the PI.

Assessment of the team's organization and life

Regular lab meetings take place every two weeks to share and discuss the results obtained by each member of the team. There are no other details of the lab organization.

Assessment of the team's involvement in training through research

Four of the five permanent members of the team are involved in teaching at UP7 from L1 to M2 level. Four members have a HDR diploma. They all are training master and Ph. D students in the lab. All the students left the lab after PhD defence with several publications.

Assessment of the five-year plan and strategy

In the next five years, the team wants to study the pathogenic mechanisms of FOXL2 mutations by in vitro studies of transcriptional regulation, gene expression, target interaction and signal transduction pathways. However, this plan appears to be fairly generic with experiments that can be done, but for which rationale was never presented and appeared fairly weak to the committee members. It is therefore likely that the experiments listed will produce papers but that the impact of these papers will be limited. It is therefore recommended that more discussion among the group and with external advisors be done as to ensure that the experiments performed will have significance.

The team will also work in vivo by using mice to follow tumor development, and Drosophila as model for small molecule screening. The generation and analysis of the KI mice will be expensive and very time consuming, but does not seem very risky considering the relationship between FOXL2 mutation and ovarian granulosa cancer but finding other phenotypes could get a difficult task. In the report there are only few details on the construction of the mice (they will be done in collaboration) and their housing and analysis. There is no information on the funding of the mouse studies.

Conclusion:

● Strengths and opportunities:

- There is some international visibility by their reviews.

- There is a high involvement in teaching and training of students.

- The team seems to be well managed.

- Very high number of publications.

● Weaknesses and threats:

- Narrow focus on one gene/protein, from upstream to downstream.

- If Team 23 has produced a very large number of publications in the FOXL2 field, none of them is in a high profile journal and the significance of most of them is limited. One suggestion is to favour quality over quantity and to encourage the younger members of the team to focus on defining the rationale of experiments to be performed.

- The teams is using well known reagents but has not developed specific tools that could help devise original experiments that would secure future success in the field.

● Recommendations:

- The FOXL2 mutation link to ovarian granulose cancers renders the topic more interesting for a larger scientific community and should result in high IF publications but the approaches proposed are often generic rather than addressing specific questions that could help our understanding of this important biological question.

- The PI should more carefully choose research directions in order to perform experiments that are more significant rather than follow a fairly generic approach around a single gene.

5 • Conduct of the visit

Visit dates:
Start: Monday 10 December 2012 at 8:30 AM
End: Wednesday 12 December 2012 at 12:30 PM

Visit site: I Institut Jacques Monod
Institution: Université Paris-Diderot
Address : 15 rue Hélène Brion, 75013 Paris

Conduct or programme of visit:

Monday 10 December 2012

9:00 – 9:30 :	Closed door committee meeting
9:30 :	Starting of plenary presentations
9:30 – 9:45:	Presentation of the AERES evaluation committee
9:45 -10:45:	Presentation of the research unit by the director (including 15-20 mn questions)
10:45 – 11:00 :	Break / Debriefing of the committee
11:00 – 11:45 :	Three sub-committees meet with - Technical and Administrative Staff - Thesis Students - Researchers and Postdocs
12:00 – 1:00 :	Lunch
1:00 – 2:00 :	Teams 20 and 9
2:00 – 3:00 :	Teams 7 and 11
3:00 – 4:00 :	Teams 16 and 4
4:00 – 4:15 :	Break / Debriefing of the committee
4:15 – 5:15 :	Teams 13 and 17
5:15 – 6:15 :	Teams 12 and 21

Tuesday 11 December 2012

8:45 – 9:15 :	*Closed door committee meeting*
9:15 – 10:15 :	Teams 10 and 19
10:15 – 11:15 :	Teams 1 and 5
1:15 – 11:30 :	Break / Debriefing of the committee
11:30 – 12:15 :	Meeting with representatives of Institutions supporting the unit (could be extended during lunch)
12:15 – 1:30 :	Lunch
1:30 – 2:30 :	Teams 15 and 6
2:30 – 3:30 :	Teams 18 and 8
3:30 – 4:30 :	Teams 22 and 2
4:30 – 4:45 :	*Break / Debriefing of the committee*
4:45 – 5:45 :	Teams 3 and 14
5:45 – 6:45 :	Team 23

Wednesday 12 December 2012

9:00 – 9:30 :	Meeting of the committee with the head of research unit
9:30 :	*End of visit*
9:30 – 9:45 :	Break
9:45 – 12:30 :	*Closed door meeting of evaluation committee*

6 • Statistics by field: SVE on 10/06/2013

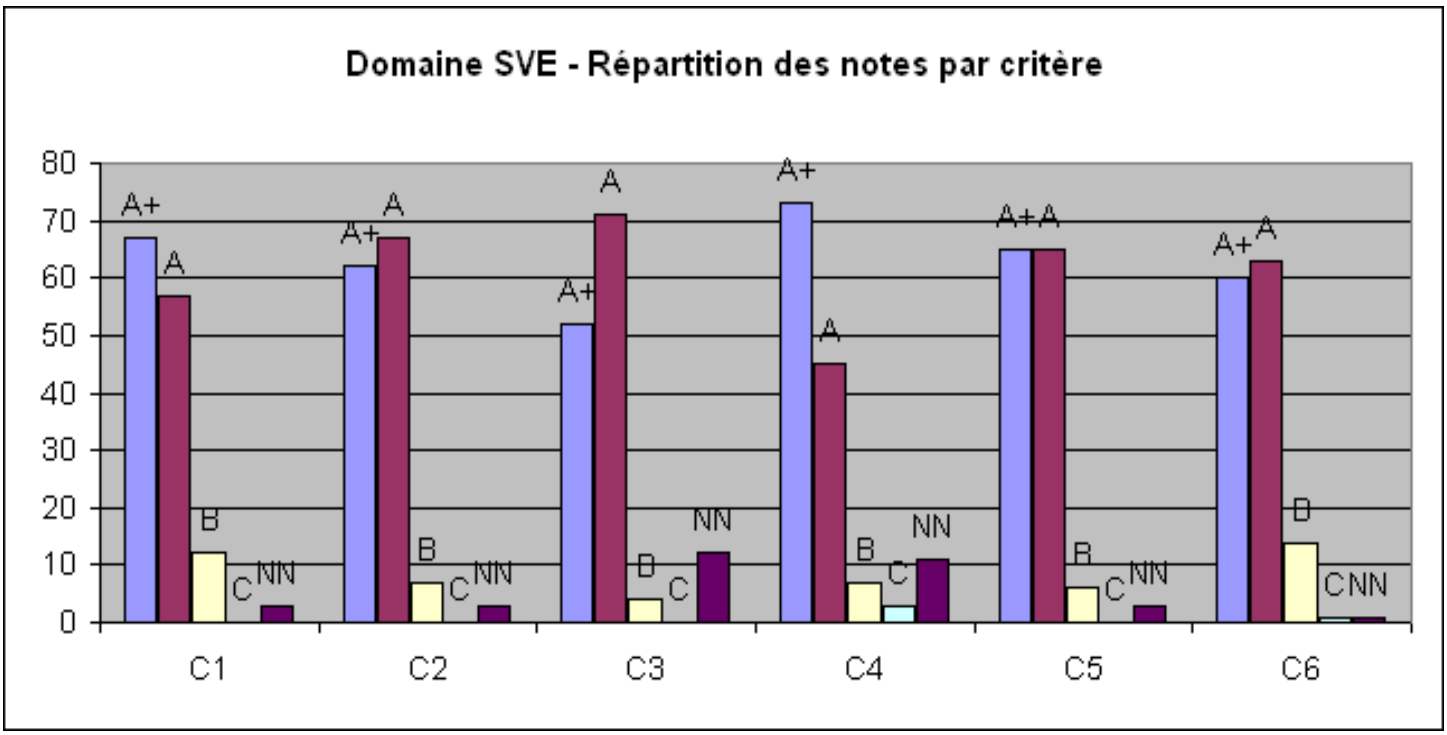
Notes

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	67	62	52	73	65	60
A	57	67	71	45	65	63
B	12	7	4	7	6	14
C	0	0	0	3	0	1
Non Noté	3	3	12	11	3	1

Percentages

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	48%	45%	37%	53%	47%	43%
A	41%	48%	51%	32%	47%	45%
B	9%	5%	3%	5%	4%	10%
C	0%	0%	0%	2%	0%	1%
Non Noté	2%	2%	9%	8%	2%	1%

Histogram



7 • Supervising bodies' general comments

www.ijm.fr

Professeur Giuseppe Baldacci
Directeur
: +33 1 5727 81 39
baldacci.giuseppe@ijm.univ-diderot.fr

To the chair and to the members of the AERES Expert Committee for the Institut Jacques Monod

We thank the AERES committee for their commitment to the IJM and for their thoughtful advice, not only on the overall direction of the institute, but for most of the individual research groups as well. The analysis of the strengths and weaknesses of the IJM was appreciated for its pertinence and perspicacity. Their analysis will greatly assist us in confronting the challenges in the next few years.

Most of the research teams were satisfied with the critical analysis of the committee, and plan to reflect on the points raised to improve their research. One team (team 4) felt however that the committee profoundly misunderstood the goals of its research program and thus did not appreciate the group's progress in achieving those goals. Another group leader (team 23) was disturbed by remarks disparaging the quality of his many publications. In addition, other group leaders (team 9, 18, 19, 20 and 21) raised specific comments. We ask the committee to consider what these colleagues estimate conceptual errors in the AERES report (Appendix 1-d).

We agree with the committee's assessment of the IJM's strengths, but we do have some remarks concerning the perceived weaknesses and the committee's recommendations to ameliorate them.

Weaknesses 1 and 2: Some teams are not doing work that reaches the top level and the IJM has published relatively few papers in "the most prestigious journals".

We are of course aware of the need to publish as much as possible in these high profile journals. We note only that the frequency with which IJM teams succeed in publishing in Nature, Science, and Cell has accelerated in recent years (2 in the last year alone).

Weakness 3: No international grant e.g. ERC or prestigious awards (EMBO YIP);
Recommendation R1: Be more ambitious in applying for them.

This is not strictly accurate. While we certainly could do more to encourage group leaders to apply for these grants and awards, we point out that Team 22 leader had indeed been awarded an ERC but was obliged to decline it because he had also obtained an EURYI award the same year. We also note that two IJM applications to the ERC and one to EMBO YIP made it to the auditions last year but were unfortunately not awarded. This year we have two more applications pending that have been preselected for auditions.

Weakness 4: Some of the teams appear to be isolated and to not receive the feedback necessary to orient their research towards more significant goals;
Recommendation R6: Dramatically improve mentoring at all levels.

We are surprised by the remark that "mentoring appears to be lacking." The IJM does indeed promote several levels of mentoring, not only for young groups but for all the group leaders.
Firstly, there is administrative mentoring: every new research group, regardless of scientific experience, is officially assigned a "tutor" (an established group leader) to guide the new group through the administrative labyrinth and help it integrate more smoothly into the IJM.

Secondly, all the research groups profit from the biennial discussions with our Scientific Advisory Board, a group of internationally renowned scientists.

Thirdly, there's the constant scientific give-and-take from colleagues, formalized by two internal seminar series, the Monday seminars before the whole institute, and the Wednesday chalk talks, before the other group leaders. These two forums provide an opportunity for colleagues to question the research goals and methodologies of the presenting group leader.

We also strongly encourage all group leaders, but especially those having difficulty obtaining grants, to discuss their grant proposals with their colleagues prior to submission. This is not formalized by an official Mentor, but rather is simply a part of our daily collegiality. Finally, the Director's door is always open for anyone desiring to discuss any aspect of life at the IJM.

Weakness 5: Some common services only serve one group (e.g. ancient DNA) while receiving technical support.

There is only one "common service" that serves only one group. But this is just a misunderstanding, partly caused by our use of the word "platform." The Ancient DNA platform is not a common service of the IJM, nor does it receive any technical or financial support. It is a platform only in the sense that the Paleogenomics group collaborates with labs all over the world who wish to profit from its unique technology. It should not be considered in the same category as the imagery, animal, proteomics, and genomics facilities.

Weakness 6: Poor initial support for junior teams ("Startup") if those do not come with an ATIP-Avenir.

It is lamentable that the Direction's discretionary funds from the supervising organizations have shrunk considerably in the last few years. However we have always endeavoured to provide the financial resources necessary to get a lab running. The basic package is 25K Euros, but if a group makes a case for requiring more, it can receive more (provided the funds exist, of course).

Weakness 7: Insufficient involvement of CNRS/INSERM scientists of IJM in the administrative structure of the Université Paris Diderot that hosts the Institute.

We are aware of the need for greater involvement in the scientific and administrative councils of the University. We note that many of the IJM staff scientists are active in teaching, and some even in organizing, master level courses at the university. The university professors however usually retain the administrative control over these courses.

Recommendations (not treated above)

***R2**: Better interactions among teams to orient research towards more significant goals.*

This recommendation is one of our top priorities already. We will continue to implement policies to promote better interactions among the groups. It is with this goal in mind that the IJM chose to abolish the departments ("programs"), and replaced them with overlapping loose confederations of groups with shared interests ("themes"). In addition, we are about to begin an internal financial incentive program to promote new collaborations between groups.

***R3:** Attract more international scientists at every level, including postdocs and junior group leaders.*

Although the IJM already has scientists from 27 different countries working here (including 5 group leaders) we would be delighted to have even more. During our recent call for new group leaders more than half the applicants came from abroad. However, our low salaries are set by the French State, and permanent positions cannot be offered by the IJM, only by our supervising organizations (CNRS, INSERM, and the university). This situation discourages foreign applicants, and makes recruitment from outside of France very difficult.

***R4:** Provide teaching relief for teaching scientists.*

This is an excellent idea. Unfortunately, teaching relief can only be accorded to teaching scientists by our supervising organizations. We support their applications, but the decision is out of our hands. Two professors are currently exempted from teaching responsibilities; one assistant professor enjoyed teaching leave last year, and three assistant professor applications for next year are pending.

***R5**: Provide better technical help for teams that have no technicians.*

We would like to be able to do this. Every time a research group closes, we redeploy the technicians (if any) to groups who have none. However national employment policy in the public sector is making it increasingly difficult to hire new technicians, even for temporary positions, and even if they could be paid for with the research funds of the team.

Other Recommendations

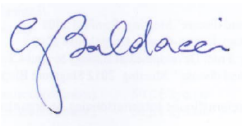
The committee strongly encouraged the development of Bioinformatics expertise in the IJM.

We entirely agree. In fact, in 2011 we launched a search for a Bioinformatics group leader. The candidate chosen (a Spanish national working in Japan) was excellent, and initially accepted our offer, but then backed out when he learned about the salary he would be getting.

The committee encouraged better integration with the neighbouring institutes of the University.

The IJM has a formal partnership to run the Genomics Platform with four different institutes at Université Paris Diderot (Paris 7), plus one with Institute Cochin de Biologie Moleculaire, at Université Paris Décartes (Paris 5). Moreover, several groups have ongoing collaborations with physicists of Paris 7 and elsewhere. Finally, several collaborative research projects between teams at Institute Cochin and IJM have been supported by seed money from the two institutes.

Paris, le 4 avril 2013



Professeur Giuseppe Baldacci

Directeur de l'Institut Jaques Monod

Appendix 1 - Document a

ERRORS OF FACT
(corrections are in **red**)

Introduction

(page 4)

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1 = Permanent professors and similar positions	35	31	100 %
N2 = Permanent EPST or EPIC researchers and similar positions	50	44	100 %
N3 = Other permanent staff (without research duties)	68 (65,4)	65 (62,4)	
N4 = Other professors (PREM, ECC, etc.)	2	2	100 %
N5 = Other EPST or EPIC researchers (DREM, Postdoctoral **fellows**, visitors, etc.)	29	7	100 %
N6 = Other contractual staff (without research duties)	23	5	
TOTAL N1 to N6	207	154	100 %

Percentage of producers	**100 %**

(page 5)

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	**36**	
Theses defended	**60**	
Postdoctoral students having spent at least 12 months in the team	**9**	
Number of Research Supervisor Qualifications (HDR) taken	**20**	
Qualified research supervisors (with an HDR) or similar positions	**55**	49

Team-by-team analysis

Team 1: *Evolution and development of* ***metazoans***
Name of team leader: Mr Guillaume BALAVOINE and Mr Michel ***VERVOORT***
(Page 11)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1 = Permanent professors and similar positions	1	**2**	100 %
N2 = Permanent EPST or EPIC researchers and similar positions	1	**1**	100 %
N3 = Other permanent staff (without research duties)			
N4 = Other professors (PREM, ECC, etc.)			
N5 = Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	2	100 %
N6 = Other contractual staff (without research duties)			
TOTAL N1 to N6	6	5	100 %

Team 2: ***Pathologies*** *of DNA replication*
Name of team leader: Mr Giuseppe BALDACCI
(Page 14)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1 = Permanent professors and similar positions	3	**3**	100 %
N2 = Permanent EPST or EPIC researchers and similar positions	1	**-**	100 %
N3 = Other permanent staff (without research duties)	**1**	**1**	
N4 = Other professors (PREM, ECC, etc.)			
N5 = Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	**1**	100 %
N6 = Other contractual staff (without research duties)			
TOTAL N1 to N6	**6**	**5**	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		**1**
Theses defended		
Postdoctoral students having spent at least 12 months in the team		**1**
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

Team 3: *Mitochondria, metals and oxidative stress*
Name of team leader: Mr Jean-Michel CAMADRO
(Page 17)

Team workforce	Number as at 30/06/2012[1]	Number as at 01/01/2014	2014-2018 Number of project producers
N1 = Permanent professors and similar positions	4	**4**	100 %
N2 = Permanent EPST or EPIC researchers and similar positions	**2**	2	100 %
N3 = Other permanent staff (without research duties)			
N4 = Other professors (PREM, ECC, etc.)			
N5 = Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	**1**	**1**	
N6 = Other contractual staff (without research duties)			
TOTAL N1 to N6	**7**	**7**	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the team	**1**	
Number of Research Supervisor Qualifications (HDR) taken	**2**	
Qualified research supervisors (with an HDR) or similar positions	**5**	**6**

(Page 18)
Team 3 includes **2 DR2** CNRS, **3 MCU P7**, 1 MCU P6, 1 DR1 Emeritus, 2 PhD students. Since 2007, 1 CR1 has left the lab while 2 MCU have joined the group.

Team 4: *Regulation of cell fate specification in the mouse*
Name of team leader: Mr Jérôme COLLIGNON
(Page 20)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	1	**2**
Postdoctoral students having spent at least 12 months in the team	2	**2**
Number of Research Supervisor Qualifications (HDR) taken	1	**1**
Qualified research supervisors (with an HDR) or similar positions	**3**	3

(page 21)
Assessment of scientific quality and outputs
…. the mapping of movements of the ICM, construction of useful early transgenics for the identification of enhancers and study of an endolytic receptor Cubilin, which are all interesting but

somewhat tangential. …
This sentence is wrong on three counts.
- We did not map the movements of the ICM. We tracked the fate and position of primitive endoderm cells, which derive from the ICM and go on to form the visceral endoderm (VE)
- This study is not tangential but central to our research interests because the VE plays a critical role in the establishment of embryo polarity, and its formation is concomitant to the maturation of the underlying epiblast, two of the key Nodal-dependent processes we are actively studying .
- Neither is the production of reporter transgenic lines for specific Nodal enhancers tangential to our research interests. It is at the core of our strategy to understand how diverse regulatory influences (Activin/Nodal signalling and other signalling pathways, pluripotency factors) are integrated at the Nodal locus to modulate Nodal expression and cell-fate specification.

… Team 4 studies of nonneural ectoderm, microelectroporation …, while all interesting, represent promising beginnings but rather preliminary findings, all of which have been reported to a greater or lesser extent by others…
This sentence is inaccurate and minimizes the novelty of these studies
- « non-neural ectoderm » refers to the production of a fatemap of the anterior ectoderm and an ablation study of a particular territory that appears to be critical for forebrain development. It has definitely not been done before in the mouse. The best evidence of its novelty is that the fatemap paper was accepted within 2 weeks by development with no rereview. When the ablation study was presented at the Mouse Molecular Genetics meeting at Asilomar, USA, in October 2012, it won first prize in the poster competition.
- « microelectroporation » refers to a collaboration with a team of physicists from the laboratory of photonics and nanostructures. Its aim was to devise an apparatus capable to electroporate a very small number of cells in mouse embryos while achieving reproducibility and survival. All these goals have been attained and this has never been done before.

Assessment of the team's involvement in training through research
..Team 4 head teaches Master courses in France and European Union (ENS Paris and Lyon, Univ Paris-Diderot, UPMC, Sweden, Italy, Spain). He has mentored the work of three PhD and four undergraduate students, one technician. He was reviewer for only one PhD Thesis, and one HDR, which is surprisingly low.
- Team 4 head taught courses in the US (Cold Spring Harbor), Institut Pasteur, Univ. d'Auvergne, Univ. Paris-Diderot, UPMC.
- Team 4 head was reviewer for 5 PhD thesis (member of PhD jury) and one HDR. In addition he was tutor for one PhD student at the Pasteur Institute (member of PhD committee).

Team 7: *Membrane Epigenetic regulation of genome organization*
Name of team leader: Ms Sandra DUHARCOURT
(Page 30)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	**2**
Theses defended	1	
Postdoctoral students having spent at least 12 months in the team		**1**
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

Team 9: *Membrane traffic in neuronal and epithelial morphogenesis*
Name of team leader: Mr Thierry GALLI
(Page 36)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		
Theses defended	3	
Postdoctoral students having spent at least 12 months in the team	5	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	4	4

Assessment of scientific quality and outputs

The report states in error that *"The team also significantly contributed to **collaborative work**, most notably in their report of a transmembrane protein Vezatin that participates in dendritic spine morphogenesis (J Neuroscience, 2012)."*

This article **is a publication of the team**, and does not correspond to a collaborative work, because the study was directed by team members, most of the data were acquired in the team, with the first and last two authors being members of the team. (Danglot L, Freret T, Le Roux N, Narboux-Nême N, Burgo A, Hyenne V, Contremoulins V, Dauphin F, Bizot JC, Vodjdani G, Gaspar P, Boulouard M, Poncer JC, Galli T, Simmler MC. 2012. Vezatin is essential for dendritic spine morphogenesis and functional synaptic maturation. ***J Neurosci*** 32:9007-9022.)

In addition, publications with a team member as first (or co-first), last (or co-last) or corresponding author in ***J Cell Sci, Biophys J, EMBO reports, EMBO Mol Med, Psychiatric Genetics, J Biol Chem, Biol Cell*** and reviews in ***FEBS J, Dev Cell, FEBS Lett,*** **Médecine/Science, *Biol Cell* should be listed as publications of the team bringing the total to ten research articles and five reviews as stated in the summary sheet**.

Team 11: *Polarity and morphogenesis*
Name of team leader: Mr Antoine Guichet
(Page 43)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	2
Theses defended	2	3
Postdoctoral students having spent at least 12 months in the team		1
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

Team 12: *Membrane dynamics and intracellular trafficking*
Name of team leader: Ms Cathy JACKSON
(Page 46)

Team workforce	Number as at 30/06/2012[1]	Number as at 01/01/2014	2014-2018 Number of project producers

N1 = Permanent professors and similar positions	1	1	100 %
N2 = Permanent EPST or EPIC researchers and similar positions	2	2	100 %
N3 = Other permanent staff (without research duties)			
N4 = Other professors (PREM, ECC, etc.)			
N5 = Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	**2**	
N6 = Other contractual staff (without research duties)	1		
TOTAL N1 to N6	7	4	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the team	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	**2**

(Page 47)

Assessment of scientific quality and outputs

Team 12's research is focused on deciphering the mechanisms mediating membrane trafficking. The works done have **has** contributed to identifying interactors that revealed new mechanisms by which Arf and Rab small G proteins cooperate in the membrane trafficking **pathways**. More recently, the team has found a novel class of amphipathic membrane curvature sensors that might be involved in the process.

Assessment of the team's academic reputation and appeal

The PI is member of the editorial board of J Cell Sci, Cellular Logistics and a member of the reviewing editors for Mol Biol Cell, **and is an academic editor for PloS One.**

Assessment of the five-year plan and strategy

The team will focus on the Arf1 GTPase exchange factor GBF1. Three mains goals will be pursued:

(1) the dual role of GBF1 in trafficking and lipid droplet metabolism. Research will focus on interacting partners common to the two interactomes. Experimental approaches will be based on super-resolution and CLEM microscopy on **using RPE1 and HeLa cell lines, and in silico modeling;**

Team 13: *Molecular virology*
Name of team leader: Ms Isabelle JUPIN
(Page 49)

Team workforce	Number as at 30/06/2012[1]	Number as at 01/01/2014	2014-2018 Number of project producers
N1 = Permanent professors and similar positions	1	1	100 %
N2 = Permanent EPST or EPIC researchers and similar positions	1	1	100 %

N3 = Other permanent staff (without research duties)	1	1	
N4 = Other professors (PREM, ECC, etc.)			
N5 = Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	**2**	
N6 = Other contractual staff (without research duties)			100 %
TOTAL N1 to N6	5	**5**	

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		**1**
Theses defended		
Postdoctoral students having spent at least 12 months in the team		**1**
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

***Team 14**: Regulation and dynamics of cell division*
Name of team leader: Mr Roger KARESS
(Page 53)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the team		
Number of Research Supervisor Qualifications (HDR) taken	**1**	
Qualified research supervisors (with an HDR) or similar positions	4	4

***Team 16:** Computational modelling and biomethematics*
Name of team leader: Khashayar PAKDAMAN
(Page 59)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1 = Permanent professors and similar positions	3	3	100 %
N2 = Permanent EPST or EPIC researchers and similar positions			
N3 = Other permanent staff (without research duties)	1	1	
N4 = Other professors (PREM, ECC, etc.)			
N5 = Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6 = Other contractual staff (without research duties)			
TOTAL N1 to N6	**4**	**4**	

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	6	2
Theses defended	3	2
Postdoctoral students having spent at least 12 months in the team	-	-
Number of Research Supervisor Qualifications (HDR) taken	1	1
Qualified research supervisors (with an HDR) or similar positions	2	3

(Page 60)

Assessment of the team's involvement in training through research

All Team 16 permanent staff are faculty members, strongly involved in interdisciplinary training at all levels. The PI is the French representative of the ERASMUS MUNDUS Complex Systems Sciences masters program. **Seven** PhD students were or are supervised, two in co-direction with Team 3 PI, three in co-direction with external collaborators. Graduate students co-authored papers of the team.

Team 17: *Genetics and development of the cerebral cortex*
Name of team leader: Ms Alessandra PIERANI
(Page 62)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1 = Permanent professors and similar positions		1	**100 %**
N2 = Permanent EPST or EPIC researchers and similar positions	2	2	100 %
N3 = Other permanent staff (without research duties)	1	2	
N4 = Other professors (PREM, ECC, etc.)			
N5 = Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	2	100 %
N6 = Other contractual staff (without research duties)	1	1	
TOTAL N1 to N6	7	7	100 %

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		2
Theses defended	3	
Postdoctoral students having spent at least 12 months in the team	1	1
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

(Page 63)

Assessment of scientific quality and outputs

"Since 2007, they have published 7 research articles in peer reviewed journals, 2 in peer reviewed journals in journals of high quality (4<IF<15), 3 in 2010 (comprising 1 in Nature Neurosci), 1 in 2011 and 1 in 2012. In addition, they have also produced 1 review in Current Opinion in Genetics and Development IF 8 (2010), 1 in Development, Growth and Differentiation (2009), 1 book chapter (2012).

should be:

"Since 2007, they have published 7 research articles in peer reviewed journals of high quality (4<IF<15), 3 in 2010 (comprising 1 in Nature Neurosci), 3 in 2011 and 1 in 2012. In addition, they have also produced 1 review in Current Opinion in Genetics and Development IF 8 (2010), 1 in Development, Growth and Differentiation (2009), 1 book chapter (2013)".

Assessment of the team's academic reputation and appeal

"Team 17 attracts many applicants a year for both post-doctoral and student positions from European Union and US: 5 Post docs in total (1 Japanese/Korean, 1 British), 3 have now left the team) and 2 just recruited (02/2010 and 04/2011)."

should be:

"Team 17 attracts many applicants a year for both post-doctoral and student positions from European Union and US: 3 Post docs in total (1 Japanese/Korean, 1 British, 1 Italian), 1 has now left the team and 2 just recruited (02/2010 and 04/2011)."

Assessment of the team's organization and life

"In the evaluated period, the PI has mentored the work of 2 PhD and 10 undergraduate students, 6 post doctoral fellows and 3 technicians."

should be:

"In the evaluated period, the PI has mentored the work of 2 PhD and 10 undergraduate students, 3 post doctoral fellows and 3 technicians."

Assessment of the team's involvement in training through research

"Team 17 leader teaches Master courses in France and European Union (ENS Paris and Lyon, Univ Paris-Diderot, UPMC, Sweden, Italy, Spain). She has mentored the work of two PhD (now in post-doc training) and ten undergraduate students, six postdoctoral fellows and three technicians."

should be:

"Team 17 leader teaches Master courses in France and European Union (ENS Paris and Lyon, Univ Paris-Diderot, UPMC, Sweden, Italy, Spain). She has mentored the work of two PhD (now in post-doc training) and ten undergraduate students, three postdoctoral fellows and three technicians."

Team 18: *Cell cycle and development*

Name of team leader: Mr Lionel PINTARD

(Page 67)

Assessment of scientific quality and outputs

There has been a steady flow of articles in good journals over the past years (J Cell Sci, Development, PLoS Genetics (~~**in revision**~~)).

Assessment of the team's involvement in training through research

This involvement is sufficient and effective. A high number of rotation students have been educated/supervised (>10). Lab retreats are organized, together with a nematode group in **Geneva**. Management of supervision is sound.

Team 19: *Development, signalling and trafficking*
Name of team leader: Ms Anne PLESSIS
(Page 69)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1 = Permanent professors and similar positions	1	2	100 %
N2 = Permanent EPST or EPIC researchers and similar positions			
N3 = Other permanent staff (without research duties)	1	1	
N4 = Other professors (PREM, ECC, etc.)	1	1	100 %
N5 = Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	**1**	
N6 = Other contractual staff (without research duties)			
TOTAL N1 to N6	5	**5**	

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		
Theses defended	1	
Postdoctoral students having spent at least 12 months in the team		
Number of Research Supervisor Qualifications (HDR) taken		**1**
Qualified research supervisors (with an HDR) or similar positions	1	1

(Page 70)
Assessment of the team's organization and life (last line)
"including Master II students, one of which is now applying for a fellowship in order to pursue her thesis."
Should be
"including Master II students, one of which is now pursuing her thesis in the team".

(Page 71)
Assessment of the team's involvement in training through research (line 2)
"Team 19 contributes to about 600h teaching/year"
should be
"Team 19 contributes to about **300 h** teaching/year".

(Page 72)
ll Weaknesses and threats: (last line)
"The technician is not recruited under a permanent position and there is a risk that he leaves the team."
should be
"The technician **did not get recent promotion** and there is a risk that he leaves the team."

Team 20: *Morphogenesis, homeostasis and pathologies*
Name of team leader: Ms Françoise Poirier
(Page 73)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		
Theses defended	1	
Postdoctoral students having spent at least 12 months in the team		
Number of Research Supervisor Qualifications (HDR) taken		**1**
Qualified research supervisors (with an HDR) or similar positions	3	4

(Page 74)

Assessment of the five-year plan and strategy

The proposed research program aims at ..... One difficulty is the multiplicity of cell types to be analyzed (epidermal –mice & human-, enterocytes, ~~chondrocytes,~~ intestinal epithelium, cultured cells), as well as of that of the cellular processes (migration, division, morphogenesis…).....

Appendix 1 - Document b

CONCEPTUAL ERRORS AND COMMENTS

Team 4: *Regulation of cell fate specification in the mouse*
Name of team leader: Mr Jérôme COLLIGNON
(Page 20)

We find the report minimizes our achievements.
Our published findings on the regulation of Nodal at preimplantation stages contributed to a better understanding of epiblast maturation and primitive endoderm patterning. It also led us to the identification of a novel Nodal enhancer, HBE, which we found to be regulated by pluripotency factors – the characterization of HBE is finished and is currently being written up. In the course of this work we produced a number of valuable reagents (transgenic reporter lines, ES cell lines, KO), which allow us to further pursue our investigations of the regulation of early cell-fate specification.
As part of our research on the formation of the forebrain we published the most detailed fate map of the E7.5 mouse anterior epiblast to date, pinpointing the non-neural origin of the signalling center known to be critical for forebrain formation. An exhaustive investigation of the role of this region was then undertaken and is now nearing completion.
In collaboration with a team of physicists we also produced a micro-electroporation apparatus, capable of reproducibly targeting fewer than five cells in an early mouse embryo, without compromising viability. This is the first device of its kind available to mouse embryologists. This project is now finished and ready for publication.
None of these advances is properly acknowledged.

We find the report presents an incomplete, sometimes misleading, view of our research plan.
The studies on Cubilin and Notch, to which we contributed our developmental biology expertise, are finished and about to be published; they are *not* part of the five-year plan.
The study of the non-neural epiblast region critical for forebrain formation is *not* part of the plan either, as the researcher who is responsible for this topic will leave the lab and pursue this line of research elsewhere.
In contrast, our five-year plan details six research projects, all aimed at understandings the role of Nodal and Activin/Nodal signalling in the regulation of early cell-fate specification. Of these six projects, only one, the follow-up study of HBE, is mentioned in the report; in particular, the report completely neglects our use of the *in vitro* models we have established.
This confused view of our research plan may explain the reviewer's apparent failure to perceive its coherence.

We find the report unduly negative on our prospects.
The report presents things as if our future depended entirely on the outcome of our study of HBE, the novel Nodal enhancer. As mentioned above, this study is only a part of our research plan. Even so, the three objections raised against this specific project appear unfounded:
- The HBE reporter transgene *does* in fact identify (not "may or may not") a subpopulation of the post-implantation epiblast. Thus, we now have the means to find out what this subpopulation is.
- The CreER approach has already been used successfully by others (Takaoka et al., 2011).
- We now know that the deletion of HBE does indeed abrogate the expression of Nodal in embryonic stem-cells.

Last but not least, the report fails to take into account the fact that we have secured the necessary funding to achieve our aims. Indeed, over the past two years we have obtained grants from the ANR, the FRM, the Ligue National Contre le Cancer, and the Stempole Ile-de-France. These successes attest of the confidence our current research plan inspires in experts in our field.

Team 9: *Membrane traffic in neuronal and epithelial morphogenesis*
Name of team leader: Mr Thierry GALLI

Assessment of the team's interaction with the social, economic and cultural environment

The depository of three mouse lines (tetOmin-GFP, GFP-TIVAMP, GFP-Longin) to the European Mouse Mutant Archive (EMMA), a license agreement for mAbCl158.2 with Synaptic Systems, a collaboration under MTA with the UK biotech company Syntaxin, activities to raise pupils' interest in science in primary school, and the presence of the PI in several scientific councils, advisory boards, and steering committees are mentioned in the report.

Assessment of the five-year plan and strategy

We are grateful for the very positive comments.
Aim3: Our proposal includes "anatomical and biochemical investigations to characterize alterations of the synapses [… and] the screening of metabolic changes". The study of "behavioral phenotype of mutants affecting trafficking" **was not included in our projects**. Indeed, we have already carried out and published studies **exploring behavioral abnormalities** in TI-VAMP/VAMP7 KO (Danglot et al, *J Neurosci* 2012). In addition, VAMP2 KO mice die at birth preventing any such experiments.

Conclusion

Weaknesses and threats

VAMP KOs are animal models which provide important tools to dissect novel molecular mechanisms, as described in our "Scientific Project". After the considerable effort in obtaining the TI-VAMP/VAMP7 KO mouse (which has been **published)** (Danglot et al, *J Neurosci* 2012), we now wish to capitalize on our investment. The power of studies combining cellular and whole organism studies using mouse KO is exemplified by our recent paper (Larghi P, Williamson DJ, Carpier JM, Dogniaux S, Chemin K, Bohineust A, Danglot L, Gaus K, Galli T**§**, Hivroz C**§.** The SNARE protein VAMP7 controls T cell activation by regulating recruitment and phosphorylation of Lat subsynaptic vesicles to the TCR activation sites. ***Nature Immunol*** 2013 May 12. doi: 10.1038/ni.2609; **§ equal contributions**).

Recommendations

The team will certainly continue to focus "on a limited amount of central questions", and make all efforts in "consolidating and keeping the scientific excellence" as suggested by the Committee.

Team 18*: Cell cycle and development*
Name of team leader: Mr Lionel PINTARD
(Page 67)

The work performed in collaboration with P. Mains (Genetics 2009 and JCB in revision) is not mentioned in the report. Likewise, the work performed in collaboration with the group of Monica Gotta on the regulation of mitotic entry in the early emrbyo is not discussed in the report.

General comments

We will take the recommendations of the committee into account. We acknowledge that the identification of substrates by proteomic approaches might be challenging but as mentioned in our report we are also using genetic approaches to achieve this goal and we have already identified candidates. Alternates approaches are investigated. We would also like to stress that this part is only one part of the project. Our work on the regulation of cell cycle timing in the early embryo is not discussed or mentioned in the report.

***Team 19**: Development, signalling and trafficking*
Name of team leader: Ms Anne PLESSIS
(Page 69)

General comments
The three year gap in the publication records is largely due to the fact that the team started in 2010, meaning that novel members arrived that started new projects. The team is only starting to harvest the full products of its investment in these novel projects.

***Team 20:** Morphogenesis, homeostasis and pathologies*
Name of team leader: Ms Françoise Poirier
(Page 73)

Assessment of the five-year plan and strategy
The proposed research program aims at investigating the influence of galectin3/7 on various aspects of cytoskeletal organization in epithelial cells and exploring their relevance to some human pathologies. The team will address roles of galectins either in epidermal cell migration or in "centrosome biology", in each case engaging collaboration with clinical groups. The two projects are well supported by preliminary evidence. One difficulty is the multiplicity of cell types to be analyzed (epidermal –mice & human-, enterocytes, chondrocytes, intestinal epithelium, cultured cells), as well as of that of the cellular processes (migration, division, morphogenesis…). How these different investigations will synergize remains hard to predict.

This sentence is inaccurate.
We are indeed working on 3 cellular processes (migration, division, morphogenesis) in the context of two target tissue: the epidermis and intestinal epithelium of mutant mice. The molecular mechanisms will be dissected with the help of only two well established cell culture systems: human epidermal cells (HaCat) and human enterocytes (Caco2).

***Team 21:** Chromosomal domains and DNA replication*
Name of team leader: Ms Marie-Noëlle PRIOLEAU
(Page 76)

Several factual points are incorrect and needed to be modified. Moreover, some factual and important points have not been mentioned and should be added.

Assessment of scientific quality and outputs
This important point should be emphasized.
The team has also been the first to develop a genetic system to study DNA replication in vertebrates. This system is based on the use of the unique capacity of avian DT40 cells to do homologous recombination at very high rates.

Assessment of the team's academic reputation and appeal
The financing resources are not correctly described. Only two are mentioned and the two more important sources are eluded. The correct description is as following:
Team 21 has had 3 sources of financing from the French National Research Agency. The PI has been the coordinator of one "ANR blanc" that has been allocated exclusively to this team from 2009 to 2011. However, the PI is not the
coordinator of the other two. One is a very important consortium that involved several institutes and will allow the team to develop collaborative studies with new groups. The other one is a large bio-

informatic grant, the team is among the few biologists belonging to this consortium. This grant has allowed the team to recruit one PhD student who is doing both experimental studies and bio-informatic training in order to reinforce the capacity of this team to interact with bio-informaticians. Finally the team has been supported since 2011 by the Ligue National contre le cancer in the prestigious program named Equipe Labellisée.

Students are not exclusively "local" as mentioned in the text
The team does not have students from abroad, working half with local students from Université Paris-Diderot and half with students from the Université Pierre et Marie Curie.
Finally two researchers have joined the laboratory and not only one. The truth is the following
A researcher joined the team from a closing team in another Parisian Institution. A second researcher attracted by the originality and quality of the projects of the team and the availability of a highly competent imaging core facility at the Institute, has joined the team to develop an imaging approach using molecular tools perfectly mastered by the team

Finally, the description of the participation of the leader in conferences and important committee is again far from been complete.
The team leader was invited in 4 conferences, 3 abroad (2 in UK and 1 in Russia, one was a FEBS congress) and 2 at international meeting in Paris (Institut Curie and Institut Pasteur). The team leader is reviewer of a number of specialized journals and has been the editor of a special issue on DNA replication in Chromosome Research. The team leader has been for two years in a committee of the National French agency (committee svs8) and since September 2012 is in the committee of the Ligue National contre le Cancer. The team leader has organized two international meeting (one as the principal organizer) and two national meetings.

Assessment of the team's interaction with the social, economic and cultural environment
The technical advances made by the team should interest the DNA replication community and her methodology has been already disseminated to other teams. The use of DT40 cells as a model genetic system to study DNA replication has already lead to one fruitful collaboration with the team of Michelle Debatisse on the study of common fragile sites. Finally, the work of the team has long term implications on cancer research.

Assessment of the five-year plan and strategy
We do not agree with the comment that some projects need important technological development.
The aim 6 relies on the use of DNA micro-arrays to study the temporal program of DNA replication and the team has already used it.
Aims 4, 5 are newer but rely on cell models and molecular tools perfectly mastered by the team. Regarding the new imaging tools necessary for these aims, close and permanent collaboration with the members of the ImagoSeine/imaging core facility of the Institute, together with the availability of highly performing equipment have already enable successful first development of these approaches.

Team 23: *Molecular oncology and ovarian pathologies*
Name of team leader: Mr Reiner VEITIA
(Page 82)

According to the committee, "the field of FOXL2 research is quite small (430 publications)". We think there is no field of Foxl2 but a field of reproductive biology and endocrinology where FOXL2 stands as a key gene. Coming down to numbers, a pubmed search with the keyword "Forkhead" retrieves 10747 refs, barely different from the popular "homeobox" genes (13179 refs). FOXL2 is a model.

Concerning the international visibility, the PI of the group has an H index=31 (age 43 y). We agree we do not create tools but we do produce lot of genomic data for the community. Moreover, we follow technological developments to a point that a journal of the Nature family (IF>19) is about to accept a MS of which the PI is the last author.

Concerning our project, the main point is deciphering the impact of a pro-oncogenic FOXL2 mutation on structure, interactions, target-gene recognition and function. We admit that our genomic/proteomic approach is "generic" but we firmly believe this is a first and mandatory step to generate hypothesis-driven experiments. The fact that the oncogenic mutation is known since 2009 and we are still looking for its molecular and cellular effects, clearly shows there is no obvious a priori experiment to perform at this point.

The phrase "One suggestion is....to encourage the younger members of the team to focus on defining the rationale of experiments to be performed" is totally unfounded (nothing was said about this point neither in the written document or in the oral presentation). Actually, this is the way we already proceed in the lab.