UGBD - Génétique et biologie du développement

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Genetics and Developmental Biology Unit

Under the supervision of the following institutions and research bodies:

Institut Curie

Centre National de la Recherche Scientifique

Institut national de la santé et de la recherche médicale

Université Paris 6 - Pierre et Marie Curie

January 2013

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

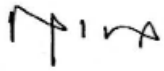
Research Units Department

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: Genetics and Developmental Biology Unit

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

- Grading table of the team: Mammalian Development Epigenetics

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

- Grading table of the team: Polarity Division and Morphogenesis

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

- Grading table of the team: Germ Cell Development

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

- Grading table of the team: Epigenetic Decisions and Reproduction in Mammals

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

- Grading table of the team: Mechnism of Repression by Polycomb Proteins

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

- Grading table of the team: Neuronal Circuit Development

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

- Grading table of the team: Stem Cells and Tissue Homeostasis

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

- Grading table of the team: Ms Sylvia FRE 's Team

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

- Grading table of the team: Ms Alena SHKUMATAVA's Team

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

Evaluation report

Unit name:	Genetics and Developmental Biology Unit
Unit acronym:	
Label requested:	Institut Curie, CNRS, INSERM
Present no.:	UMR 3215-U934
Name of Director (2012-2013):	Ms Edith HEARD
Name of Project Leader (2014-2018):	Ms Edith HEARD

Expert committee members

Chair:

Mr Pierre LEOPOLD, Institut de Biologie Valrose, University of Nice

Experts:

Mr Cédric BLANPAIN, Université Libre de Bruxelles, Belgique

Ms Claire CHAZAUD, Génétique Reproduction et Développement, University of Clermont-Ferrand, (Representative of CNRS)

Mr Joël DREVET, Génétique Reproduction et Développement, University of Clermond-Ferrand, (Représentative of CNU)

Mr Robert FEIL, Institut de Génétique Moléculaire de Montpellier, University of Montpellier

Mr Saadi KHOCHBIN, Institut Albert Bonniot, University of Grenoble

Ms Nadine PEYRIERAS, Institut de Neurobiologie Albred Fessard, CNRS, Gif sur Yvette

Mr Alain VINCENT, Centre de Biologie du Développement, University of Toulouse

Mr Jean-Paul VINCENT, MRC National Institute for Medical Research, London, UK

Scientific delegate representing the AERES:

Mr Pierre COUBLE

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

Mr Daniel Louvard (Institut Curie)

Mr Laurent Kodjabachian (CNRS)

Ms Marie-Pascale Martel (INSERM)

Ms Delphine Duprez (University Pierre et Marie Curie)

1 • Introduction

History and geographical location of the unit:

The Genetics and Developmental Biology Unit was created in January 2009 through the strong will of Mr Daniel LOUVARD and Mr Spyros ARTAVANIS TSAKONAS and after the construction of a new building on the campus of the Curie Institute in Paris. The starting aim of this new institute was to bring together researchers of different expertise in Developmental Biology in a context of strong medical expertise, where both fundamental and medical researches could foster each other. Four founder teams, two senior (Ms Edith HEARD, Mr Yohanns BELLAICHE) and two junior (Ms Deborah BOURC'HIS, Mr Jean-René HUYNH) occupied the recently constructed building in 2009, rapidly followed by a total of 5 other junior teams recruted in three successive waves of open international calls. The Unit currently counts 9 teams for a total of 71 staff. The teams and the administration of the unit occupy 2227 square meters in the building, the rest of the building being occupied by the Computer Science Department of the Curie Institute (103 square meters total). Currently, part of the 3rd floor is occupied by equipment and staff from a sequencing facility, which should be relocalized soon and part of the 4th floor could be made free to allow the arrival of one/two newly recruted teams (see evolution perspectives below).

Management team

The direction was originally given to Mr Spyros ARTAVANIS TSAKONAS, who initially maintained a small team in the Unit in addition to his main lab at Harvard Medical School. The delay in the construction and his increasing duty as a full Professor of Harvard Medical School compromised his capacity to maintain his position as a director. From its start, the Unit was practically run by Ms Edith HEARD and Mr Yohanns BELLAICHE, and the advisory Board of the Curie Institute asked Ms Edith HEARD to become the new director of the unit, which she accepted in the course of 2009. Since 2010, Mr Yohanns BELLAICHE is deputy director.

AERES nomenclature:

SVE1 LS1, SVE1 LS2, SVE1 LS3

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		1	1
N2: Permanent researchers from Institutions and similar positions	13	13	12
N3: Other permanent staff (without research duties)	15	16	
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)			
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	34	30	26
N6: Other contractual staff (without research duties)	9	5	
TOTAL N1 to N6	71	65	39

Percentage of producers	***100 %***

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	10	
Theses defended	8	
Postdoctoral students having spent at least 12 months in the unit*	36	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	7	8

2 • Assessment of the unit

Only four years after its creation, the unit has reached mature size and is now composed of the two founder senior teams, five young teams and two starting teams. Although the Unit is still in its early years, the research is outstanding and highly visible internationally as judged by the list of scientific papers in high profile journals and competitive fundings obtained from both national and european agencies (ERC, AVENIR, Schlumberger, etc.). The projects are in most cases cutting edge and ambitious and carry very strong potential for future outstanding contributions.

Strengths and opportunities

The main strengths of the Unit are its outstanding research, its youth and enthusiasm and its strong potential for future accomplishments. The Unit is hosted in a new research building, which provides full support for top of the art biology research. The two senior groups are conducting outstanding research and represent charismatic examples for the Unit. The young group leaders have been highly selected and most of them already benefit from a full support and recognition from national and European granting agencies. The Unit has developed a highly collegial atmosphere, which is reinforced by geographic unity, strong complementarity in the research themes and a rather overall limited size. The close proximity of the Curie computer science department has allowed developing important collaborations with several teams of the Unit. The set up within the Unit of a versatile and efficient imaging platform maintained by three talented engineers allows developing state of the art imaging techniques and represents an asset for the teams. Finally, the Unit benefits from an excellent local scientific environment both in other Curie units and in closeby institutes (ENS, ESPCI, Jussieu campus).

Weaknesses and threats

The unit is funded by the CNRS, INSERM and Institut Curie. These research agencies have decreased their funding to the Unit in the last three years (except for the Curie Institute, which provides equal budget despite a strong mass increase of the Unit). Therefore, most of the research is funded by individual contracts, including exceptional equipments (OMX super resolution microscope, 1M€ ; confocal microscope, 250K€, both being inserted in a Curie platform). Due to the recent start of the Unit, a large number of young teams will apply for senior selection rather synchronously in the coming years, with the risk of strong internal competition and major changes in Unit composition. The 5 years period given to young groups appears rather short compared to european standards; moreover a clear agenda of the selection procedure should be given to the young group leaders.

Recommendations

The committee is unanimously impressed by the outstanding quality of the current research and the very strong potential of this young Unit, which represents a unique and very successful example in the French biology research landscape. Given the present trend of institutional funding, the committee strongly recommends that new young teams are selected according to their ability to fund themselves through competitive funding agencies. The present Director of the unit is not willing to prolong her office for a second 4-year period and has started a search for new directorship. Given the tight schedule, discussions should progress rapidly, either towards the emergence of a director amongst the present group leaders, or the recruitment of a new director.

3 • Detailed assessments

Assessment of scientific quality and outputs

The scientific production of the Unit during the last four years is simply outstanding. The composition of the Unit is heterogeneous in terms of team experience, with two senior teams, five young teams with 2-4 years of experience and two starting teams. Nevertheless, almost all PIs have produced outstanding research and published in journals of highest profile, either as PIs or postdocs (since 2008: 4 Nature, 2 Science, 4 Cell, 2 Mol Cell, 2 Dev Cell, 2 PLoS Genetics, 2 Nat Cell Biol, 2 Genes&Dev). Ongoing research is highly innovative and has led to several paradigm-shifting papers on the topological organization of chromosomes (Nora et al. 2012), the mechanisms of X inactivation (Okamoto et al. 2011, Chow et al. 2010), the morphogenesis of epithelial tissue (Bosveld et al. 2012), the conserved role of lincRNAs in embryonic development (Ulitsky*, Shkumatava* et al. 2011) or the processing of visual information (Del Bene et al. 2010).

Assessment of the unit's academic reputation and appeal

The strong national and international reputation of the groups in this unit is attested by the numerous invitations to international meetings and institute seminars, as well as the award of both national and international competitive fundings (4 ATIPE/AVENIR, 5 ERC, 1 EURYI, 2 Schlumberger prizes, 2 Emergence Ville de Paris, plus several other grants obtained through collaborative work with other groups: ANR, EU networks, NIH, HSFP etc…). In addition, the Unit has been awarded a Labex funding of 7M€ co-headed with the Unit of G. Almouzni (UMR218) for the next 8 years. The recent recruitment of highly talented PIs coming from internationally recognized institutes and universities is an obvious sign for the strong drawing power of the Unit. The most senior members of the Unit have received prestigious national (FRM prize, CNRS silver and bronze medals, Paoletti prize, College de France Chair) and international (Otto Mangold prize, Science Herloom for Women in science) awards. Two PIs are EMBO members. Many PIs of the Unit participate in expert committees (FRM scientific council, SABs for national institutes, EMBO YIP committee, ATIP scientific board, INSERM recruitment committee, ANR committee, Agency for Biomedical Ethical Authorization) or editorial committees (Invited editors or members of editorial boards for PLosOne, Cell Reports, Epigenetics and Chromatin, etc.) and participate actively as referees in scientific reviewing. Several PIs of the Unit have participated or are currently participating in the organization of national or international meetings (EMBO Symposium on Germline and Totipotency 2012, Cold Spring Harbor meeting on Dynamic organization of nuclear functions 2012, Mechanism of Tissue Meeting 2013, International European Light Microscopy Initiative Meeting 2013). Finally the Unit has hosted famous scientists like John Seddat (expert in super resolution microscopy) and Elizabeth Blackburn (Nobel prize Medecine 2009) for sabbatical periods and collaborative work.

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

The Unit is still young but has noticeably contributed several initiatives towards public diffusion of science (TV broadcast on France 5 –a national TV-, live interview on French radio, articles in Science et Santé, Le Monde, partnership with the French Science Academy and the National congress, public conferences “Les Mardis de Curie” on French radio) and education activities (High school children classes for biology experiences organized by the PIs and taking place in the Unit department).

Assessment of the unit's organisation and life

The Unit is run by the director, helped by the deputy director and a lab council. A prestigious SAB meets regularly with the representatives of the Unit (last SAB meetings : 2010, 2012) and a lab council meets approximately 3 times per year to help in decision making concerning the life of the Unit. A strong collegiality has been established, which is reinforced by internal interactions taking place during common meetings (weekly join Unit meeting, monthly group leader science lunch, weekly tea time shared with UMR218, yearly lab retreat, etc.). This contributes to a most convivial atmosphere, which was attested by the three categories of personnel during their meeting with the committee (ITA, PhD/Post-doc and Researcher). In general, all categories are very happy with the scientific and technical opportunities offered by the Unit. The technical staff attests for the dynamic and rewarding atmosphere, as well as the strong organization of the different services of the Unit, allowing them to work in optimal conditions. PhD and Post-docs are all satisfied by the general organisation and are conscious to be « lucky to work here ». One point worth mentioning is the need for help concerning housing. The Curie Institute should think about providing specific help to foreign students who have difficulties filling the conditions to rent a flat in Paris. The community of permanent researchers (small, 5 people total without the team leaders) had no specific remarks.

However, all the staff, together with the Director, mentioned that the Unit has greatly increased in size since its creation in 2009 and, as a consequence, faces a chronic deficit in technical staff for the research teams, only partially compensated by CDDs payed on the teams' contracts. All the staff complains about this situation, which puts strong pressure on the teams to pay CDDs that are limited in time by law and therefore has a disruptive effect on the employees in the research teams.

Assessment of the unit's involvement in training through research

The unit is affiliated to the University of Paris Pierre et Marie Curie. Despite the absence of funding from this University, group leaders from the Unit participate in several Master programs (Génétique des Caractères Complexes; Epigénétique, Chromatine et Organisation Nucléaire; ENS Master on Molecular Genetics; International Developmental Biology Course Curie/UPMC/Harvard, etc.). The various teams and platforms of the Unit have hosted 32 M1/M2 students, 21 PhD students and 32 postdocs during the last 4-year period. Eight students have graduated and obtained their PhD. PhD students working in the unit are affiliated to the Curie International PhD program (http://curie.fr/en/enseignement/international-phd-program), which provides support for their PhD work and career. Part of the Labex funding obtained in collaboration with the UMR 218 will be used to support PhD fellowships for the Unit. During the discussion with the committee, PhD students and Postdocs expressed their general concern for career possibilities. This is unfortunately a very general question that extends beyond the limit of this unit.

Assessment of the five-year plan and strategy

The five-year project of the Unit derives from individual teams projects, which have all been highly favourably evaluated (see individual team evaluations).

One axis of research addresses various questions concerning genome organization and modification of the genetic program by epigenetic mechanisms. This is the major strength of the Unit today with contributions from 4 teams including the team of the Director. All teams in this axis of research are outstanding and the future projects ambitious and cutting edge.

The Developmental Biology axis is very strong too, with one senior team benefiting from strong international recognition and three young teams proposing novel and exciting projects. The new addition of a neurobiology and behaviour project to this axis is not a will to specifically develop neurobiology but was rather considered as an attractive opportunity to introduce the fish model to address developmental biology questions. This enabled the further installation of a new team addressing the role of lincRNAs during fish neural development. The very recent addition of a cancer/stem cells team allows the Unit to extend its research interests towards the biology of cancer cells, which remains an important aim for the different Units hosted at the Curie Institute. This team has a good integration within the Unit and proposes scientific connexions with many different projects (gut stem cell biology, epigenetic regulations). Nevertheless, the team needs to consolidate funding and visibility to insure its viability in a highly competitive context.

The scientific policy for young groups at the Curie Institute imposes a selection after 4-5 years to upgrade to senior status. Many of the young groups in the Unit will reach this cut with synchrony in the three coming years and will be engaged in a competitive selection (70% cut in average over the last 10 years, according to the Curie scientific Director). Therefore, attention should be given to avoid a drastic reduction of team number and/or a destabilizing remodelling of scientific directions in the three coming years. In this respect, clearer vision of the future selection procedure for the young teams should be given to the group leaders by the Curie Direction. Although youth is an obvious strength of the Unit, the committee also recommends that a better balance is found between junior and senior teams.

In conclusion, through a major collective effort, the Unit has developed over the last four year into an outstanding Institute where science is produced at cutting edge level in a very convivial atmosphere. Expectations for future contributions are at their highest. This unit obviously constitutes a reference for excellence in biology research in France.

4 • Team-by-team analysis

Team 1 : Mammalian Development Epigenetics

Name of team leader: Ms Edith HEARD

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
N2: Permanent EPST or EPIC researchers and similar positions	4	3	3
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.)	10	7	7
N6: Other contractual staff (without research duties)	2	1	1
TOTAL N1 to N6	18	14	12 (100 %)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	13	
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

The team has a leading position in the field of epigenetics through its major contributions to the understanding of X chromosome inactivation. The work of the team has impacted the general understanding of epigenetic mechanisms. In the past 5 years, the team has made several startling discoveries ranging from the fundamental basis of chromosome organization to evolutionary aspects of X inactivation in mammals, the fine-tuned regulation of inactivation propagation and the faith of X inactivation in cancer. Within the four-year period the group has published a remarkable series of high profile papers (Nature 2012, Cell 2011, Nature 2011, Cell 2010), all under the direct leadership of the team leader.

Assessment of the unit's academic reputation and appeal

The team has gained outstanding recognition in its field and is involved in remarkable collaborations and highly visible research networks. The team has been the training field for many talented post-doctoral research fellows coming from various countries. The appointment of the team leader as the Head of the Unit has been decisive for attracting talented junior scientists as new team leaders. The team leader is member of EMBO since 2008 and has received since one scientific price every year, including very prestigious ones like the CNRS Silver Medal (the group Leader is EMBO member since 2008). The team was awarded an ERC advanced grant in 2010 and is participating in numerous French and European consortia (EpiGeneSys, Syboss, ANR). In 2012, the group leader was awarded a prestigious nomination as Professeur at the Collège de France.

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

The team leader is very active in disseminating information and concepts on genetics and epigenetics to the public. This includes contacts with the press and journalists and the management of thematic issues of large audience magazines (INSERM Santé Magazine).

Assessment of the unit's organisation and life

The outstanding scientific outputs obtained in the past 5 years testify for a very efficient team management.

Assessment of the unit's involvement in training through research

The team has trained a significant number of students and post-docs (currently 8 post-doc and 1 PhD student in the team). The team leader participates in several Master programs and is in the Scientific Committee of the International PhD Course on Epigenetics of the Curie Institute.

Assessment of the five-year plan and strategy

Projects and future plans are prolonging the excellent work made on XCI in the past 5 years. A special focus is made on the link between XCI and chromosome instability in breast and liver cancers for which the team benefits of its unique expertise and of an excellent environment at the Curie Institute. Additionally, emerging findings made by the team like the discovery of monoallelically expressed loci in the mouse genome are opening exciting avenues of research for the coming years. The recognized expertise of the team and its outstanding past research are a good warranty for the success of the proposed research.

Conclusion

This is a very strong group with promises of additional startling discoveries. The directorship of the Unit could have been a threat for the team leader, but this is not the case and the research of recent years has propelled the team to the highest international level.

There are no weaknesses, and the only possible recommendation is that the team continues with excellent work.

4 • Team-by-team analysis

Team 2 : Polarity Division and Morphogenesis

Name of team leader: Mr Yohanns BELLAICHE

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	2	1	1
N3: Other permanent staff (without research duties)	2	1	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	6	5	5
N6: Other contractual staff (without research duties)	2		
TOTAL N1 to N6	12	7	6 (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	9	
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

During the past 5 years the lab has published 4 high quality research papers that are clearly led by the lab and a further 3 collaborative papers. This is a very good output especially considering the multidisciplinary nature of the work. Moreover, it appears that additional manuscripts are either under review/revision. The work is characterized by methodological advances combined with important insight. This is particularly clear for the Science 2012 paper, which involves multiscale imaging, an interesting substractive approach to phenotyping and insight in the role of PCP in tissue shape control. All the papers published are in high-end journals. During the past 5 years, the PI has established himself as an international leader in the biophysics of tissues.

Assessment of the unit's academic reputation and appeal

The PI is a rising star in cell and developmental biology. Evidence includes: invitations to international meetings, election to EMBO, membership of editorial boards of Developmental Cell and Cell Report, award of ERC starting grant. He has assembled a strong team of scientists. All the named personnel have good CV. The recent recruitment of a physicist is very positive as it will help establish the group at the interface between cell biology and physics.

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

The group is developing computation methods of image analysis that are original and may have a wider impact in the long term. However, the group's strength is in cutting edge basic research. There should be no pressure to translate the findings unless this is driven by the group leader.

Assessment of the unit's organisation and life

The members of the team have diverse expertise in cell and developmental biology, physics, and computer science. Assembling such diverse expertise in a small group is an achievement. In addition, the group leader has been able to arrange collaborations that further expand his expertise base. Over the last four years, the group leader has moved from cell behavior to tissues. His expertise in cell biology will serve him well in his attempt to understand tissues making. The diversity of questions being addressed is about right. Diverse enough to allow individual members of the lab to develop while still fostering synergic interactions.

Assessment of the unit's involvement in training through research

The PI has participated in setting up an international course for Developmental Biology Curie/UMPC/Harward. The PI also provides teaching courses to various Master and PhD programs. The team has trained a significant number of students and post-docs (currently 4 post-doc and 2 PhD students in the team).

Assessment of the five-year plan and strategy

The proposed research builds on previous achievements and aims at a cellular and physical understanding of tissue behaviour and morphogenesis. The program is ambitious, including the analysis of PCP components and adherens junction dynamics, multiscale imaging and mechanical modelling and biochemical identification of new components. All the aims might not be achievable in the next 5 years although, on the basis of the lab's track record, major advances are in the offing. Perhaps, the aims should nevertheless be prioritized.

The issue of time is important for morphogenesis but a more specific hypothesis is needed as a basis for the proposed research. To be able to perform multiview microscopy would be an advance but it is not clear how this will directly benefit the research programme. There are several labs in Germany who are already developing such approaches and it is not clear whether the PI has a novel angle or technical advantages that the others have not.

Conclusion

- Strengths and opportunities:

Original approaches, uniquely positioned to pursue innovative multidisciplinary approaches.

- Weaknesses and threats:

Need to prioritize, avoid spreading too thin, and build on strength.

- Recommendations:

Keep up with excellent work, prioritizing on strong projects.

4 • Team-by-team analysis

Team 3 : Germ Cell Development

Name of team leader: Mr Jean-René HUYNH

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	2	2	2
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	2	2
N6: Other contractual staff (without research duties)	1	1	1
TOTAL N1 to N6	7	6	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	3	
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

This team is one of the Unit's founding teams and was created as a new emerging team in 2008. The team is interested in understanding the mechanisms of germ cell development using the Drosophila female ovary as a model. Drosophila oogenesis is a well-studied process that is particularly amenable to genetic screens, allowing deciphering the many biological processes leading to oocyte formation. A few years ago, Team 3 launched a mosaic screen to isolate new genes involved in early cellular processes of oogenesis, focusing in particular on the biology of the Germ Stem Cells (GSCs). This is a typical scenario where an unbiased screen is performed, and based on the observed phenotypes various projects develop, opening new and diverse areas of research. As of today, the team has uncovered a specific role for the localization of component of ribosome biogenesis in GSC maintenance (Fichelson et al, Nat cell Biol, 2009) and shown that the polarity genes par are not sufficient to induce oocyte polarization, but also require the function of a tumour suppressor gene called lethal giant larvae (lgl) for their proper posterior localization (Fichelson et al, Development, 2010).

Ongoing research focuses on the role of another set of candidate genes found in the screen and related to the function of the Chromosome Passenger Complex (CPC) in the final step of cell division (abscission). This important complex acts at different steps during cytokinesis, first by promoting the ingression of membranes, and second by blocking the very last step of sister cells separation called abscission through a checkpoint mechanism called the Nocut pathway, ensuring that complete chromosome segregation takes place before sister cells split. Work in the group nicely demonstrates the developmental inhibition of abscission by the Aurora/Survivin complex in the GSCs and the following cystoblast cells, allowing all the progeny of the GSC to remain attached through cytoplasmic bridges called ring canals. Very interestingly, the group uncovers a novel cross-inhibitory loop between AuroraB/surviving and CyclinB/Cdk1 explaining the developmental inhibition of abscission. The group is currently testing the functional conservation of these findings in vertebrate systems including mammalian HeLa cells and zebrafish. A manuscript describing the work on abscission is under revision at Cell. Two other projects derived from the screen are developed in parallel: one concerns the potential role of AuroraB/Survivin in chromatin remodelling, a new project in a new area that could benefit from the great expertise on epigenetic mechanisms in the Unit. Another one concerns the role of a novel class of small RNAs derived from tRNAs in germ cell development.

Overall, this young and very dynamic group has succeeded in developing a very creative and high impact research over the last years. The initial technical investment now pays off and opens several new and exciting lines of projects. They all benefit from well-mastered classical expertise of the fly system by the young group leader and his colleagues and should lead to strong conceptual advances in the field in the coming years. The conceptual novelty of the findings has so far allowed publication in good to high profile journals (Genes Genome Genetics, Development, Nat Cell Biol). The ongoing research is very promising and should be published soon at this level or higher.

Assessment of the unit's academic reputation and appeal

The team is young and rather small, but has good visibility as assessed by its independent funding (ANR 2007, Schlumberger, Ville de Paris, Deep Labex 2012). Special care should be given for the timely publication of the ongoing work to allow renewing the funding of the team in the coming years. The team leader has good contacts with the leading labs in the field of germ cell biology.

Local collaborations for ongoing projects are mentioned. The group is not participating in national or international network. The PI is a brilliant scientist who was awarded the CNRS Bronze Medal in 2007. The publications of the group have so far reached very good standard (GGG, Development, Nat Cell Biol).

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

The research of the group was highlighted in a documentary presented on TV this year (France 5, Le Magazine de la Santé, Sept. 2011) as well as several communications in large audience journals (Science et vie 2009, Science et Avenir 2009, Pour la Science 2009, Le Monde 2009).

Assessment of the unit's organisation and life

The present team consists of 2 permanent researchers, 2 post-docs, 1 PhD student and 1 technician. The group leader has attracted a permanent researcher but is keen in promoting the future independence of this person. The size of the group could nevertheless become rapidly limiting given the number of ambitious projects that are proposed and the committee recommend that attention should be made to fit the size of the team to the number of projects.

Assessment of the unit's involvement in training through research

The PI has participated in setting up an international course for Developmental Biology Curie/UPMC/Harvard. The PI also provides teaching courses to various Master programs in the Paris area. The teams comprises two postdocs and one PhD sutdent, who are adequately trained by the PI.

Assessment of the five-year plan and strategy

The group will continue studying the role of the CPC in abscission, as well as develop two new original projects on the role of Aurora B in chromatin remodeling and the role of new small RNAs in oocyte development. All projects have high potential. The two first topics are potentially risky given the competition at play in the field of cell cycle control. So far, most of the projects in the team have had a rather short life, which in terms of strategy represents high energy cost for a small team. It is therefore crucial that the PI finds the right balance between the size of the team and the number of projects to be completed in the next few years, specially considering the great variety of topics that are proposed. The PI has clearly demonstrated his ability to enter new fields and develop new concepts with success. Overall, the technical feasibility of the proposed project is very good given the strong expertise of the team.

Conclusion

- Strengths and opportunities:

The group leader has developed strong and independent thinking over the recent years, which places the team in a strong position to make significant contributions in various aspects of the biology of germ cells in the coming years. The local environment in the Institute is very favorable to the development of these new projects.

- Weaknesses and threats:

The team has a limited size and caution should be taken to adapting the number of projects to this constraint. The publication of ongoing work will be key for the renewal of funding in the coming years.

- Recommendations:

The team should adapt its size to provide full support to ambitious ongoing projects. The committee recommends that the PI focus on germ line development on which he is presently building up his recognition, and care should be taken to avoid full exposure to competitive fields like hard core cell cycle control.

4 • Team-by-team analysis

Team 4 : Epigenetic Decisions and Reproduction in Mammals

Name of team leader: Ms Deborah BOURC'HIS

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	1
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	4	2
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	5	6	3 (100 %)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	4	
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 last years, the PI has made important contributions to the understanding of the developmental regulation of DNA methylation in mammals, using the mouse as model system (but performing collaborative studies on humans as well). The group has produced several excellent publications related to the developmental ontogeny of DNA methylation and the role of the DNMT3-like protein Dnmt3l in this process. The team discovered several novel imprinted gene loci in the mouse, on which mechanistic studies have been performed. This work represents one of the three themes of their coherent research programme. The PI contributed several timely review articles as well, in which novel ideas are being discussed, also on the repression of transposons, which constitutes one of the other themes of the research programme. Overall, this is an excellent output for a junior group, particularly since they also generated preliminary data in their novel projects as well.

Assessment of the unit's academic reputation and appeal

The PI has acquired a good international visibility during the last four years, particularly now that the first studies from her new lab have been published in high profile journals. Team 4 PI is frequently invited for seminars and was invited speaker at two international conferences. She is grant coordinator of an ANR-funded collaborative research programme (2011) and participates in the LABEX 'Deep' of the Institut Curie. The group is associated to the European NoE EpiGeneSys.

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

The PI has been co-active at this level as well. She has been involved in the bio-ethics and regulation of research on human stem cells and early embryos (ie, she is Member of the Scientific Council of the Agence de Biomédecine, France) and has been member of different grant proposal evaluation committees.

Assessment of the unit's organisation and life

The group has grown considerably since it was initiated in 2009. Currently, it has one permanent researcher (the PI), two postdoctoral researchers, 2 PhD students and one research technician. An advantage of their current size is that the group is internally highly collaborative and really as one team. For instance, some members of the team are leading scientists in different projects. This has contributed to the coherence and efficiency of their projects.

Assessment of the unit's involvement in training through research

The PI has been lecturing to Master and PhD students on a regular basis. She also taught at international training courses, some of which she co-organised herself. The PI has been part of several 'HDR' and PhD thesis committees. In her own team, she has supervised several PhD and Master students. Overall, this is a considerable training output for a junior group leader.

Assessment of the five-year plan and strategy

The different projects are well structured and clearly explained. They address the three main themes of this group: 'Trans and cis determinants of de novo methylation', 'DNA methylation and genomic imprinting' and 'DNA methylation and transposon control', each with two or three proposed projects. Two exiting new projects which follow on from their earlier studies concern a new imprinted gene locus (Zdbf2) in the mouse where a long ncRNA controls chromatin and DNA methylation during the early stages of development, and a project on the identification of new germline repressors of transposons in the mouse. Given their nature, these novel projects can be expected to expand during the coming years, but they are promising and have already generated convincing preliminary data.

Another novel project will attempt to achieve knock-down followed by re-expression of DNMTs, with the aim of assessing when during the process of ES cell differentiation, DNA methylation patterns and associated chromatin features become fixed at different types of DNA sequences, and whether the timing of this process diverges between different loci. This project makes use of genome-wide chromatin, DNA methylation and gene expression studies, with a particular interest in non-coding RNAs as well. Several of the other projects are more descriptive in nature, but nevertheless address important questions, including the spatio-temporal regulation of genomic imprinting, and the control of transposons in human spermatogenesis and in relation to assisted reproduction technologies. The committee finds the latter projects in humans particularly interesting. Overall, this is an attractive but rather ambitious research plan, given the current size of this group.

Conclusion

- Strengths and opportunities:

An internationally competitive group with high quality output. A very attractive combination of projects with promising novel findings and insights. The team has relevant collaborations with other groups in France and abroad.

- Weaknesses and threats:

The publications so far concern mostly one of the main themes of the team. Relative to the size and composition of the group and their scientific emphasis, careful planning is required to ensure that they remain competitive in their growing number of projects during the coming years.

- Recommendations:

This group has done very well during the period of assessment and is encouraged to continue their high-quality research during the coming years. The proposed projects are all well structured and relevant. The committee notes that those on the repression of transposons and the different studies in humans are particularly original and promising.

4 • Team-by-team analysis

Team 5 : Mechnism of Repression by Polycomb Proteins

Name of team leader: Mr Raphaël MARGUERON

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	1
N3: Other permanent staff (without research duties)		1	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	4	2
N6: Other contractual staff (without research duties)	2	1	1
TOTAL N1 to N6	7	7	4 (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	3	
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

This team is still relatively young and it is too early to assess output at this stage. The PI had a very successful post-doctoral period in the US with a number of high profile publications as first author. The research projects are important and focus on the biochemistry and regulatory roles of Polycomb repressive complexes (PRC). Several of the group's own projects build on the PI's research as a post-doctoral fellow. Recently, the group contributed to several collaborative studies, which were published in excellent journals. Given their unique expertise in biochemistry, this new group constitutes an important addition to the unit and several internal collaborations have been initiated.

Assessment of the unit's academic reputation and appeal

The PI has the international reputation expected from a good scientist of his seniority. He was awarded an ERC starting grant, a clear mark of recognition by the research community. He has attracted several post-doctoral fellows and PhD students, a good indication of future productivity.

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

Not yet applicable given the recent start of this team. However, the PI was invited for a general lecture in 2011, and the cutting edge research of this group can be expected to have societal impact in the long run.

Assessment of the unit's organisation and life

Currently, the group consists of two post-doctoral researchers, two PhD students, and two technicians. The PI wishes to recruit a permanent researcher, which should be beneficial to the group on the long run. The group is well positioned to perform the proposed biochemical and functional studies in relation to PRC mediated repression.

Assessment of the unit's involvement in training through research

The PI supervises two PhD students and has taken part in different PhD thesis committees, an involvement at the right level for his seniority.

Assessment of the five-year plan and strategy

The research program is well structured and coherent. It largely follows on from the PIs previous research on the PcG machinery, particularly the Polycomb repressive complex 2 (PRC2). Several projects are to be developed. One involves identifying genes that influence the PRC2, using genome-wide screening approaches. The PI has been successful here and identified several candidates. Another project is to follow up the study of Jarid2, which the PI identified as a cofactor of PRC2 during his post-doctoral research period. This particularly interesting project considers further the interaction of PRC2 with Jarid2, the effect of Ezh2 on Jarid2 protein and to which extent these processes impact on the recruitment of PRC2 to target loci. Amongst other questions, the project explores which role these processes could play during ES cell differentiation. Another project is to uncover how non-coding RNAs might contribute to the recruitment of PRC2 to its targets as well. This is potentially of great interest because so far little is known about the de novo recruitment of PcG components. Importantly, the group has taken care in these projects to avoid competition with the PI's former postdoctoral supervisor (with whom he is in regular contact), and has initiated several collaborations including with one other group at the Developmental Biology and Genetics unit. Linked to the (still disputed) role of PRC2 deregulation in human cancers, the team has explored different mouse cancer models. As a comparison, also explored immortalized embryonic fibroblasts are being studied. One question to be addressed in these cancer-related studies is whether there could be marked effects of PRC2 on cellular proliferation and the DNA damage response. Based on the data obtained so far, which do not suggest a significant involvement of the PRC2 complex in these models, it is not clear to the committee whether it is worthwhile to put much effort in these studies during the coming years.

Conclusion

- Strengths and opportunities:

Good research program that addresses important questions, with excellent preliminary observations.

- Weaknesses and threats:

None of the team's own research has been published and this should be one of their priorities. For this, the group may wish to initially focus its efforts on a few projects only.

- Recommendations:

This is an excellent group, which deserves continued support.

The international visibility of the group might be enhanced by developing research that diverges from the PI's earlier research as a post-doctoral Fellow.

The group may wish to develop further collaborations to explore animal models.

4 • Team-by-team analysis

Team 6 : Neuronal Circuit Development

Name of team leader: Mr Filippo DEL BENE

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	1
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	2
N6: Other contractual staff (without research duties)	1	1	1
TOTAL N1 to N6	5	4	4 (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	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions		

• Detailed assessments

Assessment of scientific quality and outputs

N.A.

Assessment of the unit's academic reputation and appeal

N.A.

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

N.A.

Assessment of the unit's organisation and life

N.A.

Assessment of the unit's involvement in training through research

N.A.

Assessment of the five-year plan and strategy

This team was established in May 2010, following an international open call. The PI benefited from an EC-IRG re-integration grant and obtained an ATIPE-AVENIR INSERM grant. In 2012, it was awarded an ERC Junior grant, attesting of the novelty of his projects.

The PI is an expert of optogenetics applied to zebrafish neurodevelopment (Rev Neuroscience, 2011), and introduced this technology and zebrafish in the unit. His main current interest is a complete understanding of the neuronal circuit which filters out low frequency visual information and increases the sensitivity for small moving objects. He has identified Superficial Inhibitory Neurons (SINs), located at the surface of the tectum, as essential players in this spatial filtering (publication in Science, 2010).

The main project includes further studying SINs function and establishing their connectivity - pre-synaptic and post-synaptic targets-, and the role of Reelin signaling in SINS development. A second, and rather unrelated topic is the role of microtubule based mobility in axogenesis and the development and function of neuromuscular junctions.

On the topic of SINs, the team is at the forefront of research, asking innovative questions and bringing novel technologies –optogenetics, enhancer-trap Gal4 lines, TALEN gene disruption (in collaboration with another group in Paris)- allowing to fully exploit zebrafish as a model system. This project has been judged outstanding: it is a coherent and logical continuation of the most exciting results obtained by the PI during his post-doc. It should remain at the centre of the team's project, and hypothesis-driven. The project on microtubule motors in establishing retinotectal synaptic connectivity is still in an exploratory phase. It might take time to dissect axonal transport in vivo, starting from morphological defects observed in microtubule motors mutants. At this exploratory stage, care should be taken to follow innovative questions, which cannot be addressed in other experimental set-ups.

Conclusion

- Strengths and opportunities:

This is a very strong team led by a PI who demonstrated clear independent thinking and conceptual innovations along the preceding period. The project on SIN connectivity and responsiveness to visual stimuli is built on recently developed tools, giving it a competitive edge. Teamwork is organized around a core of post-docs and PhD students, attesting of the team's attractiveness. Solid funding is secured for the coming years. The team can expand in size, due to strong external funding.

- Weaknesses and threats:

Recent projects on microtubule-based axonal transport are less innovative and competition in the field is very harsh.

- Recommendations:

Strong funding is secured for several years. Time flies nevertheless. Care should be taken not to disperse too much effort on topic 2 and maintain competitive edge and leading position on the main topic of dissecting neuronal circuits.

4 • Team-by-team analysis

Team 7 : Stem Cells and Tissue Homeostasis

Name of team leader: Ms Allison BARDIN

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	2	2	2
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	3	2
N6: Other contractual staff (without research duties)	1	1	1
TOTAL N1 to N6	6	6	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	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions		1

• Detailed assessments

Assessment of scientific quality and outputs

The PI is a young group leader, having been recruited only about 2 years ago. She has secured funding through the prestigious ATIP/Avenir programme.

She has been trained in fly development biologist as a postdoc at the Pasteur Institute during which she published a first author paper in Developmental Cell. While still in this lab, she began to study intestinal stem cells in fly to uncover general mechanisms regulating stem cell renewal and cell fate commitment. In order to identify novel regulators, she undertook a large-scale genetic screen. The first mutant that she followed turned out to encode an enzyme that catalyzes the formation of fucose, which through fucosylation regulates the strength of Notch signalling in the gut and promotes the differentiation of ISC into enterocytes. This is a nice study that has been published in Development and received a lot of attention in the field, as demonstrated by the invitation to international meetings that she received to present these data.

The panel felt that after two years of being independent group leader in Curie, the PI has made great progress in establishing her own new line of research while pursuing the functional characterization of the genetic mutants that regulate intestinal stem cell functions she identified few years ago.

She should continue to develop new lines of research that will distinguish her from the others in the field of intestinal stem cells.

Assessment of the unit's academic reputation and appeal

The PI has a very good international reputation, seen as a solid, rigorous, with manuscript of excellent quality (though not yet many). She has been invited to give talks in prestigious international stem cell meetings (Eurosystem, …). She secured several competitive grants.

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

N.A.

Assessment of the unit's organisation and life

The team is still relatively small, thus allowing the PI to mentor closely her PhD students and postdocs.

Assessment of the unit's involvement in training through research

The PI teaches stem cell and developmental biology within the context of MD/PhD program at the UPMC and she has also co-organized two international PhD courses on stem cell and developmental biology. She is also contributing to the mentoring of PhD students in the department.

Assessment of the five-year plan and strategy

The group has developed a well thought plan for the next few years. They will pursue three main strands: to characterize hits from a screen initiated while the PI was a postdoc, to pursue the study of Numb in stem cell fate specification, and to develop a project on the response to DNA damage.

Following a mutagenic screen, several mutants were identified leading to defect in intestinal stem cell functions. They were classified them in 20 complementation groups and some of them linked to known mutants. The team is currently concentrating on two of them (split-ends and kismet), and elaborated a good strategy to understand them molecularly and biochemically.

One such mutant, called kismet, encodes chromatin-regulating factor excluded from repressive chromatin marks. The plan is to use a genetic, cellular and molecular approach to understand Kismet function. This should be pursued even though the broad expression of kismet may complicate the identification of specific stem cell functions. The characterization of the other mutants found in the screen will need careful prioritization.

The team is also continuing to pursue the study of the role of Notch signalling in the intestine by investigating how Numb regulates endocrine cell fate decision but not EB differentiation into enterocyte renewal, which is also controlled by Notch. It is planned to perform lineage ablation of EE and assess whether EE regulate stem cell function through a non-cellular autonomous function. Numb function is also looked at in mouse mammalian SC in collaboration with one team within the unit and one team at the Pasteur Institute .

The team is also developing a new original line of research based on the preliminary observation that loss of heterozygosity occurs frequently in the adult intestine. Spontaneous DNA damage are also frequently found. The team is investigating how such DNA damage is repaired. These are still preliminary results but the team is encouraged to explore them since they could develop into an original line of research. The PI is aware of the intense competition in the field. The team will need to develop new tools such as cell sorting to gain an edge over the competition. Notwithstanding the issue of competition, the project has a good mix of safe and risky elements.

Conclusion

- Strengths and opportunities:

Good project built on previous work while attempting to depart from that of previous mentor; interesting area of research.

- Weaknesses and threats:

No high profiles papers yet published. Important competition in the field.

- Recommendations:

The PI should focus on projects that are most likely to have impact and that help define a scientific niche for the team.

4 • Team-by-team analysis

Team 8 : Team name

Name of team leader: Ms Sylvia FRE

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	
N3: Other permanent staff (without research duties)		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		3	

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		

• Detailed assessments

Assessment of scientific quality and outputs

N.A.

Assessment of the unit's academic reputation and appeal

N.A.

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

N.A.

Assessment of the unit's organisation and life

N.A.

Assessment of the unit's involvement in training through research

N.A.

Assessment of the five-year plan and strategy

This team was created in October 2012. The PI has previous expertise of the Notch signaling pathway in tissue homeostasis. The project encompasses studying Notch expression and function in intestine stem cells, colorectal cancer cells, and mammary gland stem/progenitor cells. The general goal of the project takes advantage of recently established N(1–4)-CreERT2SAT knock-in mouse lines allowing the lineage analysis of cells specifically expressing one of the four Notch receptors, both in vivo, and ex vivo in “miniguts” and “mini mammary glands” organotypic cultures that are well mastered by the team. Several aspects of the project have high potential, although it is difficult to precisely assess some of the expectations, since experiments are still in the descriptive phase in particular those that rely on the establishment of long term ex vivo imaging and cell tracking. The possibility to perform cell clonal analysis in organotypic cultures derived from the Notch reporter lines is a major original aspect of the project. Studying intestine normal and cancer stem cell lineages is highly competitive and it is not certain that studying Notch expression in ISC will allow novel discoveries to be made. There is also a risk, since the PI mentions collaboration/competition with a European leader group in the field. The situation seems more open in the mammary gland, since progenitors in this tissue have only recently begun to be characterized. The Notch reporter lines can certainly bring new insights into cell lineages in the luminal epithelial layer and in tubulogenesis. Furthermore, the Curie Institute provides an excellent environment to link studies on normal tissue and mammary gland tumours. Nevertheless, the task force needed to pursue all the proposed directions should not be underestimated. Overall, the feasibility of the proposed project over five years is good, given the past expertise of the PI and the Curie environment. It is, however, essential that the PI finds the right balance between the size of the team and number and cost of proposed projects. Because part of the project is to study cancer stem cells, this new team should benefit from all possible support.

Conclusion

- Strengths and opportunities:

The PI has developed independent thinking over the past few years and the project is built on recently developed tools, giving it a competitive edge. Some of these tools could allow bringing novel insights into mammary normal and pathological mammary gland development. The team introduces studies on cancer stem cells in the unit, and productive collaborations with other teams are expected.

- Weaknesses and threats:

The team has limited size and financial support. Caution should be taken in adapting the number of projects to these constraints. Publication of ongoing work will be key for funding in the coming years and if the work is too descriptive, it can take some time until reaching publication in excellent journals. Competition on intestine stem cells is very high.

- Recommendations:

The team should rapidly choose among its different projects in order to optimize the chance of success. This is essential to publish and obtain competitive grants.

4 • Team-by-team analysis

Team 9 : Team name

Name of team leader: Ms Alena SHKUMATAVA

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	
N3: Other permanent staff (without research duties)			
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		1	

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		

• Detailed assessments

Assessment of scientific quality and outputs

N.A.

Assessment of the unit's academic reputation and appeal

N.A.

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

N.A.

Assessment of the unit's organisation and life

N.A.

Assessment of the unit's involvement in training through research

N.A.

Assessment of the five-year plan and strategy

The PI has just been recruited after a post doc in David Bartel's at MIT. The project is based on the PI's post-doctoral work on lincRNAs and their conserved role in vertebrate development (Cell 2011).

The project goal is to highlight the role and conservation in vertebrates of lincRNA and the mechanisms underlying their contribution to gene expression regulation in brain patterning and neurogenesis. In this context, the project addresses the question of biological function of lincRNAs, the molecular and biochemical mechanisms of lincRNAs action and the evolution of vertebrate lincRNA genes. The project is original on a rather new subject, but competition in this fast evolving field is certainly to increase rapidly.

The consistency of the project relies on the lincRNA concept and all the questions left open by the discovery of these non-coding RNAs. The loss of function approach might however lead to very different phenotypes and drive the whole project toward specific morphogenetic process rather than help documenting more generic features of lincRNAs. The current knowledge on the several hundreds of zebrafish lincRNAs identified is still very sparse and more systematic categorization of their characteristics and properties could be an insightful step. Overall, the strategies are well thought and already produced preliminary results. The diversity of directions envisioned will require an important task force.

The threat identified is the increasing competition in the field. It is unlikely that all the directions proposed might be pursued at the same time by the new team.

Conclusion

- Strengths and opportunities:

The PI had a major contribution to the lincRNAs new field of research. The Unit is definitely the best possible environment for success.

- Weaknesses and threats:

The PI comes from the RNA field and should take advantage of these skills rather than focusing too fast on any particular morphogenetic process through the morphant approach. The field is likely to become very competitive.

- Recommendations:

It might be wise to progress further in the categorization of lincRNAs properties in the zebrafish for which little is known. Assessing synexpression groups might lead to the identification of GRN modules involving lincRNAs and opening the possibility to more directly assess of their role in the gene network dynamics.

5 • Conduct of the visit

Visit dates:

Start: Thursday, 17 January 2013, at 8:80 AM

End: Friday, 18 January 2013, at 5:00 PM

Visit sites :

Institution: Institut Curie

Address :

BDD Building
11-13 Rue Pierre et Marie Curie, 75005 Paris

Institution: Institut Curie

Address :

Burg Building
12 rue Lhomond, 75005 Paris

remises visited:

A lab tour was organized at the end of the first morning

Conduct or programme of visit:

Thursday 17 January 2013
BDD Building
11-13 Rue Pierre et Marie Curie, 75005 Paris

8:30 – 8:45 AM:	Welcome Coffee, Ground floor, BDD Building
8:45 – 9:00 AM:	Welcome (with Daniel Louvard), Amphitheater BDD
9:00 – 9:30 AM:	Closed-door Committee meeting, Salles Annexes 1, 2, 3
9:30 AM:	Start of plenary presentations, Amphitheater BDD
9:30 – 9:45 AM:	Presentation of the AERES Committee
9:45 -10:45 AM:	Presentation of the research unit by Ms Edith HEARD
10:45 – 11:00 AM:	Break / Debriefing of the Committee, Salles Annexes 1, 2, 3
11:00 – 11:15 AM:	Imaging Facility (Plateforme Imagerie)
11:15 – 11:45 AM:	Tour of Lab
11:45 – 12:30 PM:	Meeting with representatives of Institutions supporting the unit(CNRS, Institut Curie, UPMC), Salles Annexes 1, 2, 3
12:30 – 1:30 PM:	Lunch – with whole Unit - Ground floor, BDD Building
1:30 - 2:30 PM:	Group Ms Edith HEARD
2:30 – 3:30 PM:	Group Mr Yohanns BELLAICHE
3:30 – 4:30 PM:	Group Mr Jean-René HUYNH
4:30 – 4:45 PM:	Break, Ground floor, BDD Building
4:45 – 5:45 PM:	Group Ms Deborah BOURC'HIS
5:45 - 6:45 PM:	Group Mr Filippo DEL BENE
6:45 – 7:25 PM:	New group Ms Alena SHKUMATAVA

Friday 18 January 2013
Burg Building
12 rue Lhomond, 75005 Paris

8:30 – 8:45 AM:	Welcome Coffee, Green Café, Ground Floor, Burg Building
8:45 AM:	Start of group presentations, Amphitheater Burg
8:45 – 9:45 AM:	Group Ms Allison BARDIN
9:45 -10:45 AM:	Group Mr Raphaël MARGUERON
10:45 -11:25 AM:	New group Ms Sylvia FRE
11:25 -11:45 AM:	Break, Green Café, Ground Floor
11:45 –12:15 AM:	Meeting of the committee with technical and administrative staff
12:15 –12:45 AM:	Meeting of the committee with post-docs and thesis students
12:45 – 1:15 PM:	Meeting of the committee with researchers (without lab director)
1:15 – 2:15 PM:	Lunch – committee and group leaders, Green Café, Ground Floor
2:15 – 2:45 PM:	Meeting of the committee with the head of the research unit, Salle Annexe 2
2:45 – 3:00 PM:	Coffee Break, Green Café, Ground Floor
3:00 – 5:00 PM:	Closed door meeting of Committee, Salle Annexe 2
5:00 PM:	End of visit

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

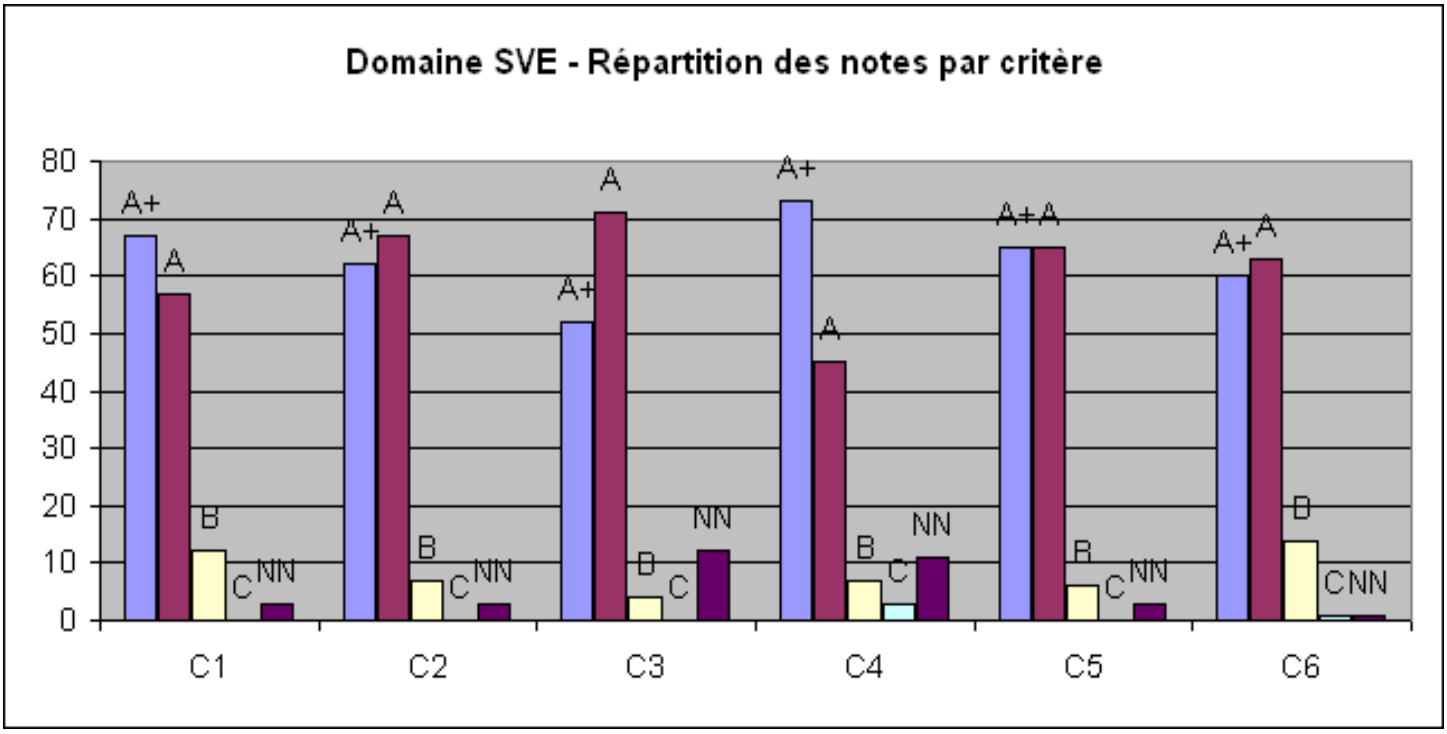
Grades

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

CENTRE DE RECHERCHE

institutCurie
Ensemble, prenons le cancer de vitesse.

AERES
Section des Unités
20, rue Vivienne
75002 PARIS

Paris, le 18 avril 2013

Concerne : Rapport S2PUR140006121 - Génétique et Biologie du Développement - 0753172R - Unité IC/CNRS UMR3215/INSERM U934 - Directeur : Edith Heard

Chers Collègues,

En tant qu'organisme hébergeur et déposant unique des rapports des unités de recherche du site de Paris de l'Institut Curie – Vague D, je vous informe avoir bien reçu en date du 29 mars 2013, le rapport d'évaluation de l'AERES sur l'unité IC/CNRS UMR 3215/INSERM U934.

J'ai lu ce document avec attention et je tiens à remercier le Comité AERES et le Comité d'experts pour leur évaluation consciencieuse et leurs commentaires constructifs à propos de notre unité (Génétique et Biologie du développement, Institut Curie, INSERM U934, CNRS UMR3215). Nous tenons également à les remercier pour leur retour motivant et utile durant leur visite. Nous sommes très satisfaits de l'appréciation du Comité notifiée dans le rapport et n'avons aucune réponse spécifique à apporter hormis celle de poursuivre nos efforts pour une science toujours plus excellente dans le contexte de cette nouvelle unité.

Nous aurions toutefois une série de points mineurs à modifier/clarifier dans le rapport :

1) Nous souhaiterions que les évaluations pour les équipes Margueron et Bardin en C1-C5 soient supprimés par souci d'équité entre les différentes équipes juniors (i.e les équipes qui n'ont été présentes que 2 ans ou moins pendant la période d'évaluation comme les équipes Bardin, Del Bene et Margueron). Dans le rapport actuel, seule l'équipe Del Bene n'a pas de commentaires dans les sections C1-C5. Or, les équipes Margueron et Bardin en ont, bien qu'elles soient arrivées au même moment ou après l'équipe Del Bene. Par conséquent, je demanderais à ce que les commentaires en C1-C5 soient retirés pour les équipes Margueron et Bardin. De plus, le Président (Pierre Léopold) et le représentant AERES (Pierre Couble) m'ont informé que les discussions ont bien été menées en ce sens lors de l'évaluation.

2) Correction d'une erreur dans l'Annexe (conduite de la visite) p.35 : A la place de "18.45 – 19.25: Nouvelle équipe Mr Spyros ARTAVANIS TSAKONAS" il faut lire "18.45 – 19.25: Nouvelle équipe Dr Alena SHKUMATAVA".

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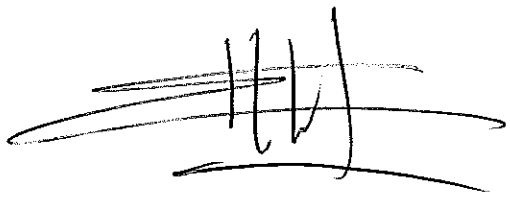
3) Modifications des commentaires pour la section C5 concernant l'équipe de Yohanns Bellaiche. Bien que le commentaire n'ait pas de connotation négative, il reste ambigu et nous souhaiterions qu'il soit clarifié en le remplaçant par la phrase suivante :

"The PI has participated in setting up an international course for Developmental Biology Curie/UPMC/Harvard. The PI also provides teaching courses to various Master and Ph.D programs. The team has trained a significant number of students and post-docs (currently 4 post-doc and 2 PhD student in the team)"

Afin d'assurer le succès continu de cette unité, j'ai bien noté les recommandations du comité pour appuyer ce plan en tenant compte de l'évolution de cette unité et tous les efforts seront faits en coordination avec les tutelles : l'Institut Curie, le CNRS et l'INSERM et notre partenaire l'Université Marie-Curie (Paris 6) pour assurer les soutiens nécessaires.

Je tiens à exprimer tous mes remerciements aux membres du comité d'évaluation pour leurs commentaires et recommandations très pertinents qui sont basés sur un travail d'analyse approfondie. Je remercie également l'équipe de l'AERES qui a soutenu la mise en oeuvre de l'ensemble de cette évaluation.

Je vous prie d'accepter, Chers Collègues, mes plus cordiales salutations.



Daniel LOUVARD
Directeur de la Section de Recherche
INSTITUT CURIE