Dynamique nucléaire

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Nuclear Dynamics and Genome Plasticity

NDGP

Under the supervision of the following Institutions and Research bodies:

Institut Curie

Centre National de la Recherche Scientifique

January 2013

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

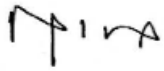
Research Units Department

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, its in-house teams received the following grades:

- Grading table of the unit: Dynamique Nucléaire

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

- Grading table of the team: Chromatin Dynamics

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

- Grading table of the team: Epigenetic Plasticity and Ploarity of the Embryo

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

- Grading table of the team: Compartimentalization and Dynamics of Nuclear Functions

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

- Grading table of the team: Chromosome Dynamics and Recombination

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

- Grading table of the team: Chromatin Pathways to Genome Integrity

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

Evaluation report

Unit name:	Nuclear Dynamics and Genome Plasticity
Unit acronym:	NGDP
Label requested:	UMR
Present no.:	218
Name of Director (2012-2013):	Ms Geneviève ALMOUZNI
Name of Project Leader (2014-2018):	Ms Geneviève ALMOUZNI

Expert committee members

Chair:

Mr Saadi KHOCHBIN, INSERM/université Joseph Fourier

Experts:

Mr Peter BECKER, Ludwig Maximilians University, Germany

Ms Wendy BICKMORE, MRC Human Genetics Unit, UK

Ms Julia COOPER, Cancer Research UK

Ms Eileen FURLONG, EMBL Heidelberg, Germany

Ms Ambra GIGLIA-MARI, (CoCNRS representative)

Scientific delegate representing the AERES:

Ms Sylvette TOURMENTE

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

Mr Daniel LOUVARD, Institut Curie

Mr Domenico LIBRI, CNRS

Ms Catherine JESSUS, UPMC

1 • Introduction

History and geographical location of the unit:

This evaluation marks the 12th year of the leadership of the director as the head of the unit with a continued activity at Curie Research Center, Paris. During the considered period (2007-2012), two junior teams left the unit and were replaced by two young teams ; one ATIP in 2009 and one ATIP/AVENIR in 2010. The PI of one junior team (N°3) established in 2007 (ERC 2009), was proposed for promotion which has been granted very recently by the International Research Council of the Center.

Management team:

The director of the unit (53), is helped by two administrative managers (100% and 80% respectively). The director is also supported by the board of group leaders, each of them taking specific responsibilities. The leader of team 3 has recently taken an even more active part in the managerial activities of the unit.

AERES nomenclature:

SVE1_LS2

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	9	8	7
N3: Other permanent staff (without research duties)	10,8	10,8	10,8
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)			
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral researchers, students, visitors, etc.)	28	21	17
N6: Other contractual staff (without research duties)	4	4	4
TOTAL N1 to N6	51,8	44,8	39,8

Percentage of producers	*100 %*

* This person has changed from DR to PR but was present on June 30, 2012 and will be still present in 2014-2018.

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	10	
Theses defended (from Janv 2007 to June 2012)	9	
Postdoctoral students having spent at least 12 months in the unit*	12	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	5	5

2 • Assessment of the unit

Strengths and opportunities:

The director of the unit is among the top world-class scientists and one of the most active among European and French researchers in the field of chromatin and epigenetics. As a consequence, her position as the unit director has brought high visibility to the unit and opened numerous opportunities for the unit's team leaders.

Additionally, the director has proven to be an outstanding manager, who not only is ensuring an excellent optimal organization of her unit, but also and additionally, is having an important impact on the organization of Science in Europe and the promotion of epigenetics at an international level. This internationally prominent position of the director and her involvement in many central "decisional nodes" is also clearly helping to establish thoughtful strategies and minimizing the adverse effects of the intense international competition in the areas covered by the unit's teams.

The unit had also been the cradle for the rise and development of several prestigious French teams: two of the past juniors unit's teams are now successful scientists directing their own groups elsewhere. A third one is now establishing her group in an Epigenetic Paris 7 University/CNRS Institute. In this respect, it is of note that the present very successful director of the Genetics and Developmental Biology unit (Institut Curie), started as a junior group leader in this unit. Today the unit is hosting equally promising group leaders and the committee foresees successful dissemination of these groups in the French science landscape in the future and hence the strengthening of this country's place in the field of epigenetics.

The unit has therefore served as a relay and enhancer of excellence and is hence playing a pivotal role in stimulating research in chromatin and genome biology, worldwide.

The other strength of the unit is the thoughtful and strategic development of research programs and core facilities, which have been put in place to increase the synergy between the units projects. A particularly remarkable example is the newly established Synthetic Genetic Array (SGA) in development under the responsibility of team 5, which will also have a high impact on the projects not only of teams 3 and 4, using yeast as a model, but also on the two other groups, studying non-yeast model systems.

In addition, the imaging facility provides training, helps design the experiments, choose the best reagents, choose the best system on the imaging facility, provides expertise for imaging analysis and treatment. The contribution of the facility to several projects is attested by the authorship of the manager of several publications and by numerous acknowledgements. The facility also develops its own image treatment tools. The number of users is between 30 and 40 using the facility for an average of 3000 hours of occupied systems per year.

The outstanding strategic scientific governance can also be illustrated by the development in the unit of transversal themes tackling different model systems to uncover the role of a particular mechanism, i. e., chromatin assembly, in different settings, or tackling a common model, i. e. yeast, to converge different concepts, i. e., meiotic double-strand break and nuclear compartmentalization.

In conclusion, the research programs and the accompanying appropriate actions are tremendously increasing the coherence of the whole and greatly strengthening the unit as a whole.

Weaknesses and threats:

The director of the unit has been very recently nominated as the director of "Curie Research Center". This is an important new responsibility that adds to her already heavy tasks.

Although the accumulation of responsibilities could at first be seen as a threat, taking into account the outstanding capabilities of the director of the unit in terms of administrative and scientific management, the committee feels this new appointment could rather be taken as an opportunity for the unit. In fact this will give rise to emerging possibilities for one of the newly appointed senior PIs and will ensure a smooth transfer of the leadership from the present director, who has been in charge of the unit for 12 years, to the head of the new senior group.

The director has proven in the past that she could efficiently conduct her unit and act at the same time as a coordinator of several European and National networks. During the same period, she has been the organizer of a significant number of high-profile prestigious international meetings. All these actions, among others, testify to the extraordinary working capabilities of the director and guaranty the success of the new configuration.

Additionally, the director is proposing specific actions to be undertaken at the level of the unit as well as that of her team to face her new additional responsibility as a Curie Research Center Director.

The first proposition is to promote team 3 leader as the unit deputy director. The second action aims at securing the team management by promoting a senior researcher of the team to the deputy team director position.

The committee has therefore paid a special attention to these propositions. Detailed subsequent discussions revealed here again a thoughtful strategic plan that convinced the committee of its validity and viability, without any major foreseeable pitfall. The actions proposed in the frame of this plan should reasonably compensate for the increased responsibility of the unit director and maintain the excellence of the unit. The plan however implies additional supports from the institutions (please see below).

Recommendations:

The director of the unit has now been nominated the director of "Curie Research Center". She wishes to keep her responsibility as the director of the unit with a progressive transfer of this leadership to the deputy director, which would fully take over after a defined period of time. The leader of team 3 has been recently promoted as a senior team leader by "Institut Curie Research Center" after the recommendation of the International Scientific Council. This PI has been already significantly involved in the management of the unit at different levels and gives all the signs of a capable unit leader. Discussions with both the director and the future deputy-director clarified the way the responsibilities will be shared and how the transfer will progressively occur.

Taking into account all the above-mentioned parameters, the committee approves and supports the proposed unit management plan, which appeared thoughtful and credible to the committee.

To support this decision, the committee recommends a series of actions, some already proposed by the director herself.

Accordingly, it appears critical that a full-time technical staff (engineer) is recruited and affected to team 3. This should help this team to stabilize its position as a senior group and also help its team leader to better ensure her increasing responsibilities.

Additional points

Discussions with technical staff, researchers, post-docs and students also revealed some important points that the committee has considered as serious issues that need urgent consideration. However, the committee also realizes that actions to face these problems sometimes exceed the responsibility of the unit and could engage the Curie Research Center.

1 - Space constraints appear as an acute issue, limiting an optimal accomplishment of the research programs in a safe environment. Indeed, this "space problem" is clearly creating a number of security issues. An example is the impossibility for the unit to respect the new European law regarding autoclaving of laboratory wastes containing GMOs. Respecting the law would require setting up an additional autoclave, which is presently impossible due to the acute space problem.

2 – The discussion with students and post-docs also revealed a need to undertake an action to support the administrative requirements for them, specifically foreigners, which are of significant numbers, to obtain housing.

3 – The third issue more specifically concerns the unit administrative management. Indeed, presently the unit has the benefit of two administrative managers (100% and 80% time, respectively). All five teams of the unit have many national and European grants with very complex management rules, which come in addition to the core funding as well as to the requirement to face specific units actions, i. e., teaching, AERES visit, etc. Discussions with corresponding staff members revealed a subsequent and unusually heavy workload and hence appeals for corrective actions.

3 • Detailed assessments

Assessment of scientific quality and outputs:

The published achievements of the unit are outstanding. All the team leaders published articles as senior author in journals of high visibility and impact. All the teams including the two junior groups that left during the considered period, have published 96 papers between 2007-2012 with an average impact factor of 10.634 (15 papers with an impact > 20 and 39 with an IF > 10).

The research programs of the five teams of the unit cover mostly the chromosome structure/dynamics, regulation of chromosome stability and gene expression. Interestingly an exquisite balance of model systems are in use hence ensuring a comprehensive approach to the issues considered. The examinations of the projects and discussions with the team leaders revealed the specific place of each model system and their complementary contribution to the unit research program as a whole. Model organisms encompassing yeast, Drosophila, Xenopus and mouse nicely complement efforts undertaken on human cell lines and cancer samples. A wide range of investigations specifically considering the mechanisms of chromatin assembly/disassembly, genome stability, nuclear organization, in specific settings such as early embryonic development and sexual differentiation uncover concepts that are readily applicable to disease-oriented issues, mainly cancer. The strong Curie environment in oncology has been taken as a ground for applications of the teams' discoveries in the pathological setting of cancer.

In conclusion, the unit is clearly one of the prime leaders in the wide field of chromatin dynamics worldwide.

Assessment of the unit's academic reputation and appeal:

Through exceptional achievements and leadership in international and European actions the unit has influenced the entire field of epigenetics and chromatin, making the unit highly attractive to young and older scientists from all-over the world.

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

To illustrate the outstanding contribution of the unit only several examples are presented below.

The involvement with the NOEs 'The Epigenome' and 'EpigeneSys', the unit has been able to engage in a number of highly visible outreach activities, involving artists, moviemakers and journalists. Not only the unit director but all the team leaders have been involved in various actions to disseminate knowledge and educate the public.

The unit is also very actively pursuing links to cancer research. The unit has been involved with several networks at the national level (SIRIC and PACRI) and participates in European networks that address the cancer epigenome. Several patents have been applied for with the potential to translate some of the fundamental findings of the unit into clinical practice.

Of particular interest is the organization of the course on Epigenetics. Each year the unit organizes a course with positions for students from European, National and Parisian Universities. In 2012 the 8th course was held.

Overall, the unit activity directly impacts the society through education and medicine.

Assessment of the unit's organisation and life:

The governance, communication and infrastructure are exemplary. The decision making within the unit is transparent, the level of infrastructure coordination is very high and the level of mentoring very good. Due to their successful expansion the unit currently suffers from space limitations and technical support (see above). The existence of unit retreats, a scientific advisory board and formalised procedures for promotions etc. testifies the excellent "lab culture". The unit provides services outside teams through the Imaging Facility and the robotic "Synthetic Genetic Array" platform.

Assessment of the unit's involvement in training through research:

The unit has been the training ground through research for an important number of students and post-docs. All PhD students enjoy PhD committees and proper mentoring. Additionally, following their PhD defense they are supported in their search for post-doctoral positions and above all, a significant number of post-docs has obtained a permanent position in France and abroad following their work in the unit. The training through research has therefore been a relay and enhancer of excellence in numerous cases.

Assessment of the five-year plan and strategy:

For all the teams, the five-year plan follows the excellent achievements during the reporting period. With promotion of team 3 as a senior group, the unit will be composed of three senior groups and two junior teams. One of these groups will shortly reach the end of the 5-year period and hence would need to consider its evolution outside the unit. The director has however mentioned to the committee that, following discussions at the Curie Research Center, this period could be extended to 7 years. This would allow this team to pursue its outstanding research in the unit. Overall, the level of established methodology and development of novel approaches is balanced, and, as could be judged from the preliminary data that have already been obtained, all the proposed programs are feasible. The projects are ambitious and will certainly ensure continued leadership of the unit in the field.

4 • Team-by-team analysis

Team 1 : Chromatin Dynamics

Name of team leader: Ms Genevieve ALMOUZNI

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	4	4
N3: Other permanent staff (without research duties)	3	3	3
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral researchers, students, visitors, etc.)	17	12	10
N6: Other contractual staff (without research duties)	2	2	2
TOTAL N1 to N6	27	21	19

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	5	
Theses defended (from Janv 2007 to June 2012)	4	
Postdoctoral students having spent at least 12 months in the unit	8	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs:

The 5-year reporting period must be considered one of the most productive phases in PI's lifetime research to date, both with respect to quantity, quality and originality. Her published achievements are outstanding, with senior author papers in journals of high visibility and impact. Importantly, her trajectory appears to be still on the rise. Starting from her specialization in chromatin assembly during replication she expanded her interest to cover the dynamics of all major variants of histone H3, which are deposited outside of S-phase. The discovery of specialised chaperones and histone "assembly" lines during interphase has led to a number of novel and original models that inspire the entire field. The novel concepts that revolve around histone level homeostasis and its regulation by synthesis, degradation and a network of specialised chaperones has opened an entirely new field of study.

Their in-depth analysis of heterochromatin formation led them to consider factors "on top of" the nucleosome infrastructure. The discovery, that HP1 sumoylation and binding of non-coding satellite-derived RNA is required for heterochromatin formation must be considered seminal. The realisation that DNA replication and the repair of DNA damage – the two main processes that rely on chromatin assembly – are functionally compromised in cancer cell led the team to search for cancer-related phenotypes involving chromatin assembly factors (4 patents were filed). The team covers a broad range of methods from basic biochemistry to advanced microscopy and molecular biology. High level collaborations pave the way to organisms studies.

During the reporting period a number of methodological achievements have been instrumental, among them use of SNAP-tags to follow histone dynamics, the combination of stable cell lines expressing tagged histones for sensitive identification of chaperone complexes. The PI and her team not only generated an enormous amount of highly novel and interesting data, but they also cover the conceptual background in a series of highly authoritative review articles. The PI has become one of the prime leaders in the wide field of chromatin assembly and dynamics worldwide.

Assessment of the team's academic reputation and appeal:

A direct consequence of the PI's research achievements is her reputation in the field. She is one of the most popular faces of the "Chromatin and Epigenetics" community in Europe. Her standing is documented by the "FEBS/EMBO women in Science" award, which honoured her life-time achievements. Among the competitive grants she has obtained, the ERC advanced grant stands out, which characterises her as one of the most successful researchers in Europe. Her standing in the field is documented by more than 80 invitations as a speaker during the last 5 years, by her contribution to a large number of national and international advisory panels (most prominently the EMBO council). Through her unmatched engagement in the European Scene, notably as coordinator and inspiration of the NOE "EpigeneSys", she has influenced the entire research landscape in Europe. She serves as a role model not only for all women in science but for any ambitious, hardworking group leader in the Life Sciences. Her group is highly attractive to young scientists from all-over the world. The team is highly qualified, highly motivated and highly successful.

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

Through her involvement with the NOEs 'The Epigenome' and 'EpigeneSys', the PI has been able to engage in a number of highly visible outreach activities, involving artists, moviemakers and journalists. She is one of the articulate "faces" of the Epigenetics community that takes every opportunity to propagate her enthusiasm and to educate the public.

Realising that chromatin assembly is a limiting process during all proliferation, and may be compromised in cancer cells that loose the integrity of their genomes, the team has very actively pursued links to cancer research. It coordinates several networks at the local and national level and participates in European networks that address the cancer epigenome. Four patents were filed that illustrate her ambition to translate some of her fundamental findings into the clinical realm of cancer prognosis and eventually treatment.

The unlimited willingness of the Pi to share her experience and give advice is illustrated by her involvement in SABs for several research institutes. The benefits for society through (1) shaping the research landscape at the local, national and European level, (2) translating her research into clinically relevant areas and (3) disseminating and educating the uninitiated cannot be overestimated.

Assessment of the team's organisation and life:

The PI not only leads a very productive team, but she also heads the entire unit. The documentation provided on governance, communication, infrastructure is exemplary. The decision making within the unit is transparent, the level of infrastructure coordination very high and the level of mentoring very good. Due to their successful expansion the unit currently suffers from space limitations and technical support. The existence of unit retreats, a scientific advisory board and formalised procedures for promotions etc. testify to an excellent lab culture. The unit provides services outside teams through the Imaging Facility and the robotic "Synthetic Genetic Array" platform. Bioinformatics support will continue to be very important in the near future, particularly since global analyses are likely to increase.

Assessment of the team's involvement in training through research:

Formal teaching commitments are very low. Yet the team leader has engaged in a number of teaching activities at the local and international level. Since 2009 she is deputy director of the Institute Curie-Research Center Educational Programme. All staff is encouraged and has the opportunity to participate in training courses (language skills, technical tutorials). The unit runs a highly successful "Course of Epigenetics" already in it's eight year and popular with PhD students from across Europe.

PhD students enjoy PhD committees and proper mentoring. The number of PhD students being promoted under the PI's direction is rather low. The main body of the work is carried out by post-doctoral fellows. Nevertheless, the PI participated in some 30 thesis committees during the reporting period.

Assessment of the five-year plan and strategy:

The five-year plan builds firmly on the achievements during the reporting period. The level of established methodology and development of novel approaches is balanced, and, judged by the preliminary data that have already been obtained, is feasible. The programme is ambitious in the sense that the aims are chosen such that the successful research will assure continued leadership.

Conclusion:

- Strengths and opportunities:

The leader and her team continue to work at the forefront of competitive, cutting-edge research at an international level. Their overall achievements are outstanding.

- Weaknesses and threats:

None.

- Recommendations:

The generation of knock-in / knockout mice is being outsourced. Once these mice have been generated histological analysis of these animals will require new collaborations.

Given the enormous number of tasks and responsibilities, undertaken by the PI herself the promotion of a senior team member to deputy Team Leader is highly appropriate.

The bioinformatic support needs to be accessible to the team's projects. This is why it is highly appropriate to embed informaticians in the unit / team, provided that they network with the general bioinformatic unit of I Curie. The space constraints are clearly limiting future development. The team leader is challenged with many administrative tasks. Some of this burden could be eased by hiring further personnel, but she also may have to learn to say "no" once in a while.

4 • Team-by-team analysis

Team 2 : Epigenetic Plasticity and Ploarity of the Embryo

Name of team leader: Ms Nathalie DOSTATNI

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	1		
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral researchers, students, visitors, etc.)	1	3	1
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	3	5	3

* This person has changed from DR to PR but was present on June 30, 2012 and will be still present in 2014-2018.

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended (from Janv 2007 to June 2012)	3	
Postdoctoral students having spent at least 12 months in the unit	0	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs:

Throughout, the team has done an excellent job in exploiting the unique advantages of the chosen model system, *Drosophila*, to address important biological questions. This is exemplified by the work on CAF-1, where genetics has been used to dissect its role in endocycling cells, meiotic cells and cells undergoing asymmetric division, three important contexts for a developing embryo for which there are no tissue culture models.

New technologies have also been used in innovative ways by applying them to answer still open questions in the field. For example, the work on the Bicoid gradient is very original, taking a different methodological approach (FCS vs. FRAP) thereby leading to very different measurements of the establishment of the Bicoid gradient compared to previous studies. This work has directly challenged many assumptions in the field and contradicts a number of models of the early gap network.

The team's work measuring the dynamics of the Bicoid gradient may lead to a paradigm shift in our understanding of how early patterning by the segmentation network is thought to occur. For over two decades, it has been hotly debated if a morphogen gradient is sufficient to provide the robustness required to form the precise borders of gap gene expression. The teams' Development paper, which lead to the measurement of a much faster diffusion coefficient for Bicoid than previously observed, challenged the current dogma in the field.

Assessment of the team's academic reputation and appeal:

The team's work on the Bicoid gradient has been widely recognized. The latest papers have directly challenged the conclusions and hypothesis of many of the 'big players' in the field. This has lead to international recognition.

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

Although this is a very small team, with a high teaching load, the team leader has participated in the Paris Science Festival for several years.

Assessment of the team's organisation and life:

From discussing with the students and post-doctoral fellows, the team leader is very supportive of her group and participates in organizing and managing the unit. She clearly manages the team with a coherent and logical scientific objective in mind. Given the small group size (only 4 people), the team is very productive, indicating that the work of all team members is coordinated and maximized to make a very efficient group. The convergence of the 'big questions' of chromatin reassembly, and thereby transcriptional regulation after nuclear division is a very productive way to get the most out of the group's expertise and resources.

Assessment of the team's involvement in training through research:

The team leader has made an outstanding contribution to training and teaching. She has taught at the Polytechnic Ecole for 12 years. She takes this role very seriously, spending a lot of time in preparation. Her excellence in teaching is emphasized by the fact that the University has made her a permanent Professor.

Assessment of the five-year plan and strategy:

The five-year proposal is both very feasible and very original. For the CAF project, the team will take advantage of utilizing genetics, which the team has strong expertise in. For the Bicoid project, the proposal plan is very innovative and exciting. The team leader already has established strong collaborations with physicists, which is crucial to the success of the project. Given her expertise, this exciting question and her established collaborations, this project will produce very exciting and timely results that will have a big impact on our understanding of how morphogen gradients function.

Conclusion:

- Strengths and opportunities:

The clear strength of proposal comes from the convergence of expertise in the team, in both chromatin assembly in newly replicated nuclei and in transcriptional regulation in the early Drosophila embryo, which are both essential to tackle the very interesting question of how transcriptional memory is maintained during cell division. There is currently very little known about this process, and the tools and expertise developed in the team provide a great opportunity to tackle it.

- Weaknesses and threats:

The small size of the group will limit their ability to be competitive. They need to expand, but given the lack of space for the unit, this is currently very difficult.

- Recommendations:

No specific recommendations.

4 • Team-by-team analysis

Team 3 : Compartimentalization and Dynamics of Nuclear Functions

Name of team leader: Ms Angela TADDEI

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	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral researchers, students, visitors, etc.)	4	3	3
N6: Other contractual staff (without research duties)	1		
TOTAL N1 to N6	7	5	5

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended (from Janv 2007 to June 2012)	1	
Postdoctoral students having spent at least 12 months in the unit	1	
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:

The team has developed original and innovative research projects based on the use of budding yeast to uncover the functional impact of the special organization of the genome.

Within the considered period, the Pi has been able to set up a highly efficient research team, giving rise to important conceptual advances in the field by producing results published in two high profile journals (J. Cell Biol. & Genes & Dev.), both under her direct leadership. The group showed that tight DNA protein complexes cause replication fork stalling and in turn, localized heterochromatin formation. The group also identified a way to separate telomere clustering from the nuclear periphery, providing both mechanistic information and tools for understanding the consequences of altering telomere localization under various environmental conditions.

Assessment of the team's academic reputation and appeal:

During the past 5 years the team has been involved in a number of important national and European networks, such as INCa, ANR, LABEX, as well as Marie Curie Actions. It is of note that the PI has been also the laureate of an ERC Grant starting in 2009.

The team started in 2006/7 as a junior group with a post-doc and within the considered period, thanks to various funding sources, a true team with additional post-docs, PhD students and technical staff has been established. In addition the PI has also able attract a professor on sabbatical leave to the team.

Finally, the PI was invited to 8 international and prestigious meetings as a speaker, attesting her international visibility.

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

The PI has actively contributed to the dissemination of knowledge by participating in public lectures and as well as science festivals and by being a board member of two different societies/foundations. She also contributes to the teaching of epigenetics at various levels.

Assessment of the team's organisation and life:

The success of the team in terms of scientific achievements testifies the capacity of the PI to efficiently and creatively manage the team. Additionally, the committee would like to highlight here the important involvement of the PI in the management of the unit revealing her remarkable managerial talent.

Assessment of the team's involvement in training through research:

During the considered period, 3 PhD and 4 master students have been supervised. Additionally, the Pi has been a member of the jury for Ph D theses (7) and of thesis committees (30). Students have authorship on the major publications led by the PI.

Assessment of the five-year plan and strategy:

In the coming years, the team will be developing various aspects of its main research theme: the functional impact of the spatial organization of the genome. The research programs are guided by questions regarding: i) the mechanisms directing the establishment and maintenance of nuclear compartments, as well as the functional importance of this compartmentalization, and ii) the relationship between active and repressive nuclear compartments.

Additionally, these projects have direct implications in the other teams' programs such as the role of nuclear organization in the control of meiotic recombination, which is the central subject of team N°4.

It is of note that the team is also developing the interface between its research and mathematics and modeling by establishing appropriate and fruitful collaborations (a manuscript is already submitted).

Overall, the team is leading original and promising research programs with foreseeable success in the coming years.

Conclusion:

- Strengths and opportunities:

The ability of the PI to lead her projects has been clearly demonstrated in the past 5 years, as can be judged by the excellent science produced and ongoing, and by her ability to secure the corresponding funding and attract people. She already occupies within the unit a very strong position, attested by her promotion to senior group leader position by the Research Center. This promotion is not only promising the development of increasing ground-breaking research programs, but also allows the team leader to upgrade her managerial responsibilities. This latter point corresponds in fact to her proposed promotion to become deputy director of the unit. The committee considers this situation as an excellent opportunity for the personal evolution of the PI, which has shown her managerial talents, as well as for increasing the attractiveness of the team and hence stimulating its development.

- Weaknesses and threats:

The committee could not identify any clear threats but has recommendations to strengthen the team, which, if not satisfied in a short term, could become threats.

- Recommendations:

Strengthen the team.

4 • Team-by-team analysis

Team 4 : Chromosome Dynamics and Recombination

Name of team leader: Ms Valérie BORDE

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	2	1
N3: Other permanent staff (without research duties)			
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral researchers, students, visitors, etc.)	3		
N6: Other contractual staff (without research duties)	1	1	1
TOTAL N1 to N6	5	3	2

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended (from Janv 2007 to June 2012)	0	
Postdoctoral students having spent at least 12 months in the unit	1	
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:

Despite being established as an independent laboratory for only 3 years, the PI and her team have already made very significant findings that shed new light on the mechanisms controlling meiotic recombination. The team work is original, both in its conception and execution, and is of the very highest intellectual and technical standard. It is an outstanding example of how the intelligent use of yeast molecular genetics can be used to provide deep mechanistic insight into fundamental biological processes. This is coupled with the team's specialized technical expertise in mapping the precise sites of double-strand breaks (DSBs) across the genome.

The finding that, in yeast, the PHD protein Spp1 promotes DSBs through association with both the chromosomal axis and with chromatin marks on chromosomal loops, has provided the basis for a new model of meiotic recombination initiation that will likely be applicable to a wide range of eukaryotes, including mammals. This may yield new insights into the origin of defects of meiotic chromosome segregation in humans (aneuploidy).

This team was only established in 2009, so there has not been much time for the PI to publish senior author papers from her own group. The team should therefore be congratulated on the very nice paper, which was just published in Molecular Cell (2013) – one of the very best journals in molecular biology. A second paper is close to acceptance in another high impact journal. This is exceptional output for a small junior group.

Assessment of the team's academic reputation and appeal:

The team leader is rapidly gaining a strong international academic reputation as evidenced by invitations to speak at major meetings (Two Gordon conferences, and an EMBO meeting). With the recent and forthcoming publication of the new papers, it seems clear that the PI's academic reputation will continue to grow rapidly. The quality of the team's PhD students and postdocs is very high which reflects the appeal of the team to young researchers.

The PI has also organized meetings on a national level and she serves on the board of the French Genetics Society. She is to be commended on this level of engagement and commitment.

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

The team leader has contributed to the Paris Science Festival and has an industrial partnership with EDF, which represents a good contribution to the dissemination of science to the wider cultural and economic environment. This is an appropriate level of engagement for a junior group.

Assessment of the team's organisation and life:

The team is well run, with the students and postdocs well supervised, engaged and productive. They play a full and active role in unit activities – journal clubs, seminars and meetings. The team leader serves on a large number of thesis committees.

Assessment of the team's involvement in training through research:

Students in the team are very well supervised and guided. The team leader also plays an active role in the International Epigenetics course run at the Institut Curie.

Assessment of the five-year plan and strategy:

By addressing chromatin events both upstream and downstream of DSBs during meiotic recombination, the team occupies a very good niche in a competitive field. The scientific questions are original and appropriately focused for a small team. Future plans combine the continued use of exquisite yeast genetics, in which the team has already demonstrated their excellence, with some bold aims. In particular, the aim to produce and compare the first genome-wide maps of DSBs and meiotic cross-overs is a big one and will have a major impact. There is a high likelihood that they will be successful in this achieving this.

The team has presented an appropriate SWOT analysis. There are constraints placed on the team and its future development by space limitations within the unit. In particular, the current placement of the SGA platform for high-throughput yeast genetics at a site some kilometers away from the PI's main laboratory is a significant barrier to the most effective use of this facility and the opportunity it should provide. The future aims to assess affects on meiotic recombination in yeast mutants genome-wide will require good bioinformatics input into data analysis and interpretation. The team would therefore benefit from enhanced bioinformatics support at unit level.

Conclusion:

- Strengths and opportunities:

The strengths of the team are the quality of their scientific approach and outputs, combined with the precise mechanistic questions that they are asking of fundamental biological processes in a tractable genetic system. The expertise of the team gives them the opportunity to make a major scientific impact and for the team leader to become a highly respected international figure in the area of chromosome biology and meiosis. All measures indicate that this team leader is on an exponential upwards curve for both her scientific output and international recognition. The excellent mentoring provided within the unit will expedite this.

- Weaknesses and threats:

None identified.

- Recommendations:

No specific recommendations.

4 • Team-by-team analysis

Team 5 : Chromatin Pathways to Genome Integrity

Name of team leader: Mr Manolis PAPAMICHOS-CHRONAKIS

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)	0,5	0,5	0,5
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral researchers, students, visitors, etc.)	3	3	3
N6: Other contractual staff (without research duties) dedicated to Plateform SGA		1	1
TOTAL N1 to N6	4,5	5,5	5,5

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	0	
Theses defended	0	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	0	0

• Detailed assessments

Assessment of scientific quality and outputs:

This junior team program aims to understand the relationship between chromatin state and DNA damage repair (DDR) processes – how do histone modifications and variants impinge upon the DDR and how does the DDR alter the histone modification state? The PI has an impressive and innovative foothold into this field stemming both from postdoctoral work (which appeared recently in very high profile journals including Cell, Nature Struct Mol Biol, etc) and the feats accomplished by the PI's own 2.5-year-old lab.

A major springboard is the identification of a role for the conserved Ino80 chromatin remodelling complex in controlling levels of the histone variant H2AZ in chromatin. The team is using rigorous biochemical approaches, molecular genetics and high-throughput screening techniques to define the relevant pathways and mechanisms and their functional importance.

The team has performed SILAC experiments to identify proteins that interact with Ino80 specifically in response to DNA damage. This approach revealed DDR-dependent interactions between Ino80 and the ATPase Cdc48, a component that has been shown to degrade RNA polymerase II in response to DNA damage; genetic analysis also shows that Ino80 becomes essential for the DDR when the Cdc48 pathway is compromised. A major (and important) current goal is the dissection of the roles and interplay between these two complexes. The team is also exploring the role of H2AZ modifications (which are clearly important for genome maintenance, in thus far poorly understood capacities).

Assessment of the team's academic reputation and appeal

The PI has an impressive set of distinctions including the FSER Prize for young group leaders, first place rankings in both CNRS and INSERM first class competitions, and five grant awards. The PI has been selected as a speaker for at least 7 international meetings and invited for seminars. Therefore, his status as a young investigator is clearly high and most likely on an upward trajectory.

In this 2.5-year period, the PI has clearly assembled a committed and effective team – we are particularly impressed by the recruitment of 3 postdocs from around the world. He has also set up the SGA platform for the Institute.

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

N/A

Assessment of the team's organisation and life:

Given the space allocated to the team, we are particularly impressed that they could have produced such high quality results; this is a testament to the PI's effectiveness. Moreover, the SGA platform is located 3 km from the unit, a suboptimal situation that presents extra challenges for the PI and his team members.

Assessment of the team's involvement in training through research:

While it is too early to comment extensively on this, the assembly of a productive team suggests the PI has already been and will continue to be highly successful in training through research.

Assessment of the five-year plan and strategy:

The centerpiece of the proposal is to extract and pursue meaningful mechanistic information from genome-wide data sets (most prominently synthetic genetic analysis, SGA). The plan is bold in tackling the large amount of data likely to be generated from several SGA screens. The PI's expertise in the fields of chromatin composition and regulation as well as DNA repair gives him a unique and promising perspective. Given this and the PI's experience with the suggested approaches, along with his plan to strategically screen mutations about which he has an extensive and unique scientific understanding, we find the plan credible and feasible. The growing expertise in SGA approaches is also of great value for the entire unit and promising collaborations with other teams (Teams 3 and 4) are already arising.

Conclusion:

- Strengths and opportunities:

The work is uniformly well-done and constitutes a significant and potentially ground-breaking set of contributions to a highly important and competitive field whose fruits are likely to include not only a basic understanding of how genetic information is maintained, but also cancer treatments (given the extensive array of relationships between altered epigenetic regulation and cancer).

- Weaknesses and threats:

None (see below).

- Recommendations:

The space issues mentioned above and the large distance between the PI's laboratory and the distant SGA platform are weaknesses that should be addressed as soon as this is possible.

5 • Conduct of the visit

Visit dates:

Start: Thursday, 31, January, 2013, at 8h30

End: Friday, 1st , February, 2013, at 13h

Visit site(s): Building Developemntal Biology

Institution: Institut Curie

Address: 26 rue d'Ulm, Paris cedex 05

Specific premises visited: Laboratories

Conduct or programme of visit:

The visit was well prepared and perfectly organized, with a detailed high-quality documents provided two months in advance. It included presentations by the director of Curie Research Center, the director of the unit and by the group leaders and with ample time for discussions with the director, group leaders, technical and administrative staff, students and postdocs.

High quality posters were set-up covering almost all the ongoing team projects. All the unit members responsible for the posters including mostly students and post-doc presented their posters to the committee members. The committee had sufficient time, albeit in a very tight schedule, to discuss various issues and meet with all the representatives of CNRS, Curie, UPMC. The visit was executed smoothly and without any problems. A visit of the labs had also been organized at the end of the first day.

Day 1 - January 31st, 2013

08:30 Welcome by Ms Geneviève ALMOUZNI & Mr Daniel LOUVARD
Overview on the research center by Mr Daniel LOUVARD

Coffee – with all members of the unit

08:45 Session with the AERES Scientific advisor
(closed-door) - visiting committee

09:00 AERES representative: the role and procedures of AERES

09:15 Presentation of past activities and future projects
Ms Geneviève ALMOUZNI (director of the unit)
Ms Angela TADDEI (deputy director)

10:00 - Coffee break -
Posters session -

Individual team presentations on past activities and project

10:15 **Team 1:** *Chromatin dynamics*
(20' talk + 20' discussion/questions + 5' private discussion with AERES committee)
Ms Geneviève ALMOUZNI (senior group)

11:15 **Team 2: Epigenetic plasticity and polarity of embryo**
(20' talk + 20' discussion/questions + 05' private discussion with AERES committee)
Ms Nathalie DOSTATNI (senior group)

12:00 **Team 3: Compartimentalization and dynamics of nuclear function**
(20' talk + 20' discussion/questions + 05' private discussion with AERES committee)
Ms Angela TADDEI (junior ⇨ senior group)

12:45 - Lunch - *Posters session -*

14:30 **Team 4: Chromosome dynamics and recombination**
(20' talk + 20' discussion/questions + 05' private discussion with AERES committee)
Ms Valérie BORDE (junior group)

15:15 **Team 5: Chromatin pathways to genome integrity**
(20' talk + 20' discussion/questions + 05' private discussion with AERES committee)
Mr Manolis PAPAMICHOS-CHRONAKIS (junior group)

16:00 **Parallel meetings with personnel:**

Discussions with engineers, technicians, administratives

Discussions with staff scientists

Discussions with students and post-docs

16h45 - Coffee break -
Posters session

17:15 Discussion with the representatives of the managing bodies
Mr Daniel LOUVARD (Institut Curie)

Mr Domenico LIBRI (CNRS)

Ms Catherine JESSUS (UPMC)

18:00 Debriefing on the team presentations

Day 2 - February 1st, 2013

Building of Development Biology (BDD) on ground floor

09:00 Discussion with Ms Geneviève ALMOUZNI : head of the unit (30 min /1h)

10:00 Private deliberation of the visiting committee
(in presence of the AERES scientific advisor)

14:00 End of the visit

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

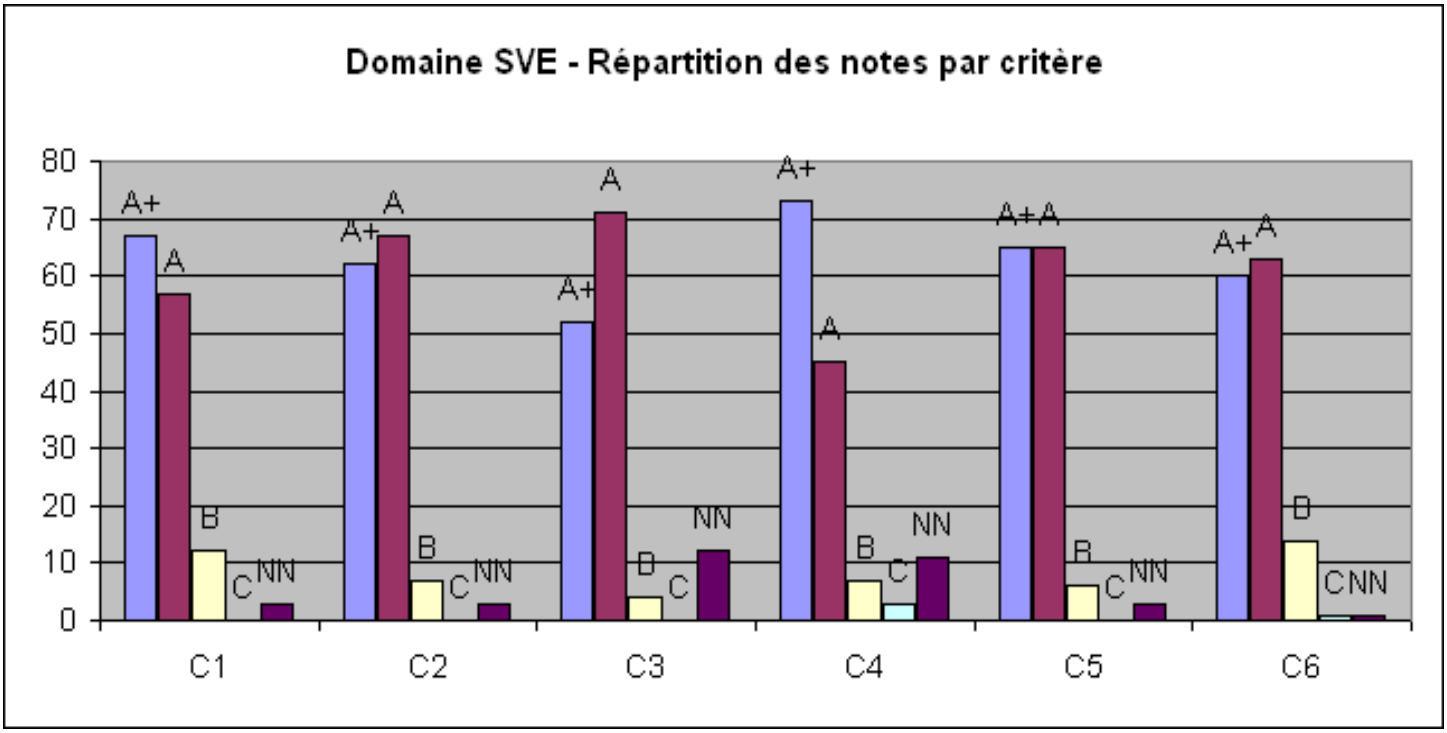
Grades

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 16 avril 2013

Concerne : ***Rapport d'évaluation S2PUR140006110 – Dynamique Nucléaire – 0753172R***
Unité IC/CNRS UMR218 : Directeur G. Almouzni

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 2 Avril dernier, le rapport d'évaluation de l'AERES sur l'unité IC/CNRS UMR 218.

J'ai lu ce document avec attention et avant de vous faire art de mes remarques, je tiens à saluer le travail réalisé par les experts.

Je me félicite de l'appréciation exprimée sur cette unité considérée comme remarquable ('outstanding') dans sa production scientifique et sa reconnaissance dans sa dimension internationale au plus haut niveau, son organisation exemplaire et son implication active dans la formation et la dissémination. Je suis particulièrement réceptif à l'avis très favorable exprimé concernant le plan à cinq ans et la stratégie proposée qui seront développés.

Afin d'assurer le succès continu de cette unité, je note bien 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 et le CNRS et notre partenaire l'Université Marie-Curie (Paris 6) pour assurer les soutiens nécessaires. En particulier :

- la prise de fonction à la direction du centre de recherche de l'Institut Curie au 1er Septembre 2013 de l'actuelle directrice Geneviève Almouzni appelle un soutien supplémentaire au sein de son unité. La proposition qu'Angela Taddei prenne progressivement la direction de l'unité après une période de transition en tant que Directrice adjointe validée par le comité est bien reçue. Il sera effectivement nécessaire d'accompagner cette transition pour cette unité compte tenu des nouvelles fonctions de Geneviève Almouzni.

26 rue d'Ulm - 75248 Paris Cedex 05
Tél. 33 (0)1 56 24 55 00 - www.curie.fr

1. Le recrutement d'un ingénieur de recherche, au niveau de l'équipe d'Angela Taddei permettra à cette dernière de dégager du temps pour prendre de nouvelles responsabilités en cohérence avec sa promotion comme groupe senior à l'institut Curie.

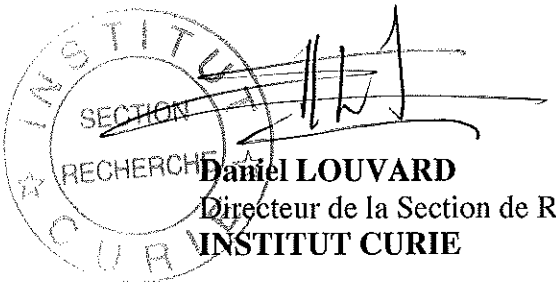
2. Il sera également important que le CNRS renforce le soutien administratif de cette unité pour qu'elle puisse continuer à jouer son rôle et se garantisse l'obtention de contrats nationaux et internationaux essentiels pour ses projets en allégeant le poids actuel sur les personnels des équipes.

- La question d'espace est un point critique pour l'ensemble des unités du site de Paris, dont l'Unité IC/CNRS UMR 218. De solutions devront être trouvées pour respecter les contraintes imposées par la législation sur le plan de l'hygiène et la sécurité.

- Les doctorants et post-doctorants, particulièrement les étrangers, ont été informés de des possibilités présentes de soutien et le seront dans l'avenir afin de répondre au mieux à leurs besoins

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