LBMC - Laboratoire de biologie moléculaire de la cellule

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Laboratoire de Biologie Moléculaire de la Cellule

From the

ENS Lyon

CNRS

Université de Lyon 1

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Le Président de l'AERES	Section des unités de recherche
	Le Directeur
Jean-François Dhainaut	Pierre Glorieux

May 2010

Research Unit

Name of the research unit : Laboratoire de Biologie Moléculaire de la Recherche

Requested label : UMR CNRS

N° in the case of renewal : 5239

Name of the director : M. Laurent SCHAEFFER

Members of the review committee

Committee chairman :

M. Laszlo TORA (IGBMC, Strasbourg)

Other committee members :

M. Jörg LANGOWSKI (DKFZ, Heidelberg, Germany)

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Committee members suggested by CNU, CoNRS, CSS INSERM, CSS INRA, INRIA, IRD

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Ms. Chantal LASSERRE, INSERM

M. Jacques SAMARUT, ENS

M. Germain GILLET, Université de Lyon 1

Report

1 • Introduction

- Date and execution of the visit

The committee visited the laboratory from February 3d to 5th, 2010. The visit was well prepared, with a detailed document provided in advance. However, the committee found that the provided documents, containing the reports and the future projects, were rather complicated and thus, not very easy to follow. On site, the visit was well organized, with presentations and discussions with the director, group leaders, technical and administrative staff, students and post-docs. The committee had sufficient time, albeit in a very tight schedule, to discuss various issues. The visit was executed smoothly and without any problems. Only those group leaders were interviewed who will stay at LBMC for the next four years. No visit of the labs had been organized.

- History and geographical localization of the research unit, and brief presentation of its field and scientific activities

The LBMC was founded in 1987, at the same time when the Ecole Normale Supérieure de Lyon (ENSL) was created. Geographically, the LBMC is hosted at the campus of ENSL. In 2006, the LBMC has acquired laboratory space at the "South Lyon" Hospital Complex, in rehabilitated teaching hospital buildings. Since its creation, the LBMC is supported by CNRS and ENSL in the form of a jointly founded research unit. The University Claude Bernard Lyon 1 and the Lyon Hospices are also supporting the LBMC in the form of joint appointments and transversal projects. INSERM support is illustrated by the presence of three scientists belonging to INSERM. In 2007, the Institut de Génomique Fonctinnelle de Lyon (IGFL) was created at ENSL from three former groups of the LBMC. Because of the delay in the construction of a new building for IGFL, the three former groups kept their laboratory surface at LBMC that created important space limitations at LBMC. The LBMC also contributed the installation of another biology laboratory at the ENS campus, the transdisciplinary Joliot-Curie Laboratory (LJC).

- Management team

The LBMC has a collegial direction with a board that is composed of the director, the administrative manager and all the group leaders. The management team of LBMC is composed of the director and the administrative manager. The administrative manager and her team takes care of the logistics and the supplies not only concerning the needs of LBMC, but also that of several other biology-related units on the ENSL campus.

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	13	10
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	22	19
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	25	20,5
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	26	26
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	10	6
N6: Number of Ph.D. students (Form 2.7 of the application file)	35	21
N7: Number of staff members with a HDR or a similar grade	16	12

2 • Overall appreciation on the research unit

- Summary

Teams at LBMC, by using numerous experimental models (i.e. yeast, C. elegans, Drosophila, mouse, and many different mammalian cellular systems), are carrying out research programs ranging from the nucleosome level to cells and tissue samples from patients. The wide scientific interests of the LBMC can be categorized in the following themes: mechanisms controlling gene expression, biology of the nucleus, epigenetics, genomics, signalling, control of proliferation, differentiation, apoptosis and senescence of cells, cell cycle, virology, immunology, neurobiology, development, muscular differentiation, cancer and aging.

Overall, the research carried out at the LBMC can be qualified as good to very good, on international standards. The committee noticed a substantial heterogeneity in the performance and the quality of the research of the various groups, yet the general feeling was positive. While most groups are clearly at the international standard, others experience some difficulties to reach a level of high visibility. This is also apparent from the recent publication records of the PIs.

A clear strength of the LBMC over the past four years has been its ability to attract many (mostly young) energetic group leaders. Out of the 15 teams that will constitute the LBMC in the next four-year period, 8 teams have been recruited recently. Four of these teams were accompanied by finance from the CNRS ATIP program for young scientists; one team obtained an ANR Young Investigator Award and another one an EU funding. The contribution of these groups to the LBMC is already excellent, or was judged by the committee very promising. Two young group leaders have also been awarded with the CNRS bronze medal.

On the other hand the departure of eight former teams in the past four years, some of them senior and well-known groups, may be a factor of risk for the future developments of the Centre. The reasons for these departures were diverse, including retirements and the creation of other biology related novel institutes, such as IGFL and LJC on the same campus or in other cities. The disappearance of senior scientists from the everyday life of LBMC may represent a significant loss of potential, competitiveness and visibility. These departures were also accompanied by the parallel departures of eight technicians.

The LBMC has also shown significant success in attracting external funding. Many ANR and EU grants were obtained during the reporting period. There has also been an equally important input from funding by charitable foundations. This capacity to attract funding has coincided with gradual erosion in institutional funding, which should be closely monitored by the CNRS and ENSL since a continuation of this trend will significantly reduce the competitiveness of the unit as a whole.

Another indicator of its activity is the publication output. Although the absolute number of publications of the LBMC may be lower than one would expect, the Institute's scientific policy is to increase the quality of publications, as revealed by the impact factor of the journals they publish: e.g. Blood, journals from the Cell and Nature press groups. The committee acknowledges this effort and encourages the teams, especially those recently started, to publish high quality scientific papers. International recognition of certain PI is also clear from the number of invited lectures.

The LBMC is also involved in developing and fostering translational research. Indeed the research topics present at the two sites (ENS and South-Lyon Hospital related sites) have the potential to do so. It seems that there is a functional communication between teams working at the two sites of LBMC.

The Institute has organized several common services and platforms that seem to function satisfactorily, however these platforms have not been involved in the presentations of LBMC.

Discussion with tenured staff, technical and administrative staff, post-doctoral and doctoral students revealed a large degree of cohesion and interaction within these groups and a general contentment in the way the Institute functions.

- Strengths and opportunities

The LBMC had a very active policy for recruiting new external group leaders, justified by the departures of many previous groups. The Institute recruited excellent and very promising young scientists, most of them at the international top level. Moreover the teams had a very good success in recruiting a lot of young scientist (PhD students and post-docs) from abroad. The PhD program of the students is well organized. There are many interactions between teams and researchers at LBMC. The scientists are satisfied with the quality of the platforms and technical services. It seems that the LBMC has an active scientific life and in general there is a good working atmosphere.

The LBMC has excellent local opportunities for interdisciplinary and translational research, for collaboration with the local hospital area to obtain relevant biological samples and information.

- Weaknesses and threats

To consolidate and develop the Institute's scientific competence, many new (8) teams have been recruited. However, this has created in certain themes and/or model systems insufficient critical mass for sufficient competitiveness. Moreover, to have so many junior groups starting more or less at the same time and without a sufficient critical mass of well-known senior PIs may also represent some risk for the further development of the Institute. To separate the LBMC into two geographical entities may also not be optimal. Due to the new recruitments it seems that in spite the efforts taken at the institution level, the available resources are not sufficient to support fully the internationally top level young groups. The lack of technicians in some of the new groups may undermine the future success of these groups. The LBMC does not have at present enough strong senior group leaders due to the departure of the former ones. The disappearance of senior scientists from the everyday life of LBMC may represent a significant loss of potential in competitiveness and visibility. The LBMC has no Scientific Advisory Board.

- Recommendations to the head of the research unit

The international visibility of LBMC has to be improved. The committee would recommend that teams at LBMC profit more from the interdisciplinary scientific interactions that they can have with other labs at the ENSL campus and at the Gerland site in general. In general there are few common internal collaborative projects within LBMC teams. Coaching and mentoring of junior group leaders should be considered. A convivial space would further foster scientific interactions between researchers belonging to different teams. Students and post-docs should participate more often in international conferences. To better balance the equilibrium between junior starting groups and more experienced PIs, the committee recommends to recruit senior groups. The LBMC has to consider developing services enabling genome-wide approaches and bioinformatics support for the community.

The lack of space at the ENSL campus, due to the delay in constructing the building for IGFL, should be solved as soon as possible. Tasks carried out by LBMC members for the other biology institutes should be better defined and made more transparent. In general the committee found that the relations between LBMC, the other biology-related institutes and ENSL are very complex and should be clarified. Since the director of the LBMC may not want to be renewed for the third time after the coming four-year period, the unit has to make considerable efforts to identify the individual(s) who will be in a good position to become the future head(s) of the Institute. It is in the interest of everyone to think in the most constructive way about the future organization of the LBMC.

- Production results

(cf. http://www.aeres-evaluation.fr/IMG/pdf/Criteres_Identification_Ensgts-Chercheurs.pdf)

A1: Number of permanent researchers with or without teaching duties (recorded in N1 and N2) who are active in research	24
A2: Number of other researchers (recorded in N3, N4 and N5) who are active in research	44
A3: Ratio of members who are active in research among permanent researchers [(A1)/(N1 + N2)]	0.88
A4: Number of HDR granted during the past 4 years	5
A5: Number of PhD granted during the past 4 years	25

3 • Specific comments on the research unit

- Appreciation on the results

The relevance and the originality of the research are generally good, but not outstanding compared to the international level. While some groups are clearly at the international standard, others experience some difficulties to reach a sufficient level of visibility and originality. The efficient collaborations between molecular biologists and biophysicists as well as between molecular biologists and clinicians were highly appreciated by the committee, and the developments of these collaborations are strongly encouraged. The epigenetic and the cell differentiation focus were considered to be excellent.

The quantity and the quality of the publications in general are very good, but not outstanding. Some PIs do not have enough international visibility since they are rarely invited to international meetings. The fact that the lab produces MD/PhD theses was well appreciated.

Within the framework of the Center for Study and Transfer in Oncology (CERVO), the LBMC has produced significant efforts to develop partnerships with different companies. Certain teams were involved in the creation of companies and several teams have filed patents. Partnership with the hospital was well appreciated by the committee.

- Appreciation on the impact, the attractiveness of the research unit and of the quality of its links with international, national and local partners

The reputation of the awards obtained by several of the young recruited PIs (i.e. ATIPE grants and Bronze medals) is outstanding. However, the number of awards and invitations to international conferences, in general, granted to researchers of LBMC was rather low and should be increased in the future.

Excellent recruitment of high level PIs and staff scientists (mainly French) Excellent recruitment of post-docs and students, many from abroad.

The teams at LBMC had a good success in getting national grants. However, only few of them got international grants.

The committee noticed a good, but not outstanding, integration into national and also international networks.

Some scientists of the LBMC make an important effort to communicate with a non-scientific audience.

- Appreciation on the strategy, management and life of the research unit

The quality and organization of the governance of LBMC was considered to be very good. The research and the functioning of LBMC are well-organized at the every-day level. The ways how strategic decisions are taken are well defined

and were clear to the scientist working at the LBMC. According to the committee the external communication strategies and tools of the LBMC could be considerably improved.

Excellent, internationally top level, recruitments of several outstanding young group leaders. The scientific animation at LBMC is well-organized. The efforts to organize LBMC retreats were well appreciated. However, the frequency of these retreats could be increased if the financial situation permits. Students and post-docs should be actively involved in scientific animation (i.e. organization of workshops and/or conferences).

The members, especially two professors, of the LBMC are involved in teaching activities. The fact that the teaching activities did not seem to be overwhelming at LBMC was highly appreciated by the committee and will help to further develop the scientific activities of this Institute.

- Appreciation on the project

The feasibility of the presented projects for the next four years is realistic. A key in the development of the LBMC for the next four years will be how their choice to increase the competence of the Institute will come to reality. In other words how the eight recently recruited junior group leaders will be able to develop and bring to completion (and publication) their planned projects.

The committee encourages the mid-term prospective for recruiting a scientist doing cutting-edge microscopy techniques applied to significant cellular or molecular biology project.

Allocation of resources to LBMC by ENSL and other local sources was not clear to the committee because of the complicated intermingling of local organizations of biology-related institutes at the ENSL campus and because of a general lack of transparency. In general the allocation of resources to teams within LBMC is good, however the allocation of resources and technical help to young teams should be a priority (either by reallocation of technical personnel or by new recruitments).

The excellent collaborations between molecular biologists and biophysicists are done in the frame of cutting-edge projects. The development of such collaborations is strongly encouraged.

4 • Appreciation team by team

Team 1: Genetics of Intra-Species Variations

Team leader: M. Gaël YVERT

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	0
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

The research of this team is first rate. The team is interested in the genetic basis of natural intra-species variation, an extremely difficult research area but one of prime importance for biology and human health. By combining approaches from multiple disciplines (experimental genetics, genomics and biostatistics) the team has successfully undertaken a few, selected and carefully designed experiments that address fundamental questions in this field. Of particular excitement are the projects on the genetic dissection of cell-to-cell variation in gene expression, which is amazingly simple but has yielded extremely interesting results, and the project on epigenetic variation across individuals, which is under review. The importance of these projects cannot be overstated: It is by figuring out how genetic and epigenetic variation between individuals from model organisms (like yeast) impacts phenotype that we will learn about approaches for personalized medicine. For this the PI is very well placed by having projects that span the phenotypic, genetic and epigenetic level.

The PI himself has published exceptionally well during his post-doc, including highly cited papers in top-level journals (like Science and Nature Genetics). Five papers have come out from his group since he started. The number of papers from his team is thus good, though not stellar, but this will likely change once the group becomes more established and papers proceed faster though the review process.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The PI is to be congratulated for obtaining two awards during his first 4 years as a group leader, including the Bronze Medal of CNRS – the highest distinction for young group leaders in the CNRS. This is excellent. The group has a solid track record of representing science at meetings (8 conferences and most as invited speaker).

The team is still young and small (4 people: the PI, one post-doc, one technician, and one PhD student). Most are French nationals. The small group size and nationality bias could be improved. The committee recommends building up the team so that the exciting scientific projects can be carried out more effectively and timely. This may have been a problem at the beginning, but given the impact and importance of the research published so far, there should be no problem in recruiting more scientists from abroad.

The group has had three grants. More effort should be placed on obtaining funding as this would help enlarge the group size.

The group has several international collaborations. He collaborates with the EMBL (one paper in review and a second one in preparation). In addition, the PI has collaborated with the University of Tokyo (one published paper) and the Faculté d'Oenologie de Bordeaux (two published papers).

A former member of this group founded a company, BioMiningLabs.

- Appreciation on the strategy, management and life of the team

Teaching is minimal which is good for the group.

- Appreciation on the project

The proposed future projects are very interesting and relevant. They delve deep and comprehensively into his key research interests, but also include additional projects beyond yeast. They appear very well selected and planned. Rather than just doing the obvious next step experiment, the proposed projects are interdisciplinary and aimed at a few key questions. For example the projects on stochasticity include analysis at multiple levels: gene expression in yeast, noise in cellular processes using microfluidics, IRES mediated translation in human cells, and the genetic basis of adaptability by in-lab evolution.

The projects are very original, interdisciplinary and at the cutting edge. The team employs state of the art technology and approaches, including tiling microarrays, microfluidic technology, computational biology and biostatistics.

- Conclusion :

  – Summary

The research of this team is first rate. By combining approaches from multiple disciplines (experimental genetics, genomics and biostatistics) the team has successfully undertaken a few, selected and carefully designed experiments that address fundamental questions in this field. The research plan is very innovative. The projects appear very well selected and thought through. Rather than just doing the obvious next step experiment, the projects are aimed at a few key questions in

each area. Although the group is small and covers not many projects, the science is very well planned and project design is impeccable.

– Strengths and opportunities

The projects are very original and at the cutting edge. They combine computation with wet lab biology. The group employs state of the art technology and approaches, including tiling microarrays and microfluidic technology. This provides an opportunity for spreading this know-how to other groups within the laboratory.

– Weaknesses and threats

Small size.

– Recommendations

The team is still young and small (4 people: the PI, one Post-doc, one technician, and one PhD student). The committee recommends building up the team so that ideas and exciting scientific projects of the PI can be carried out.

Team 2: Plasticity and Evolution of cell division

Team leader: Ms Marie DELATTRE

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	0
N7: Number of staff members with a HDR or a similar grade	0	0

- Appreciation on the results

The PI is a novel group leader who started her group little more than a year ago. Her CV is excellent, and shows highly productive pre- and postdoctoral training and includes major impact papers from her postdoctoral work. Since, she has received an ATIP grant and has been awarded a bronze medal by the CNRS in 2009.

The team currently focuses on the evolutionary conservation of asymmetric cell division. This is highly attractive as it combines an important question and hot topic in biomedical research (what are the mechanisms controlling asymmetric cell division?) with her own niche and model system (expertise in evolutionary biology of Caenorhabditis species). This combination is powerful, original and a great foundation for a productive research team. The second topic addresses the mechanisms of centrosome assembly and function. This is also an important research question and the main area of her expertise as a postdoctoral fellow.

The group is starting and still small, in part because the institute has not yet assigned a technician.

Publications as a postdoctoral fellow include first author articles in Nature Cell Biology, Current Biology and the Journal of Cell Science. Moreover, important papers have been published together with her former group leader. Given the recent start, no publications or theses have come from the group.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The CNRS bronze medal is highly prestigious. Despite her recent start the PI has been invited to give a seminar and present at "evolution" meetings.

She received a prestigious ATIP grant (150K euro, 2009-2011) and ARC funding

- Appreciation on the project

The future plans are ambitious and go in two directions.

i) Examine the robustness and evolution of the first asymmetric division in nematodes: This is a highly original and promising project. While many groups use genetics in C. elegans to study asymmetric cell division, much can be learned form comparing and contrasting this process in different Caenorhabditis species. The project is well thought out and should attract funding as well as collaborations.

ii) Identify additional components involved in the centriole cycle, through characterization of Stu mutants. The PI indicates that this project will only be initiated when the group has substantially grown. This is a wise choice, as competition in the field is fierce. While the focus on larval divisions provides a different angle from a well established lab in Lausanne, it will be difficult to compete with this group as a starting lab.

Both projects in the group are original and cutting edge

- Conclusion :

  - Summary

The PI is a highly promising group leader, who has managed to establish her own niche in an important and highly competitive field of research. Her work is original, important and first rate. She deserves full support by the institution.

  - Strengths and opportunities

The PI can use the momentum obtained by her high impact pre- and postdoctoral publications, awards and grants to establish and expand a substantial group and become a leading scientist in the next five years.

  - Weaknesses and threats

The group is currently to small to be highly productive. Help is needed, first of all a technician, but also additional graduate students and post-docs need to be recruited. Addressing two different lines of research would spread the group too thin.

  - Recommendations

The institute should provide full support for the group, in particular during the first few years of her establishing a group. A dedicated technician is highly desirable.

Team 3: Cellular and Organismal Aging

Team leader: M. Hugo AGUILANIU

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	3
N7: Number of staff members with a HDR or a similar grade	0	0

- Appreciation on the results

This team started its activity in January 2007. The written document presents the scientific activities during the period of 2007-2009.

The research activity of the team is dedicated to the study of aging using *C. elegans* and *M. musculus* as model systems. Six themes are emerging but only three of them have already led to significant production and are presented in the written document:

Theme 1: In a collaboration, the PI participated in a genetic screen for the identification of genetic determinants in the DR pathway (1 publication in Nature, co-signed by the PI). The team has pursued on its own the analysis of a negative regulator of the DR response and, in a third step, is testing the efficacy of drugs on mice in collaboration with a group in Lausanne. This project leads to one patent and an article in preparation.

Theme 2: The starting observation for this project is that worms lacking a functional germ line cannot mobilize their fat and live longer. A screen for suppression of longevity led to the identification of new genes, required for both germlineless-mediated longevity and fat mobilization. The team is pursuing the functional study of these genes, focusing on its interactions with both upstream and downstream components involved in the control of aging and fat metabolism. Collaboration with another group at LBMC is exploring the function of the orthologous genes in mammals, and the first results suggest a possible conservation across species. A manuscript in preparation covers this part of the project.

Theme 3: The project aims at understanding how the progeny is protected from aging, with a particular emphasis on mechanisms involving resetting of the aging process in the germ line. Using *C.elegans* as a model, and the visualization of a known aging marker, protein carbonyls, the team is studying the process of damage elimination.

In conclusion, in the two years of its existence, this young team has produced important original data for the understanding of different mechanisms involved in cellular and organismal aging.

The past publication record that is presented in the report concerns the period before the creation of the team. Most publications are in high standard journals (Nature, PNAS, G&D). Many publications are related to one newly established member of the group before she joined the team. The team has been created early 2007 and, so far, no publication has emerged from the work of the last 3 years. Although it is still early to make a statement on the production of the team, the Committee is concerned that the absence of publication represents a weakness for the funding renewal of the group.

Therefore, the Committee recommends that the publications in preparation are rapidly sent to journals with high probability of being accepted.

The Committee also notes the deposition of two patents with potential application in health.

The team leader works with the Valorisation and Technological Transfer Cell (PRES and ENS), two patents have been deposited.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

Recruitment of one senior scientist (CR1) in 2008.

Seven different funding sources have been obtained for a total of 338 K€ (2006-2011). Most of the funding will stop in the coming year, therefore raising the question of funding renewal. Several applications are on their way, but the chance of success will depend on the publication record of the team.

The team has established local and international collaborations (University of Southern California; Lausanne, and a collaboration in Norway not detailed in the report).

The team leader works with the Valorization and Technological Transfer Cell (PRES and ENS), two patents have been deposited. The team is involved in transferring its research to industrial firms but this is not described in the report.

- Appreciation on the strategy, management and life of the team

The position of the second tenure scientist in the team is not clarified. According to the PI, this person already has a semi-independence in the group. The Committee is not convinced that, at this point of its evolution, the team should develop independent sub-groups.

One scientist is involved in some teaching duties (Master's degree) and the two senior scientists supervise Master's students or PhD students. At least two PhDs should defend their theses in the coming period.

- Appreciation on the project

The results obtained during the last period can potentially generate many original lines of research that should be developed in a focused way. The team aims at :

- continuing on the three major projects with a special emphasis on projects 1 and 2 in order to publish and potentially patent on project 2.

- developing three new projects:

  - to understand the impact of epigenetic modifications (and more specifically caloric restriction) in aging Saccharomyces cerevisiae and Caenorhabditis elegans,

  - to study the role of Acyl Binding Coenzyme A Proteins (ACBPs) in the aging process in Saccharomyces cerevisiae and Caenorhabditis elegans,

  - to analyze single cell aging in Saccharomyces cerevisiae with four objectives: i) build a "single cell chemostat" to monitor cell division over a large number of generations, ii) describe and quantify cell transition to senescence, iii) investigate mother-daughter inheritance: the mechanism of cell rejuvenation and iv) decipher the control principles of aging.

The projects are original and rather cutting edge. Nevertheless they all reside in a very competitive area of research, where finding its niche remains a challenge for an emerging group.

- Conclusion :

  - Summary

In conclusion, the production of knowledge and the quality of the work during the last two-three years appears promising, although the group still needs to validate its production through publications in high profile journals. The project for the upcoming period is in the continuity of the work done and part of this work could have potential for practical application. The team follows a positive trajectory, with the arrival of new members.

  - Strengths and opportunities

The group leader has a strong expertise in the field of aging and a good evaluation of the key questions in its field. The reinforcement of the team by a second senior researcher is a very strong sign for the medium/long term stability of the group (see also comments above about subgroups). Several interesting projects have reached a state where the group can publish them and two publications are currently submitted.

  - Weaknesses and threats

One of the potential weaknesses is the limited size of the team compared to the large number of projects proposed. At this point of development, the group leader should not lose his focus and the Committee considers that the translational part of the project might not be a priority. By contrast, a very strong priority should be given to the publication of the acquired results, in order to validate the ongoing projects and allow a renewal of the team's funding. The area of research where the team is developing its projects is highly competitive and a niche must be found (not obvious at the moment).

  - Recommendations

The committee recommends strongly that the results achieved by the team are quickly validated by publications in journals where they have a strong probability of being accepted rapidly. This will be key in obtaining novel grants.

Team 4 : Epigenetic regulation in development

Team leader : Ms Francesca PALLADINO

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	1,5
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	0
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

The research focuses on the important question how chromatin structure is regulated in the context of animal development, and how this provides developmental control of gene expression. The group uses an original approach, based on

genetics in the nematode C. elegans, to study the function of heterochromatin Protein 1 (HP1) family members and histone methyltransferases. The genetic characterizations are performed in detail, experiments are of high quality and analysis and interpretation of the results are thorough. While this work is well respected within the C. elegans field, limited molecular analysis and focus on C. elegans specific phenotypes have somewhat hindered the broad impact of the work.

The group has published 5 articles in the 2006-2009 period, which is productive for a C. elegans lab. Three of the papers are in Developmental Biology and one in Genetics, which are good quality journals.

In addition, two theses have come from the group and have been defended in 2006 and 2008.

The group has been represented at national and international meetings, mostly C. elegans meetings, but also some chromatin and epigenetics symposia.

Collaborations have been established with international leaders in the chromatin field.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The PI has listed two invited seminars and two oral presentations at C. elegans meetings. The general visibility of the group should be improved.

The recent recruitment of an experienced post-doc with expertise in the C. elegans field, who received excellent training in the Plasterk lab, the Netherlands, is an important acquisition for the lab.

The group received funding from several sources. Four of the five are smaller grants but in 2007 substantial funding (264K, "ANR Blanche") has been obtained.

Collaborations have been established with several major research groups. These collaborators perform ChIP on chip experiments and provide expertise for the analysis of microarray data.

Both of these groups have a great scientific reputation and are experts in the field.

- Appreciation on the strategy, management and life of the team

The contribution by the group to teaching is very limited, a total of 6 hrs/year is listed. This is divided over three different Master courses. However, low level of teaching is important for the development of the team and for staying competitive in the field.

- Appreciation on the project

The future projects lists four different topics with several different sub-aims:

i) Global analysis of HPL-2 targets by "ChIP on Chip" in collaboration.

This is an interesting and sophisticated strategy. The lab may receive little credit for this work, however, the PI indicates that early insights in the results will be valuable for the group.

ii) HPL-2 function in stress and innate immunity

This project examines a class of HPL-2 target genes with a role in the ER unfolded protein response and an antagonistic relationship with the CTBP corepressor. This work will produce insights in stress and innate immunity, as well as the competitive interactions between CTBP-1 and HP1

iii) Characterization of C. elegans histone methyl transferases (HMTs)

This project examines the in vivo set-2 HMT function, localization and pattern of methylation

iv) Epigenetic remodelling in dietary restriction.

This project will be carried out in collaboration with another lab at LBMC.

This is an interesting set of projects that are all doable, include state of the art techniques and will lead to significant publications. The range of topics appears rather broad, and for that reason it would be better to focus in one or

two areas. The increased molecular focus of the work is encouraged and the impact of the work would benefit from strategies that allow resolution at the single cell level.

The ChIP on Chip experiments are certainly cutting edge. The LBMC should try to establish an infrastructure, which facilitates carrying out such experiments and bioinformatics analysis of the data by the group.

- Conclusion :

  - Summary

The PI is a well-respected scientist in the C. elegans community. She has assembled a small but high quality team, and addresses an important question of developmental control of chromatin remodelling. The publications attest of a productive group and the established collaborations are excellent. Four related lines of research have been initiated that hold promise.

  - Strengths and opportunities

The topics addressed in the lab fit well with the interests and strength of the research environment. This provides critical mass (epigenetics), while at the same time a niche (chromatin remodelling in C. elegans) is present. The PI could take a leading role in bringing together researchers from several different groups in the institute to bridge model organisms and improve the impact of the experimental results.

  - Weaknesses and threats

Improved understanding of the general mechanisms of chromatin remodelling should remain the focus of the work. The projects go in too many different directions and focus too much on the details and peculiarities of the C. elegans system.

  - Recommendations

The group might benefit from more interactions with other groups in the unit that focus on epigenetics or use C. elegans. Together, these teams could have quite an impact in the field of developmental control of chromatin organization and gene expression. The lab should try as much as possible to address the "big questions". This probably requires continued focus on molecular mechanisms in combination with establishment of novel methods for examination of chromatin structure at the level of individual cells or tissues.

Team 5 : Apoptosis and Neurogenetics

Team leader: M. Bertrand MOLLEREAU

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	3	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	1
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

The team started at the LBMC in September 2006, after moving from the Rockefeller University, NY (USA). The major interest of the team is the study of apoptosis during developmental processes as well as in response to external stress, with a particular emphasis on neuro-degeneration and -protection mechanisms. The model used is the Drosophila retina where developmental apoptosis is highly regulated and contributes to morphogenesis. Two main lines of projects are followed up:

- The study of neuro-degenerative and -protective mechanisms. This project is based on earlier observations made by the group that mild ER stress protects from apoptosis. The team aims at studying the mechanisms by which ER stress protects the cells from apoptosis, and in particular how ER stress can induce autophagy as a protective mechanism. A distinct project will allow testing this protective effect in a mouse model for Parkinson's disease. Finally a genetic screen for mutations perturbing the survival of photoreceptors in the adult eye has been conducted in order to identify genes involved in neural degeneration. The candidate genes already obtained will be further analyzed.

- The study of apoptosis during development. Two main approaches will be carried out for this project: a study of apoptosis in the retina using live imaging and the study of the Drosophila p53 tumor suppressor and its function in apoptosis and development.

The team has produced one publication in EMBO J. in 2009. The previous publication of the PI (EMBO rep. 2006) was issued before the establishment of the group at the LBMC. Given the state of evolution of the group and the fact that the project was initiated earlier in a previous environment, one could expect a more developed publication record.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The team leader has several invitations for seminars in research institutes, both in France and abroad.

The team is currently composed of seven members and has recently recruited three postdoctoral fellows and one staff scientist with good expertise in the fields of apoptosis and fly development.

The team has been allocated an ATIPE grant (2008-2011) and a FRM label (2008-2011), which should provide enough funding for up to 8-10 lab members, until 2011.

- Appreciation on the strategy, management and life of the team

The team does not benefit from a supportive environment with other Drosophila labs at LBMC. The existence of a critical mass for a given model system is key for the development of young groups and should not be underestimated.

The PI is a Professor of the ENS. Because of his ATIPE label, he benefits of a 50% reduction of his teaching load. In addition, another permanent member has been recruited as an Assistant Professor of the ENS with a CNRS chair. He therefore benefits from a 66% reduction of his teaching load.

- Appreciation on the project

The lines of projects are quite numerous for a small team, but each project seems to be assigned to a specific lab member. The recognized expertise of the team in the field of apoptosis and fly genetics is a good warranty for the feasibility of the proposed projects.

Both grants will end mid 2011 and the group leader should already think about their renewal

From what is provided in the proposal, the projects are well planned and interesting, without being exceptionally creative and original. The Committee was not fully convinced that the proposed projects were addressing the most significant questions in the field of apoptosis and neurodegeneration.

- Conclusion :

  – Summary

The team is still establishing and has produced interesting work in the last three years of its creation. For the coming years, it will need to demonstrate a real impact in the very competitive field of apoptosis through the development of ambitious and innovative projects.

– Strengths and opportunities

The team has recruited talented young members in the recent years and should benefit from this increase to reinforce the ongoing projects and develop more innovative ones.

– Weaknesses and threats

The funding will stop next year and its renewal will depend on the quality of the published work. The field of apoptosis in Drosophila is very competitive and necessitate embarking on innovative and cutting-edge projects. The lack of surrounding groups working on the Drosophila model is a weakness that should not be underestimated.

– Recommendations

The group should focus on developing ambitious research and should rapidly be involved in recruiting other Drosophila groups in the environment of the LBMC.

Team 6 : Differentiation and Cell Cycle

Team leader: M. Brian B. RUDKIN

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	2	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	5
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

The scientific objective of the research in this team is to characterize signalling pathways involved in the fundamental cellular processes of proliferation, differentiation and apoptosis and to study more precisely the expression and fate of NGF receptors (TrkA and p75NTR) by selecting several key responses characteristic of NGF action. In parallel, this team has developed the peptide aptamer technology and different applications of this technology for dissection of signalling pathways. Using this technology and employing people from this team, a start-up, Aptanomics, has been created in 2001, but this company stopped its activity in 2005/2006. The team leader says that the cessation of the activity of Aptanomics marked a major change in the scientific activities of the team. The Committee had difficulties evaluating this “major change” because the relationships between the team and the company have not been presented very clearly. After the cessation of Aptanomics, the team pursued its research on the peptide aptamer technology and its applications to basic research for dissecting signalling pathways.

In the written document, some applications of the Aptamer technology are described in collaboration with local, national or international groups about different subjects: muscle atrophy, anti-apoptose in Drosophila, osteoclast differentiation, breast cancer, spermatogenesis, self-renewal of human embryonic stem cells, role of kalirin in the signalling pathway of NGF etc. However, the importance of these applications and the main focus of the team itself has not been clearly presented during the evaluation.

The results of the applications of the technology used in this team are well recognized internationally as testified by the 12 publications in good international peer-reviewed journals (Mol Cell Biol, Drug discov Today, Oncogene, Nat Protoc, J Cell Physiol, Mol Cell Proteomics, Mol Biol Cell, PloS One, Meth Mol Biol). However, the team leader as a last author signs no publication. This represents a weakness for the legibility of the team. Moreover, the role played by this team in these applications is not clearly described.

The Committee also notes the deposition of one European patent with potential application in health.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

Many invitations are reported in different countries (Japan, China, USA, Israel, Norway, Germany, Italy, Switzerland), sign of an international recognition of the team leader in his field.

Several PhD students were recruited from abroad (mainly from China) due to an important collaboration with East China Normal University (ECNU), where the PI has another position.

Five different funding sources in collaboration with public or private partners have been obtained for a total of 1005 K€ (2005-2011). Most of the funding will stop in the coming year, raising the question of funding renewal.

The team has established local, national and international collaborations.The main collaboration is with the East China Normal University (ECNU), four PhD students are under co-supervision and a "Programme International de Coopération Scientifique" (PICS) has been established by the CNRS: it constitutes the origin of a new joint research institute between the ECNU and the ENS Lyon "Science and Society". A European project was recently started with six other teams.

The team has also collaboration with a group from University of Connectitut in USA about the role of kalirin in the signalling pathway of NGF.

Aptanomics has been involved in a preferential partnership with the team, but it was not really defended by the team leader, both in the written document and during the evaluation.

The Committee recognizes a good expertise of the team leader who presents many activities in Innovation, Valorisation of the Research and Technological Transfer in France, Europe, USA and China. He is a member of the "Investment Committee" in the Incubator CREALYS. He was in charge of the relations between the "Grand Lyon" and Philadelphia. Invited as "Asgard Scholar", he visited many centres involved in Innovation and Research. He has also many activities in Italy for the reorganisation of the Research.

One European Patent Application has been deposited in 2006 and could have potential for practical application.

- Appreciation on the strategy, management and life of the team

It was difficult to clearly understand the organization of the team. The Committee has not been convinced by the strategy and the general organization of this team.

The team leader participates in teaching duties (4-8 hours per year in France and in China), but he has an important charge as a supervisor for 5 PhD students during the last period. No information was given about two students who started their theses in 2005.

- Appreciation on the project

Many lines of projects planed for the upcoming period represent a continuation of collaborative works engaged by the team presently, but no clear, focused scientific project is presented for the next four years.

According to the document presented during the presentation, after July 2010 the team will have only one research grant for their numerous planed activities.

The peptide aptamer technology is in itself original and rather cutting edge. Nevertheless, the absence of a focused project and the general feeling of confusion emanating from the presentations (both written and oral) preclude a good evaluation of the team's projects.

- Conclusion :

– Summary

In conclusion, the scientific production of this team during the last four years reveals a number of productive collaborations. The Committee recognizes the implication of the team leader in technology transfer and creation of innovative companies. Nevertheless, the participation of the team itself to innovative scientific projects is not clarified and appears in some instances marginal. The very large dispersion of the presented projects is not good and in the absence of a solid team project, the Committee has strong doubts concerning the strategy of the team in the coming period.

– Strengths and opportunities

The group leader has strong expertise in the aptamer peptide technology and its potential applications. He participates actively in technology transfer activities, in France and other countries.

Further coming patents should have a positive impact on the development of some of the projects.

– Weaknesses and threats

The main weakness is the lack of a clear, well-structured and focused project with assigned people to it.

– Recommendations

The committee is not convinced by the long-term viability of the team and its scientific projects. In any case, a very strong priority should be given to the definition of main objectives for the upcoming period.

Team 7: Chromatin Dynamics and DNA Repair

Team leader: M. Dimitar ANGELOV

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	3
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

This is one of the top teams at LBMC. The team studies the fine structure of nucleosomes and chromatin, using innovative and original techniques that he worked out over the last years in his fruitful collaboration with a group in Grenoble. The recruitment of the PI into a stable position some years ago, after having been a regular visitor to the lab in Grenoble for quite some time, was an excellent choice.

In particular, the PI has to be congratulated for having built up a very strong program on the effect of histone variants on nucleosome structure. He skillfully combines several state-of-the art biophysical techniques to arrive at a detailed picture of these structural effects and how they influence the accessibility of the nucleosome to transcription.

The discovery of the 'remosome', an intermediate in nucleosome remodeling, is a fundamental advance in the field of chromatin biophysics that should receive worldwide attention. Together with the innovative hypothesis that chromatin is held by remodeling factors in a 'fluid state', for which the team presented first evidence, this puts the team into the forefront of international chromatin research.

Finally, the studies of DNA base opening using UV laser photolysis as a probe are highly original; he has managed to develop a very powerful new technique that produces new insights into the mechanism of DNA denaturation which were impossible before.

The publication output of the PI is excellent, both in quantity and quality. All of his publications are in highly visible journals, some of them 'top of the crop' like PNAS. Also, it should be noted that in almost every single publication a new idea is developed; a positive distinction compared to people who merely produce many 'variations on a theme'. During the review period he has directed two PhD theses, which is a good output given the limitation on the number of PhD students per researcher in the French system.

Other than local partnerships, the PI has a number of national and international collaborations. All these partnerships have resulted in high-quality scientific output.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

While PI has not been invited to large-scale international conferences, he has been an invited speaker to two specialized meetings at the reputed Les Houches center. Furthermore he and his team have been present at many international meetings, mostly giving presentations. The Committee considers the team highly visible in this aspect. He is also a member of the Bulgarian academy of sciences.

In addition to the PI and a research engineer, the team consists of one post-doc and three PhD students. His visibility and the contacts should facilitate the recruitment of more exchange scientists from abroad at the PhD student and post-doc level.

The PI has been quite successful in securing grant support for his group. He is member of one Marie Curie network, one FP7 EU network and has obtained several other regional and international grants. A new ANR grant has started in 2009. For the small size of his group, this is excellent.

- Appreciation on the project

The proposed project, largely based on the work of the previous four years, bears great promise. The team plans to expand in the direction of nucleosome remodeling, DNA damage and base excision repair and proteins associated with this processes, and mechanisms of inflammation. It is very encouraging to see how the groundwork laid in the previous evaluation period has led to the definition of several new cutting-edge projects.

The projects are very original and absolutely cutting-edge. The PI combines a large variety of experimental biophysical skills with original thinking at the forefront of biophysics and chromatin biology.

- Conclusion :

  - Summary

All in all, the research of the team is by all standards cutting edge and top quality.

  - Strengths and opportunities

The combination of state-of-the-art biophysical experiments (AFM, EM, laser photochemistry) with forefront biological problems is what gives this team its particular strength. The skills present in this group are a great asset for the other members of the LBMC.

  - Weaknesses and threats

The only concern is that the PI has been hired at a rather late stage in his career; he will reach retirement age after the next four-year period. However, this activity fits in very well with the rest of the laboratory and complements it with

important biophysical techniques. Therefore, care should be taken to find a replacement within the next four years, who can continue a research activity in experimental molecular biophysics and/or chromatin structure. Ideal would be a combination of the two.

– Recommendations

This group should by all means given the opportunity to grow. For strengthening the wet lab side, addition of technical help seems to be important. Given the success in getting funding, the group should be given the opportunity to expand its space if necessary.

Team 8: Chromosome Architecture and Functional Dynamics

Team leader: M. Pascal BERNARD

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	0
N7: Number of staff members with a HDR or a similar grade	0	0

- Appreciation on the results

The PI is a young group leader who has been recruited on an ATIP grant in late 2008. His research focus is on sister chromatid cohesion, heterochromatin assembly and mitotic chromosome condensation using Schizosaccharomyces pombe as a model organism. While the first two topics were part of his excellent training with his former mentor, condensin function is the focus of his current group. The work is of high quality and the topic of great importance. Despite the early stage, the group seems to have gained momentum.

The PI, being at a very early stage of his career, his publication output is necessarily small in quantity, and he has not finished the supervision of theses so far. However, the two publications that he presents have appeared in rather high-level journals such as EMBO Journal and Current Biology and the productivity of the group promises to be high in the next few years. He and his coworkers seem to be very motivated.

The PI has international collaborations with Swedish and British researchers, the latter of which has resulted in a significant publication.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The ATIP award given to the PI is a prestigious grant. The project into which he is embarking is very timely and promises to result in further recognition. Invitations to international conferences will certainly follow.

For a three-person team consisting of the PI, a post-doc and a stagier, the productivity of the team is excellent. Recruiting a post-doc into the team was a good move; the PI should consider to supplement the team by at least one PhD student.

- Appreciation on the project

Existence, relevance and feasibility of a long term (4 years) scientific project

The proposed project is a timely and promising continuation of the work done in the previous two years. The future plans focus on the condensin complex, in particular on its interactions with cellular factors and chromosome association. The strategy, starting from synthetic lethal interactions in S.pombe, is probably unique and appears well thought out and set up. The group leader appears talented and on top of his research.

This project is interesting, important and probably will be productive. Although another highly interesting study on centromeric heterochromatin has been completed and is in press, the lab will not continue in this direction. The ability to focus is an important skill, in particular for the leader of a starting group.

The projects are original and cutting-edge. The planned genetic screen for proteins involved in condensin-mediated association has high potential.

- Conclusion :

  – Summary

The research of the team is of top quality and should be strongly supported.

This is a promising young investigator working on an important and interesting topic. The genes identified through synthetic lethal interactions in S. pombe may provide a niche for him within a very competitive field

  – Strengths and opportunities

The structure-function relationship of cohesin in chromosome condensation is a very timely subject, and the PI has already made his imprint in the field. His plan to use genomic screens to find cohesin interaction partners presents great opportunities.

  – Weaknesses and threats

A risk might be that condensin functions in multiple processes and that genes identified through lethal interactions may be hard to link to a specific molecular function or protein complex.

  – Recommendations

The group should be given the opportunity to grow; the addition of a technician would greatly help in this respect. If the PI is successful in getting further grant funding, lab space should be adjusted accordingly.

Team 9: Nuclear Architecture and muscle differentiation

Team leader: M. Alexandre MÉJAT

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	0
N7: Number of staff members with a HDR or a similar grade	0	0

- Appreciation on the results

The team was created by the end of 2009 and thus the evaluation is mainly based on the future projects. The PI has carried out his Ph.D. thesis at LBMC and continued his scientific work at the NIH.. At both places, the PI has published at least one first author paper of high impact. Thus, he is certainly a promising candidate for a team leader. Moreover, the PI is still very young (32 years old) so that he still has many years to establish himself as a leader in the field.

The number of publications is reasonable and they are all of highest quality. Thus, the track record seems to be good. The Committee would have liked to see even more papers from his post-doc work considering the reputation of the hosting laboratory.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The PI is well recognized for the current stage of his career. He has been invited to several international meetings already.

The PI is at the beginning of his career as an independent group leader, which makes it more difficult to attract collaborators. Compared with his peers, he seems in a better position to be attractive for high-level scientists than many others.

The topic of the research of the PI is attractive for funding agencies and his track record make him certainly a very good candidate for getting funded. The interests of the PI to test potential drugs for the treatment of laminopathies in mouse models can make him also an interesting candidate for funding from industry.

The PI is very well connected to other groups working in the field of laminopathies. This is the case both on the international and national level. In this context, it is also important to note that France is very strong in this particular field.

- Appreciation on the project

The PI proposes three specific aims on the role of nuclear organization for synaptic gene transcription and strategies for the treatment of laminopathies, which cause severe forms of cardiac diseases and muscle dystrophies. One specific aim is a rather long-term project (regulation of AChR subunit expression using FISH) and requires some technological development and substantial financial resources. The project to test the use of cyclosporin A for the treatment of laminopathies in mice is rather straightforward although it requires a substantial number of mice, which are also expensive.

The drug-testing program is feasible for this period. The screening for "factor" that influences synaptic gene transcription requires long-term commitment and is likely to yield results only within a few years.

- Conclusion :

  - Strengths and opportunities

The PI has all the necessary expertise to be successful in the proposed projects. He is also well connected in the community so that the projects seem feasible. He has proven (publications) in the past that he can be successful. The project on the influence of nuclear architecture on synapse-specific gene expression at the NMJ is unique in the field.

  - Weaknesses and threats

The team does not have many collaborations at the current stage. It is therefore impossible to tackle all the questions simultaneously. It is not entirely clear to the Committee, which project will be prioritized. Thus, if the team does not concentrate on tackling fewer projects there is the clear danger that the team will not be successful.

  - Recommendations

Prioritize projects and concentrate on getting enough and very good collaborators. Do not lose too much energy in collaborations that are not at the focus of the team and ask for support to install the imaging capabilities. Overall, the team is highly promising, the team leader is brilliant, has a very good project, is still very young. Thus, the team has all the chances to become a leading figure in the field. It will, however, be important that he has enough support and that he focuses on a few, very promising projects.

Team 10: Neuromuscular Differentiation

Team leader: M. Laurent SCHAEFFER

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	6	5
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3	3
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	2	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	2
N7: Number of staff members with a HDR or a similar grade	1	2

- Appreciation on the results

The research topic of the Team concerns the mechanisms involved in the establishment and maintenance of the neuromuscular junction (NMJ). To approach this, the team employs a multitude of techniques and animal models with the aim to generate a rather complete view of this biological system. The projects concern the role of chromatin modifications, of cytoskeletal adaptors and of growth control genes for the regulation of gene transcription at synaptic myonuclei. One of the focus' is the elucidation of the role of the PI3K pathway. As this pathway is also involved in several "non-NMJ" aspects of striated muscle function, several side projects have also been tackled. For example, the role of mTOR for whole-body metabolism and for the control of heart function has also been initiated. Moreover, the group collaborates with other French teams on identifying mutations in new genes that may underlie neuromuscular diseases. Finally, the team has created smaller subgroups that tackle questions of nerve-muscle communication in zebrafish and Drosophila.

The team has published few but highly significant papers over the last four years. These include one publication in Nature Neuroscience, in The EMBO Journal, The American Journal of Human Genetics and The Journal of Cell Biology. In addition, there are several papers where Laurent Schaeffer signs as a co-author. Finally, several manuscripts are being submitted or are close to submission. The team has also filed a patent for the use of HDAC6 inhibitors for the treatment of muscle atrophy. The team leader has also been invited to a few international meetings.

In summary, the publication record is good, but clearly not outstanding for a group of that size (but see also below). The fact that one patent has been filed shows the thrive of the team to do translational/applied research. This is valued as a plus.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The team leader has been invited to several international meetings, indicating that he has a good visibility.

The team consists of 5 permanent scientists who work more or less independently. Moreover, the team also includes several students and post-docs, some of which being from abroad.

The team is well funded indicating that the team leader is capable of successfully raising funds for his research.

The team is well connected within France but has not obtained funds from European networks. Nevertheless, the team has set-up a few international collaborations with teams outside of France.

- Appreciation on the strategy, management and life of the team

The team leader is also heading the laboratory, thus playing a key role in the local organization of research.

- Appreciation on the project

Many interesting, relevant and feasible projects, all focused around a unifying theme, the neuromuscular junction.

Funding has been secured, the team has a very significant technical support (3 permanent technician positions), but the number of projects is quite high and the resources allocated to each project may be too low to be fully competitive.

The team uses state-of-the art techniques, such as electroporation of muscle in vivo and invests time and manpower in the establishment of new animal models. The team is also at the forefront to further expand the imaging and the mouse animal facilities.

- Conclusion :

  – Strengths and opportunities

The initial focus of the team on the molecular mechanisms that determine gene transcription at the NMJ with the particular emphasis on epigenetic phenomena is clearly unique in the field. The focus has also led to high impact publications. The expansion to examining signalling pathways using the same experimental methods is logic and worthwhile. The team leader has a proven record of being an excellent scientist and the people in the laboratory seem happy and are committed to do good science. The PI has also committed quite some resources to the fostering of young, promising researchers and helps them create their own research program. Although this is a strength and an investment into the future, it also bares some risks (see below).

– Weaknesses and threats

The original focus on the mechanism involved in the regulation of gene transcription at the NMJ has been largely expanded in the past. This is the case for the mTOR project and the project on CKIP. This includes also the addition of new animal models, such as Drosophila and zebrafish to the laboratory. Such a large expansion bears the risk that individual subprojects lose their depth and that the efforts of the team are too diluted to generate enough timely results for high-impact manuscripts. Moreover, the splitting up of the efforts into smaller subgroups bears the danger that not enough critical mass is available to remain competitive. In addition, some of the young researchers may need more guidance and mentoring by the PI so that they do not expand their research too far at such an early stage in their career. The apparent lack of such guidance by the PI may also be due to his strong commitments as a director of LBMC.

– Recommendations

The team has all the requisites to be very successful in the field. However, it really needs to focus in the future on fewer projects so that they can have a stronger impact. The team must also make sure that the manuscripts that are now in the pipeline will be submitted in the very near future. Moreover, it is not certain that the expansion to new animal models is wise as this requires substantial resources and critical mass.

Team 11: Control of Genetic Expression and Viral Oncogenesis

Team leader: M. Pierre JALINOT

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	1
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

This team applies interesting cell biology, genetic and biochemical approaches to understanding the interactions between virus and host proteins. The results have shed light on new cellular regulatory pathways and thus the research has a fascinating basic biology component. However the research is also relevant for the treatment of viral oncologies and displays a promising translational component. In the last years the focus has been mainly on figuring out the function of INT6, a host protein that the group showed in a Science paper from 1996 to interact with viral proteins. In addition the focus has been on further developing inhibitors of HIV and viral oncogenesis and analyzing their mechanism of action. This later project builds on a novel approach, developed in the group in 2004, to identify cell permeable peptide inhibitors that bind a target protein. Very interesting results have been obtained so far, particularly with the peptides that have been identified against HIV replication and to oncogenes of leukemic cells. With this collection of both basic molecular biology expertise and new tools for inhibitor selection, the team is well placed to improve our understanding of host-viral interactions and, in a second crucial step, the group can itself apply this knowledge to develop new candidates for treatment.

The team thus applies original research to a topic of medical importance. This is broad-minded research, which joins a highly coherent basic research program, with an innovative and promising applied research aspect. The success of this team results from its perfect control of the two-hybrid assay which led to sound discoveries in the identification of partners of the

Tax oncoprotein of HTLV-1. The precise control of this technique is also highly relevant for the identification of potential targets for the innovative SHP technology initiated by the team.

The 4 years yielded 10 good quality publications mainly in specialized journals (like Journal of Virology, Oncogene, EMBO Rep., Leukemia). Members of the team presented their results at 4 international meetings. The team trained 4 Ph.D. theses during the past 4-year period. One patent for the SHP technology was obtained.

Clearly this team was able to set up efficient collaborations to complete their objectives. The work concerning the SHP technology was supported by collaboration with various teams (3) which will play a critical role during the next 4 year period. The basic work on Tal1 is also supported by collaborations which were set up for specific developments leading to publications.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The team gave 1 talk over the last 4 years and 3 posters at international meetings.

The team consists of 11 scientists, but few postdocs and students.

Regional and national grants (2 ARC and one ANRS grants) support the work of the team. The project mentions various already established and new collaborations including a future collaboration/partnership with an industrial partner (SPI-BIO).

The partners of this team are localized in Lyon (LBMC), in Paris (Necker Hospital) and Germany (University of Erlangen-Nürnberg). A recent collaboration has been established with laboratories in Australia and in the United States on the DDR studies. In the project, the team proposes to set up a collaboration with the Structural Biology group of the EMBL in Grenoble. But other not yet defined collaborations are suggested to address some specific techniques.

The research accomplished by the team during the past 4 years and the project planned for the next period are all based on 3 major observations previously published by this team i.e. (1) that the carboxy-terminal domain of the Tax protein of HTLV-1 known as the PBM (PDZ-binding motif) interacts with various cellular factors containing PDZ domains, (2) that Tax also interacts with INT6 and (3) that it is possible to prevent HIV-1 replication by using tripartite oligopeptides named SHP that prevent Rev to fulfil its positive action.

This research opens translational opportunities. Several short hybrid proteins have been identified from the technology established in the lab. Studies were undertaken to validate and improve the efficiency of the SHP inhibitory peptides including studies about the mechanism of intracellular entry and as yet unfruitful attempt to improve the binding section of the SHP peptide targeted to Rev by mutagenesis. Finally, the SPH technology was extended to target oncogenes of leukemic cells. Concerning this aspect, an active collaboration with three other teams at LBMC was initiated and planned for future developments. Such applied studies clearly require a precise knowledge about the way the specific targeted oncogene works. Thus, basic studies were initiated (1) about the signal and the post translational modifications leading to degradation of the Tal1 oncogene which was done in collaboration with one team, (2) about how Tal1 and the HTLV-1 Tax oncogene interfere leading to increased activation of both the Tal1 and the HTLV-1 promoters and (3) about how both Tal1 and Tax inhibit hTERT expression, an effect reverted by the viral HBZ factor.

- Appreciation on the strategy, management and life of the team

The PI teaches Fundamental Virology for Master M2 at the Pasteur Institute in Paris and for Master M1 at the Faculté de Médecine in Lyon. He is a member of various research associations and Foundations.

- Appreciation on the project

The proposed future projects are very diverse. The team intends to focus on more developments on the INT6 activities in the DNA damage response, in replication and in the NMD. The second project area concerns the SHP technology for identifying inhibitors of target proteins. Screens against oncogenes of leukemic cells will be started. Any inhibitors will then be followed up. Clear hypothesis, aims, methodology and specific points requiring collaborations are presented in the project.

This project is very ambitious. The question is whether the team made of 11 including 4 trainees will be able to manage such an extended program or whether the team will have grants for hiring new well-trained researchers.

High input techniques are proposed to solve the functional role of INT6 including study of its distribution among different cellular protein complexes, as well as analysis of the effect of its silencing on RNA expression, DNA replication and DNA repair. This is clearly and original project which proposes to use state to the art techniques to solve specific questions.

The SHP projects also uses cutting-edge technologies developed in the team.

- Conclusion :

– Summary

This team has proven its excellence in managing concepts and techniques. The complementarities between basic and applied research is a positive aspect of the team's work.

This team applies interesting cell biology, genetic and biochemical approaches to understanding the interactions between virus and host proteins. The projects combine basic biology with translation, which was valued by the committee. The proposed future projects are interesting, though would benefit from further focusing. Particularly interesting is the SHP work. In this project screens against oncogenes of leukemic cells will be started. These and any new inhibitors will be followed up biologically.

– Strengths and opportunities

The complementarities between basic and applied research is a positive aspect of the team's work. Clearly this team was able to set up efficient collaborations to complete their objectives in the past.

The projects are tailed to clinically important questions. With a collection of both basic molecular biology expertise and new tools for inhibitor selection, the team is well placed to improve our understanding of host-viral interactions and, in a second crucial step, the group can itself apply this knowledge to develop new laboratory candidates for treatment. This is a major strength of the team that should be developed further, but requires focus.

– Weaknesses and threats

One or two researchers should be hired to increase the strength of the team and fulfill their ambitious projects.

A weakness of the team is that few training positions exist (PhD students and post-docs) and the team has given too few presentations at conferences, which would help in spreading the knowledge and impact of the research.

– Recommendations

The committee recommends that experiments be performed to determine the functional significance of the Tax-INT6 interaction in oncogenesis.

In the part of the project devoted to the SHP technology, the study of the in vivo stability, distribution and efficiency of the polypeptides in the mouse model and the proposed collaboration with a specialized team to study these aspects looks critical for the validation of such a technology for future therapeutic treatments.

The team could grow in training positions, diversify in nationalities, and increase international visibility. The scientific projects should be focused.

Team 12: Indolent B-Cell Proliferations

Team leader: M. Gilles SALLES

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	6	5
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	8	6
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	5	5
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	2
N7: Number of staff members with a HDR or a similar grade	4	4

- Appreciation on the results

In the past four years, this team analysed the biological bases of a particular type of chronic lymphomas, called « indolent B-cell lymphomas », which encompass several different types of B-lymphocyte malignancies. They thus identified a new specific type of B-cell malignancy, called «Marginal Zone Lymphoma», they have started analysing the miRNA profile of these malignant cells, and deciphering the mechanisms of B-cell senescence in terms of modifications of telomere length.

This team is thus the first to characterize a new type of lymphoma, although the results are still at the descriptive stage, they will provide in the future new ideas for treatments and/or diagnostics.

This team is the second largest team of LBMC, comprising 22 members, among which half are affiliated to the Hospital section (Praticien Hospitalier). The group is well-established in the lymphoma field, publishing around 15 publications directly stemming from their research in good international journals per year, plus numerous others as collaborations.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The group is well recognised in its field, as evidenced by numerous invitations to international conferences of the head of the group as well as of other clinicians, and by the writing of reviews for international journals.

This team recruits mostly French students with medical background, no clear international recruitment. Half of the PhD students trained are MD/Ph'D, which is an important training contribution to promote science-cantered medical research.

The group obtained several funding from participation with industrial partners.

This team is actively participating in several international consortiums on lymphoma.

- Appreciation on the strategy, management and life of the team

The team appears well managed on the Lyon-Sud campus, but better connections between team members and the ENS campus should be actively promoted. Exchanges appear limited up to now essentially to the sharing of the imaging facility.

Several members of the group participate in teaching for medical students and the team trains MD/PhD students. This is beneficial for the rest of LBMC (non Lyon-Sud location), where some medical students eventually end up working.

- Appreciation on the project

The projects for the next four years directly stem from their previous results, and will be centred on the analysis of miRNA, the identification of possible tumor suppressor genes, and the molecular alterations of intracellular signalling pathways in B cell malignancies. The projects are of great importance for future understanding of B lymphoma pathology and potential identification of new targets for therapy. The group has the right expertise and environment to successfully achieve their objectives.

- Conclusion :

  - Summary

This team provides a good connection with medical students, clinicians and translational research to the LBMC.

The group is very productive, and has provided important contributions for characterization of lymphomas.

It is the biggest group of LBMC in the Lyon Sud location, and together with the Delprat team (already present) and future arrival of the "Oncovirology and Biotherapies" team should create a strong pole of clinically-oriented research.

  - Strengths and opportunities

Strong connection with the clinics. Abundant production. Good training environment for MD/Ph'Ds. Involvement in several collaborations

  - Weaknesses and threats

The research performed in the group has led to the description of a new form of lymphoma. The data generated were so far mainly descriptive, and it will be important to provide, as planned by this team for the next 4 years, more mechanistic informations on the pathology, to allow for future diagnostic and therapeutic applications

  - Recommendations

To obtain an impact that is commensurate to the quality of the knowledge accumulated so far and to the opportunities offered by the association to the fundamental research campus of ENS, it would important to improve the scientific exchanges between the lab members of the Lyon Sud team and the ENS teams. This should facilitate the transition from descriptive to mechanistic studies, which should allow the team to enhance very significantly the importance of its contribution.

Team 13: Oncovirology and Biotherapies

Team leader: M. Eric WATTEL

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	2,3
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	3
N7: Number of staff members with a HDR or a similar grade	0	2

- Appreciation on the results

The research developed by this team is critical for the understanding of the early molecular and cellular events leading to transformation and onset of tumor development in vivo. A better knowledge of these events should improve the diagnosis of preleukemic states and enable the development of ways to treat leukemia, which are among the specific aims of this team.

Eight publications directly attributable to the team in journals with good (Virology, Retrovirology, Haematologica) or very good impact factors (J Clin Invest in 2006), including one review article in 2009 and one publication in press were published since 2006. In addition, members of the team are included as co-authors in six other publications.

This team intends to join the LBMC in 2011 and to work in close collaboration with another team at LBMC on the development of SHP peptides designed to target factors identified by the team as deregulated in various types of leukemia.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The PI presented 4 communications as invited speaker to national and international meetings since 2006. The team members also participated to a number of international conferences to which they presented 7 oral and 4 poster communications.

The quality of the previous studies and the importance of the objectives for the treatment of leukemias should favour in the future the recruitment of researchers and Ph.D. students.

The quality of the previous studies and the importance of the objectives for the treatment of leukemias should favour fund raising at LBMC and specifically the participation of the team to an industrial cluster.

Participation to networks or active collaboration is not mentioned.

This team was the first to clearly demonstrate the role of clonal expansion of infected but not immortalized HTLV-1 CD4+ and CD8+ T lymphocytes in the pathogenicity of this virus. The discovery that efficient cell cycling of infected CD4+ cells accompanied by Tax-mediated induction of genomic instability through a variety of mechanisms including alteration of telomerase activity is the basis of future developments of this team.

- Appreciation on the strategy, management and life of the team

Both the PI and a senior member of his team have teaching activities. In addition, the PI acts as a physician at the Hospices Civils de Lyon. The team trained 9 Ph.D. students since 2006 among 6 have completed their thesis.

- Appreciation on the project

The project of this team is to decipher molecular mechanisms of malignancies in two types of acute leukemias : lymphoid (ALL) and myeloid (AML). In preliminary analyzes, they have identified a few candidate genes, for further analyzes, including hTERT, WT1 and TRF2. Their plans is, at a basic science level, to analyze telomerase activity (linked to hTERT expression or regulation), and its role on RNA processing, and, as a more applied outcome of their work, to use WT1 and TRF2 as new therapeutic targets in acute leukemias.

The approaches, goals, and questions of this team seem highly complementary to those of another group of the LBMC at the South-Lyon site, and their arrival in this lab will possibly create strong collaborations. They also already collaborate with the team of "Control of Genetic Expression and Viral Oncogenesis" in LBMC, using their SHP-technology in leukemia cells.

- Conclusion :

– Summary

To summarize, this team has collected a great knowledge about the molecular events of the preleukemic state in several cases of leukemia. They intend to develop and to apply this knowledge for the prognosis and the therapeutic treatment of leukemias in the context of the LBMC. The proposed studies involve the analysis of the transcriptome and proteome characteristic of early steps in tumorigenesis, which are adequate for the identification of diagnostic and prognostic markers. This research should enable to reach the identification of putative therapeutic targets for the treatment of leukemia.

– Strengths and opportunities

By joining the LBMC, this team will bring in its medical and clinical expertise, which will be of great benefit for the collaboration with other LBMC teams.

– Weaknesses and threats

The future location of the team at Lyon Sud, although potentially beneficial for interactions with other groups working on lymphomas, is a potential threat for an efficient collaboration with the teams at the ENS.

– Recommendations

The committee recommends that the scientific collaboration is reinforced by regular meetings and exchanges of lab members between the Lyon Sud and the ENS teams.

Team 14: Dendritic cells and Immunoplasticity

Team leader: Ms Christine DELPRAT

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	2	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	4
N7: Number of staff members with a HDR or a similar grade	1	1

- Relevance and originality of the research, quality and impact of the results

The team is very recent at LBMC and during this 8-month period, it was busy with the setting of collaborations, technical environment and to the training of students. The scientific achievement is presented as 4 abstracts which have been selected for oral presentation at meetings in 2009 and are the basis for manuscripts in preparation. This work looks coherent and of good quality. The team's project to analyse the effects of IL17 on the biology of dendritic cells in various human pathologic situations (Langerhans cell histiocytosis, tuberculosis, BCG treatment of bladder cancer) is very original since the numerous groups working on IL17 throughout the world are for the vast majority focusing of its effects on T cells: this team is thus in a leading position in the field.

Nine publications with members of the team as first or last authors have been published between 2006 and 2008, i.e. before this team started at LBMC. These publications are of high quality, including one outstanding publication in Nature Medicine, which is the basis of the part of the project on Langerhans cell histiocytosis. The team is too recent to have published yet, but the ongoing results will surely give rise to several very interesting publications in the next few years.

The leader has co-supervised 3 theses since 2005.

This team has established collaborations with national researchers for most of their centers of interest and with national and international laboratories (in Italy, Holland, Sweden and Paris) for the collection of clinical samples with Langerhans cell histiocytosis. The presence of a Ph.D. student co-supervised by a team at the Karolinska Institute proves the stability of this collaboration.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The leader of the team was invited at 12 international conferences including two organized by pharmaceutical companies. She was elected as junior member of the Institut Universitaire de France in 2008 and she is a member of the national scientific council of INSERM. She is also acting as supervisor for several international and national grants. Other members of the team obtained several awards and organized scientific meetings in Lyon.

The contact established with foreign laboratories favoured the recruitment of students: 3 out of 4 PhD students are coming from foreign countries (Sweden, Lebanon and Italy) and two of these students are co-supervised by the team.

The team obtained several grants from regional, national and international associations since 2004. The reported funding for years 2009 to 2013 is 352 k€. This team appears thus successful in raising research grants.

The team participates to an international scientific network devoted to the collection of clinical samples. In addition, this team established a number of national collaborations to achieve their scientific objectives.

The research interests of this team focus on the role of the IL17A cytokine and dendritic cells in the immunopathology associated to infection with Mycobacterium and with the disease Langerhans cell Histiocytosis. They determined that dendritic cell fusion leading to aggressive granuloma producing IL17A is a common pathology of these two diseases.

- Appreciation on the strategy, management and life of the team

The PI as well as members of the team participate to the teaching at Lyon 1 University. The leader is also member of several committees for the organization of the teaching at the ENS.

- Appreciation on the project

The project includes 3 main aspects, which are each clearly attributed to defined members of the team. The first aim uses electron microscopy to check abnormal events occurring in the cytoplasm of monocyte–derived IL17A-secreting dendritic cells (DC) from Langerhans cell histiocytosis (LCH) patients. These samples will be collected thanks to the international network established by the team. The final aim of this part of the project is to test whether DC from LCH patients are susceptible to chemotherapeutic treatments including anti-IL17A. The second aim will study the mechanism of IL17A induction following infection with Mycobacterium and the subsequent cell fusion and formation of granuloma. The third aim is based on their observation, by transcriptome analysis, that IL17A affects lipid metabolism of myeloid cells. They intend to study the production of lipid mediators of inflammation as well as expression of miRNA involved in lipid metabolism. This part of the project involved the study of the lipid profile in transgenic mice expressing IL17A in DC. These studies are all targeted to the discovery of tools for care. This project appears relevant and feasible in the next 4-year period.

- Conclusion :

– Summary

The research program of this young team has clear impact on human health aspects and proposes original approaches all targeted to uncover tools to treat the two diseases studied.

– Strengths and opportunities

Regional, national and international foundations fund the research program of this team.

The team is supported by a good network of collaborations, including foreign laboratories and has most of the expertise to solve the questions addressed in their research project.

The team includes foreign students.

The part of the project devoted to the study of lipid metabolism will be done in the frame of a collaboration with a laboratory with expertise in this domain.

– Weaknesses and threats

The project on lipids requires a strong collaboration with specialists in this domain. The team leader has mentioned that such a collaboration is under way, but its efficiency will have to be demonstrated.

– Recommendations

This team needs permanent technical staff.

Note de l'unité	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	A+	A+

Team 1: Genetics of Intra-Species Variations

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	non noté	A+	non noté	A+

Team 2: Plasticity and Evolution of cell division

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	non noté	A+	non noté	A+

Team 3: Cellular and Organismal Aging

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	non noté	A+	non noté	A+

Team 4: Epigenetic regulation in development

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	non noté	A

Team 5: Apoptosis and Neurogenetics

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	non noté	A

Team 6: Differentiation and Cell Cycle

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
C	C	A	non noté	C

Team 7: Chromatin Dynamics and DNA Repair

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	A+	A+	non noté	A+

Team 8: Chromosome Architecture and Functional Dynamics

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	non noté	A+	non noté	A+

Team 9: Nuclear Architecture and muscle differentiation

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	non noté	A	non noté	A

Team 10: Neuromuscular Differentiation

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A+	non noté	A+

Team 11: Control of Genetic Expression and Viral Oncogenesis

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	non noté	A+

Team 12: Indolent B-Cell Proliferations

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A+	A+	non noté	A

Team 13: Oncovirology and Biotherapies

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	non noté	A

Team 14: Dendritic cells and Immunoplasticity

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	non noté	A+	non noté	A+

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Le Directeur général de l'ENS de Lyon

à

Monsieur Pierre Glorieux
Directeur de la section
des Unités de recherche
AERES
20, rue de Vivienne
75002 – PARIS

Lyon, le 26 mars 2010

Monsieur le Directeur,

Je vous remercie de l'envoi du rapport d'évaluation du laboratoire Biologie Moléculaire de la Cellule UMR 5239, comportant un avis globalement très positif. Le rapport d'évaluation représente un outil précieux pour le pilotage et le positionnement de l'unité. Le Comité a formulé quelques recommandations qui feront l'objet de toute l'attention de l'Ecole et de l'UMR.

Le Comité a souligné le dynamisme de l'Unité et sa capacité à recruter de jeunes chercheurs mais il craint que le faible nombre de chercheurs seniors ne pénalise la réussite de l'Unité. L'ENS a toujours soutenu, avec succès, cette politique de recrutement de jeunes chercheurs extérieurs au site et elle soutiendra l'unité pour permettre la maturation de ces équipes juniors et la réussite de cette politique.

Le Comité a noté un manque de transparence qui s'explique par la mise en place depuis plusieurs années d'une gestion commune de ressources matérielles et structurelles partagées entre les quatre unités de Biologie au sein de l'ENS de Lyon, gestion commune dont l'origine relève d'une demande des responsables de ces unités. Une réflexion sera conduite durant la période quadriennale pour évoluer vers une meilleure intégration de ces différentes unités de Biologie au sein de l'établissement.

Vous trouverez, ci-jointe, la réponse de Laurent Schaeffer, Directeur du laboratoire.

Je vous remercie ainsi que les évaluateurs pour la qualité de leurs travaux et vous prie d'agréer, Monsieur le Directeur, l'expression de ma sincère considération.

Olivier FARON

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Réponse de l'unité Laboratoire de Biologie Moléculaire de la Cellule – UMR 5239.
Directeur : Laurent Schaeffer

Overall, the work of the visiting committee was appreciated, and its competence to evaluate the activity of the laboratory was recognized.
We would like to comment a few points raised by the committee concerning the policy of the laboratory.
Several times, the complexity and lack of transparency is mentioned. Although some organizational points might indeed be complicated by the co-existence of 4 UMR of biology at the ENS, the tightness of the schedule and the absence of visit of the laboratory (although it was proposed) probably also contributed to the feeling of the committee. As we discussed with the AERES committee, the common wish of the LBMC and of the ENS is that at the end of the coming period, the four laboratories should be united in a single biology institute, with distinct departments. This should be beneficial for the visibility of the laboratories, and should limit the heterogeneity in the evaluation processes by the AERES, at least at the local level.
The committee mentioned as a positive point the recruitment of several young and dynamic groups by the LBMC, but is logically afraid that the lack of senior groups could be detrimental to the laboratory. First, among the eight groups recruited, three are senior (groups 7, 12 and 13). Second, it has always been the policy of the LBMC (that was created 20 years ago) to favor the emergence of young dynamic and imaginative group leaders. This policy allowed the laboratory to be at the origin of most of the laboratories of the Gerland area, which were created from teams initially hosted at the LBMC. The LBMC thus rather defines itself as a generator of successful senior groups than as a recruiter of senior groups. Finally, the recruitment of international senior groups cannot result from the initiative of a single laboratory of the size of the LBMC that does not have the financial supply for such operations, and should rather result from actions at the local and national level.
The committee regrets the lack of collaborations among LBMC members and within the ENS. We do not agree with this statement. There is not a single group in the project of the LBMC, which is not collaborating with at least another one. The fruitful interactions between the teams greatly contribute to create the pleasant and dynamic atmosphere that was observed by the committee.
The committee also advises the LBMC to favor interdisciplinary research. The LBMC has been the most proactive laboratory to develop interdisciplinary projects at the ENS. The interdisciplinary laboratory Joliot Curie was created at the initiative of a group leader of the LBMC and is currently directed by another group leader of the LBMC. The recruitment of group 7 is also highly illustrative of our will to favor such research. Finally, the recently recruited young group 2 has just obtained important funding from the Human Frontier Young Investigator Programm on a highly intersdisciplinary and intercontinental project.

Lyon le 26 mars 2010,

Laurent Schaeffer