LBME Laboratoire de biologie moléculaire eucaryote

Rapport Hcéres

▶ **To cite this version:**

Rapport d'évaluation d'une entité de recherche. LBME Laboratoire de biologie moléculaire eucaryote. 2010, Université Toulouse 3 - Paul Sabatier - UPS. hceres-02033883

HAL Id: hceres-02033883

https://hal-hceres.archives-ouvertes.fr/hceres-02033883

Submitted on 20 Feb 2019

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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 Eucaryote

From the

Université de Toulouse

CNRS

May 2010

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et de l'enseignement supérieur

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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

May 2010

Research Unit

Name of the research unit : Laboratoire de Biologie Moléculaire des Eucaryotes

Requested label : UMR

N° in the case of renewal : 5099

Name of the director: Mrs Michèle CAIZERGUES-FERRER

Members of the review committee

Committee chairman :

Mrs Annick HAREL-BELLAN

Other committee members:

Mr Witeck FILIPOWICZ (Friedrich Miescher Institute, Bale, Switzerland)

Mrs Cécile ROCHETTE-EGLY (IGBMC, Strasbourg)

Mrs Françoise STUTZ (Geneva University of Sciences, Switzerland)

Mr Marc TIMMERS, (University Medical Center of Utrecht, NL)

Mr David TOLLERVEY (Wellcome Trust Center for Cell Biology, Univ. Edinburgh, UK)

Committee members suggested by CNU, CoNRS,

Mr Olivier COQUERET, CNU representative (Centre de lutte contre le Cancer, Angers)

Mr Olivier JEAN-JEAN, CoCNRS representative: (University Paris VI, Paris)

Observers

AERES scientific advisor :

Mrs Catherine DARGEMONT

University, School and Research Organization representatives:

Mr Bernard MONSARRAT, University Scientific council (CS)

Mr Alain MILON, University Direction

Mr Bertrand DAIGNAN-FOURNIER, InSB CNRS

Report

1 • Introduction

- Date and execution of the visit :

The visit took place on December 17 and 18. The first day was devoted to presentations by the lab. A general presentation of the past was given by the current director and the future was presented by the proposed future director. After that, each group leader gave a 50 minutes presentation including discussion. At the end of the day, one hour was devoted to discuss the groups individually (strength and weaknesses). On the second day, the committee split to meet with the students, the scientists and the technicians of the lab. After that, the committee reconvened to meet the University representative. Finally, the committee met in private to discuss the lab in general and rank the different groups.

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

The Unit is located within the Paul Sabatier University Campus. The building, however belongs to the CNRS.The unit has a long history: it was first created in 1992, as a spin off of a CNRS research center created in 1972. The scientific focus is on RNA biology on one hand, and on chromatin and gene regulation on the other hand.

- Management team :

The head of the Unit is exchanged every 4 years. The lab director is helped by a lab council that meets on a regular basis. There will be a two years transition period during which the current director and the future director will share responsability, which the committee finds a very smart organization.

- 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)	5	6
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	18	>20
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)+ 2.7 past	18	
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	15,1	16,2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	4,5	
N6: Number of Ph.D. students (Form 2.8 past – 2.7 future) of the application file)	14	>5
N7: Number of staff members with a HDR or a similar grade	11	>18

Notes:

1. For researchers with teaching duties: One assistant professor has been recruited in June 2009, two positions are open for the LBME in 2010. 2 retirements in 2012
2. For full time researchers from research organizations : one retirement in Dec 2012
3. For HDR:

2 • Overall appreciation on the research unit

- Summary :

This lab is composed of 8 groups, 70 persons, 23 staff scientists, 16 technicians, 14 post-docs and 15 PhD students. The general focus is on exploring the biology of non-coding RNAs, from biosynthesis to physiological functions. A second topic is on chromatin structure and its impact on gene regulation. The two topics are tightly interconnected, and some groups are actually working on both aspects (for example, the group working on imprinting of small RNAs). In the past 4 years, the lab reported important results including: 1) the role of specific RNP proteins and interaction with RNA processing (splicing etc); the discovery of links between U1 RNP and with human diseases and interactions between imprinting and non coding RNAs and nucleosome positioning. Scientific productivity is very good, with numerous papers in high quality journals. The lab is attractive, with 12 new staff scientists and 2 new associate professors recruited in the last 4 years. It is well integrated into scientific networks in Toulouse, and it has strong connections with the University. It is an active part of a large merging project that will associate all biology labs in Paul Sabatier University (about half of biology labs in Toulouse). This new entity will be under the responsibility of the current director of the LBME.

Several young groups have emerged, from inside or outside the lab. The lab has been actively involved in training students (with 22 PhDs obtained in the past 4 years). Scientific activity is good, with regular meetings, seminars and an annual retreat. The lab is generally well funded. Finally, the lab is extremely well managed, with common equipments and resources.

- Strengths and opportunities :

The general quality of the science is very good. This is a very focused lab, which appears to be a strong entity per se. Few centers in Europe have such a concentration of high-quality RNA research. Moreover, the projects of the different groups have an extremely good potential for synergy. There is also a common interest in developping new sophisticated technologies.

It is a young lab, not only with young personnel but also with several new young groups. It is obvious that this lab offers good opportunities for more junior scientists to start their own projects and create their own group.

The lab is well integrated into Toulouse scientific networks, particularly within the University.

The lab provides a very positive atmosphere, and the personnel appear very confident in the future of the lab. This reflects an excellent management.

Finally, the future integration into a large consortium of labs within the University is a good opportunity for the lab to increase its visibility at the international level and was seen as a very positive move by the committee.

- Weaknesses and threats :

This lab is doing an excellent job in general, but the committee feels that it does not have the visibility that it deserves, in particular at the international level. The commitee noted that, despite the fact that many PhDs were obtained in the lab in the recent years, the ratio between students and staff scientists is rather low (15 students for 23 staff scientist). This is also true for Post-docs (14 post-docs). Moreover, there are not many foreigners among students and post-docs. The funding is also predominantly national, and in particular, the lab should make more efforts to obtain support at the international level from European Union (FP7, ERC) or from other sources (ESF etc.), and be more integrated into international networks.

Finally, the committee feels that there is a clear need for more technical posts. The committee, in particular, noted an obvious weakness in technical help provided by the University (only one technician, even though there are 6 University staff scientists in the unit).

- Recommendations to the head of the research unit :

The lab should seek more international collaborations, and participate in more EU NETWORKS.

- 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	
A3: Ratio of members who are active in research among permanent researchers [(A1)/(N1 + N2)]	26>26 92%
A4: Number of HDR granted during the past 4 years	2
A5: Number of PhD granted during the past 4 years	22

3 • Specific comments on the research unit

- Appreciation on the results :

The lab is one the few European labs in which there is such a concentration of good RNA research. It is well known in the domain. The main directions concern ribosome biosynthesis, small non-coding RNA biology and function, chromatin structure in relation to gene or small non-coding RNA expression. A wide variety of approaches are used from single molecule to genome wide or in vivo studies, with a specific emphasis on imaging and single molecule technologies. In general the science produced in the lab has a good to excellent impact in the field.

Among the 121 papers published by lab members during the last 4 years, 61 were “homemade” scientific papers published in very good to excellent journals (Mol Cell Biol, EMBO J); with 88% of them having an impact factor greater than 5. Nine were invited reviews or book chapters.Twenty PhD Theses have been defended. The lab members have participated in various scientific public manifestations such as the “Fête de la Science”.

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

Members of the lab are well recognized at the national level. Two staff have been awarded an IUF position, and several members of the lab participate in various national selection commitees.

There is also a good recognition at the international level. Some members of the lab are regularly invited to international conferences. Two members have recently obtained european awards (YIP or EMBO membership).

Members of the lab are actively participating in teaching and training students at various levels, and 22 PhDs have been defended during the last 4 years. The lab is attractive at the national level, and 12 new staff scientists have been recruited in the last period (which is quite notable given that these recruitments correspond to a highly selective procedure). In addition, two new associate professors have also been hired, demonstrating that the lab is supported by the University. However, there are too few foreigners among the students and post-docs, and the international attractivness appears insufficient. Part of it might be due to the geographic position of the lab (Toulouse) and to the general lack of attractivity of the French research system in general. However, the committee feels that this parameter could be dramatically improved by greater efforts among the group leaders to integrate into european and other international networks.

The main support of the lab comes from CNRS, but the proportion of external grants is increasing. There is a good level of funding from ANR and from charity associations. There is, however, too little international funding, in particular from EU. It is true that research in this lab is essentially basic and not application oriented but this does not preclude funding from the EU. Especially, the lab could profit from the recently increased interest in non-coding RNAs in the field.

The lab is well integrated at the national level in various networks (supported by ANR in particular). Some lab members have specific international collaborations, but generally there is too little participation in broad networks at the european level.

This is a very basic research lab in general. A few patents were, however, filed in the last 4 years.

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

The Unit is managed by the director, helped by a lab council which meets regularly. The CNRS funding is used for common purposes. In addition, 10% of each grant helps getting common new equipments.

External and internal seminars are regularly organized. In addition, the lab is organizing an annual retreat. New projects seem to be greatly encouraged, and 2 new groups have emerged in the last 4 years.

Members of the lab are generally involved in teaching and organization of teaching. The lab is actively contributing to local research networking, both at the level of technological platforms (imaging in particular) and at the level of creating strong local scientific links, through the generation of a large lab consortium within the University.This consortium will be headed by the current head of the lab.

- Appreciation on the project :

The projects presented by the lab were generally sound and solid. The potential of young scientists is very high, and the projects proposed by the different groups provide excellent opportunities for collaborations and synergy.

The resources are extremely well managed. The CNRS fund is devoted to common products and equipment. In addition, 10% of all grants are used for purchasing new equipments of general interest for the lab members.

The projects of the lab are a rather well balanced mixture of good, solid and straightforward research projects, along with some cutting-edge and more risky projects. The proportion of this last category could, however, be slightly increased.

4 • Appreciation team by team and/or project by project (to be pasted as many as needed)

Team 1 : Chromatin and gene expression

Team leader: Mrs Kerstin BYSTRICKY

- 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-*2(2010)*
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) + 2.7 past	3	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0.8	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.8 past – 2.7 future of the application file)	2	1-2
N7: Number of staff members with a HDR or a similar grade	1	2

- Appreciation on the results :

  – Relevance and originality of the research:

This is a 7-persons team, which has made many interesting and noted observations in nuclear dynamics and epigenetic gene regulation by using two model organisms, S. cerevisiae and a well-characterized mammary tumor cell culture system. The team is addressing the topic of chromatin dynamics in relation to gene activity. This topic is very timely and relevant and the group is developing new methods to study chromatin dynamics in living cells. The two model systems have specific advantages: in yeast cells, the genome can be readily modified, and in human cells, the activity of the estrogen receptor can be modulated by ligands. The performed research is original and addressing important questions in contemporary chromatin research.

In yeast, the main objectives are to determine the parameters of chromatin compaction and flexibility in living cells using live microscopy (Fluorescent Repressor Operator System, FROS) coupled to a lab-on chip system that they developed in collaboration with another group in Toulouse. The goal is also to analyze distances between the mating type loci under different circumstances in order to gain better insights into recombination.

Nuclear dynamics and epigenetic gene regulation in breast cancer cells, is developed essentially by the PI (recruited in 2004, PI since 2007), a recently (2009) promoted professor. The main objectives are to identify the epigenetic marks responsible for estrogen receptor target genes silencing and to classify these genes according to their sensitivity to chromatin modifying agents. A strong and novel point is the development of a "Combo-Fish" method in order to investigate whether the position of the ER-target genes vary in ER negative cells and in the presence of HDAC or DNA methyltransferases inhibitors.

The direction of the group has been modified during the last four years subsequently to the death of the previous group leader and the recent recruitment of a young researcher. The number and quality of publications of the previous group have been very good. The output of the current group should be regarded as reasonable to good for a young group leader and taking into consideration the small size of the team and its recent reorganization. The permanent researchers have established productive collaborations with leaders in the field of chromatin dynamics. Three Ph.D. theses were prepared and these all relate to the work of the previous group leader.

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

The group has established collaborations with leaders in the field. In addition, collaborations have been setup with local and national partners. It is too early to tell whether they will be successful in maintaining and extending the (inter)national collaborations. The issue of further developing the (inter)national profile of the group requires attention of the group leader. This can be achieved by attending the most important international meetings in the field of nuclear dynamics and chromatin/gene regulation.

The group leader has received invitations from national and international (Spain, USA) laboratories. The recruitment of an additional young scientist allows maintenance of the breath of the research (yeast and mammalian cells). The current composition of the group allows carrying two experimental systems forward, but the basis for this is rather shallow. The group has been successful in recruiting new PHD students and post-docs.

The research and the quality of the group should make the group competitive in raising more external funding. Opportunities offered by young investigator programs should be exploited. At present only one small collaborative project (k€ 12) with another university group is running.

- Appreciation on the project :

The team composition for the coming period is good with sufficient expertise in the different areas. The research plans are focussed and realistic. The development of the Lab-on-Chip system sounds promising. Recruitment of two PhD's with complementary interest and expertise should exploit the scientific potential offered by the FROS system. This can yield unprecedented insight into the 3D organization and dynamics of chromatin in living cells. This should be considered as cutting-edge science in this area. Studying histone variants in gene regulation in mammalian cells is a very good choice.

In order to allow the group leader to develop her research it is important that she will not be overloaded with teaching duties. The contribution of 100 hrs to the university teaching effort seems adequate. Increasing the teaching load bears the risk of restricting research development.

The proposed research of in vivo chromatin dynamics and histone variants is very timely. The approaches taken are (highly) original and the live-cell imaging approach should be considered as 'cutting-edge' science. The "Combo-FISH" sounds interesting, but bears a high risk.

In general, the group is in a good position to make important contributions to the chromatin and gene regulation field. The feasibility of this research extends beyond the 4-year period. Based on this and provided that the proposed research bears fruit, the Institute could consider further strengthening the composition of the group.

- Conclusion:

  - Summary

This group has good prospects. This is a young team with a good potential to make important contributions to the understanding of chromatin dynamics in relation to gene regulation. Findings in this area will be relevant for other nuclear processes and offer good opportunities for collaborations within and outside of the LBME. The threat for the group is that dispersing the efforts over two very different experimental systems might diminish the productivity. At the same time working in different systems can also be considered as an opportunity.

  - Strengths and opportunities:

The team has a longstanding expertise in the field. Its project is built on a robust corpus of interesting observations. The group leader develops promising 3D and high resolution imaging techniques (FROS, FISH, Combo-FISH) in order to follow genetic loci and nuclear architecture. Especially the Lab-on-chip approach is a novel and exciting development.

The yeast project is performed in collaboration with an American group and a group in Toulouse. It has been selected by the Scientific Operations of the University Paul Sabatier at the beginning of 2009. Since 2007, when the young researcher joined the team, the project concerning the epigenetic modifications involved in the silencing of ER-target genes seems to have substantially expanded. In addition, promising collaborations with a group at the EMBL Heidelberg and with the team of the institute have been initiated.

  - Weaknesses and threats

Increasing the size of the group will be necessary to reach the highest achievement standards. The recruitment of PhD students is required to develop both the yeast and breast tumour projects. In line with this, the recently recruited young researcher has to obtain an HDR as soon as possible as well as to increase the number of her publications. A threat for the group is divergence of the yeast and ER-breast cancer projects. Some of the approaches in the ER-breast cancer project are also followed by much larger (inter)national labs and the group is not in a good position to effectively compete with these labs.

  - Recommendations

The financial supports of the team appear to be rather limited for the future years. The team leader should apply for new grants and for this the ER breast cancer link offers good possibilities. The group should strive to find more synergies between the yeast and the ER-breast cancer project.

Team 2 : C/D small RNAs, micoRNAs and genomic imprinting

Team leader: Mr Jérôme CAVAILLÉ

- 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 (until 2012)
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) + 2.7 past	4	>1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2,5	2,5-2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	**?**
N6: Number of Ph.D. students (Form 2.8 past – 2.7 future of the application file)	2	>1
N7: Number of staff members with a HDR or a similar grade	1	2

- Appreciation on the results

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

This group includes 3 staff scientists (one due to retire in 2012), 2 post-doctoral fellows, 2 PhD students, 2.5 permanent engineers (one due to retire in 2011), and 1 short-term engineer.

The group's main interest is in the relationship between genomic imprinting and small RNAs. The group is more specifically interested in genomic loci encoding small non-coding RNAs, including snoRNAs and microRNAs,which are submitted to parental imprinting.. The group has contributed quite a large number of important observations on the biogenesis, localization and function of snoRNAs and microRNAs, using technologies ranging from state-of-the-art cellular imaging to in vivo gene deletion in knock-out mouse. In addition, the group is also involved in more clinical studies, addressing the role of miRNAs in Anaplastic large cells lymphoma (ALCL). The research carried out by the group is of top quality, highly original, and very competitive. It brings important novel information about the role of gene imprinting in general, and also addresses very timely questions regarding biogenesis, cellular localization, and function of snoRNAs and miRNAs.

The group has a very good publication record. In the last four years, the group has contributed 3 papers in J Cell Biol, Mol Biol Cell and Nucl Ac Res, 4 collaborative papers published in Development, Curr Biol, Nucl Ac Res, and Nat Struct Mol Biol., as well as 3 reviews and/or book chapters. In addition, a young scientist who recently joined the group had 7 publications from his Post-Doc, including papers in Science, Cell, and Curr Biol.

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

The team belongs to the internationally recognized leaders in the fields of genomic imprinting and function of small RNAs such as snoRNAs and miRNAs. This is supported by a considerable number of invitations of the group leader to present seminars in France and abroad, and to give invited talks at international meetings. The group has many national and international collaborations, which have already resulted in a number of joint publications. It should be stressed that some of the experimental approaches taken by the group (e.g. deletion of huge genomic imprinted regions in mice, and high resolution imaging and in situ hybridizations) are technically very demanding, and do not immediately result in publications.

The members of the group are regularly invited to international meetings in France and abroad, the group leader is internationally recognized as a leader in the field. He is an EMBO YIP. He was able to raise substantial funding from various agencies (ANR, EU, and charities such as ARC and Ligue contre le Cancer). Two PhD Thesis were defended during the last 4 years.

A very bright young scientist coming back from a very succesful post-doc abroad joined recently the group, testifying to the group's attractivity at least at the national level.

This group is one of the few groups in the lab which participated in 2 European networks in the last period.

The group has filed one patent application in the last 4 years, which, given that this group's research is highly basic, is very good.

This is a very dynamic team, engaged in attractive and competitive research. All the projects carried out in the lab are highly overlapping, creating the opportunity for internal collaborations, exchange of expertise etc. Management of the team is very good. The attractivness of the team is further supported by the fact that several students carried out their internships in the group over the last review period. State-of-the-art technologies (particularly imaging and in situ hybridization methods) are of great use also for other members of the lab. The team has also contributed to dissemination of knowledge by giving public lectures aimed at lay people.

- Appreciation on the project

Most of the future projects represent logical prolongation of previous and current work. The group will: (1) Explore the phenotype of mice in which an imprinted miRNA cluster is deleted; interestingly, the mice show an "abnormal behaviour" that raises very interesting questions about a role of imprinted small RNAs in brain function; (2) Address functional and evolutionary relationship between the presence of repeated small RNA sequences and imprinting; (3) Explore the early steps of small RNA processing in particular by addressing the function of DROSHA associated proteins using a combination of imaging and genetic approaches; (4) Test an original hypothesis stating that most miRNA "targets" are only reservoirs which function as miRNA competitive inhibitors; (5) Address the function of piRNAs in development by analyzing a species (sea anemone Nematostella vectensis) with asexual reproduction, thus uncoupling sexual reproduction and development. These are all very challenging and competitive projects. They are feasible and their attractiveness should help to recruit high quality collaborators, both inside and outside.

The 3 first projects listed above are both original and straightforward, and represent timely, logical and justified continuation of previous research. The two last projects are newer and thus more risky, which comes to a rather well balanced ratio. Since, however, the two risky projects are proposed by the young scientist who joined the group recently, the committee would suggest that he additionally joins or initiates a less risky project as a backup in a case his new ambitious projects do not lead to the expected results.

– Summary

This is a very good group, with an original project, vey good past accomplishments, and a very high potential for the future. The group has an excellent publication record, is involved in many national and international collaborations and gets strong financial support from both national and international sources.

– Strengths and opportunities

The group leader was a pioneer in the field of imprinting and small RNAs. The work achieved recently is very solid and original. Technologies are up-to date. The publication record is very good. The Group leader is internationally highly recognized in the field of imprinting and small RNAs. In general, the projects are innovative, well designed, and solid. The group is well funded.

– Weaknesses and threats

The two projects proposed by the young, very promising (and already highly successful during his post-doctoral research) scientist who recently joined the group are challenging and very original. They are however risky, and he might consider getting in parallel also involved in less risky projects.

– Recommendations

This is one of the top performing groups in the lab and its activity should be supported with highest priority. It is recommended that the young scientist in addtion to initiating his challenging and very original new projects, proposes also an additional less risky project that will secure publications in a foreseable future.

Team 3 : Chromatin structure and cell proliferation

Team leader: Mr Olivier CUVIER

- 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) + 2.7 past	0	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0.8	0,8
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 2.8 past – 2.7 future of the application file)	*1* Co-direction E Käs	1-2
N7: Number of staff members with a HDR or a similar grade	0	1

- Appreciation on the results

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

This starting group is formed of 3 people (a staff scientist, an engineer and a PhD student), and is in the process of recruiting a post-doc. The group leader joined recently the lab (2009) coming from a lab in Montpellier.

The group leader showed the importance of Topo II in DNA replication during mitosis. In addition, he analyzed the factors involved in replication origin clustering in active replication factories. This last story led him to propose a project on nuclear organization of chromatin and chromosomes and more specifically on the physiological roles of insulators. The group participated in a work addressing at the genome level the loci controlled by insulators and insulator binding proteins. Following up on this study, the group is currently examining the function of these proteins in cell cycle regulation and in nucleosome positioning, as well as in long-range interactions and higher order chromatin organization. These questions are addressed mostly by genome-wide analyses and bioinformatics.

This is original, in a very competitive field. If the project is working, we can expect important transcriptional questions to be resolved from these studies. In addition, the group leader also proposes to study the formation on insulator bodies, based on BEAF-CP190 interactions. This is interesting but given the size of the group, the committee is wondering whether the first two projects are not sufficient and difficult enough (although preliminary results are described) and feels the group should avoid too much dispersion.

The group leader has an excellent publication record as a post-doc (Genes & Dev, Curr Biol, and collaborations in Cell, Nature etc.). As an independent group, he recently published a Plos Paper determining the BEAF binding sites and showing that this insulator protein prevents H3K9 methylation and is therefore associated with transcription activation. The group leader was invited to two international meetings (in Switzerland and France), and his poster was selected for oral presentation in several other meetings. This is a good record of publications and oral communications, and the last paper shows that the group, although very small and new, is already productive.

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

Two invited talks are mentionned.The team is rather small, which couls be a weakness. However, a new post-doc is expected. There is no reason to doubt that the work will be attractive.

Two fundings are secured, the ATIP-AVENIR and a grant from the University (15 000 euros). The group leader is waiting for the results of several other applications, some of which have been preselected.

A project on insulator boundaries will certainly profit to other teams in the LBME, but the group is too new to conclude anything on this.

There is no teaching activity and no clear strong involvement in local university activity.

- Appreciation on the project

The projects include 1- dissect how insulator binding proteins impact on nucleosome positioning (although the experimental plan to do that is not described in many details in the written application); 2- explore the interaction between insulator binding proteins and histone modifiers by biochemical approaches; 3-investigate how insulators impact on chromatin higher order organization, but again with no clearly described experimental plan.

The observations from a genome wide analysis performed in collaboration that insulators impact on one hand on cell cycle (although the link is not clearly established, the observations being rather preliminary) and on the other hand on nucleosome organization are timely, in a sense novel and interesting to pursue.

This project is certainly competitive and of interest and given the publication record of the group leader, it could be successful.

– Summary

This is a new group with high potential, provided that it stays focused and recruits new people

– Strengths and opportunities

The group leader has a good record of publications and masters all the necessary techniques. The projects are novel, the questions timely and the hypotheses interesting and challenging.

– Weaknesses and threats

The experimental plan is not detailed enough in the written project to fully evaluate the feasibility; this was partly corrected by the oral presentation, but some parts remain unclear. The committee does not feel that the research is focused enough, taking into account the facts that the group is small and not much funded yet.

– Recommendations

The group leader seems to have applied or plans to apply to several funding agencies; this is greatly encouraged, since it will help in organizing and ranking the experimental priorities. The committee recommends to focus a little bit more on a specific scientific question, given the current size of the group. The group leader should also not restrein himself to genomic approaches, but should also consider addressing this specific question at the cellular level, in particular if he chooses to focus on the regulation of cell cycle. He also might want to seek collaborations for the biochemical characterization of chromatin-associated partners.The committee also recommends to hire PhD students or post-docs as rapidly as possible

Team 4 : RIbosomes and Telomeres

Group leaders: Mr. FERRER and Mr Y. HENRY

- 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 (until 2012)
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	4-3 (4 until 2012)
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file) + 2.7 past	3	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	1.9
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.8 past – 2.7 future of the application file)	3	3
N7: Number of staff members with a HDR or a similar grade	3	4

Note: Two retirements in 2009 and 2010

- Appreciation on the results

Over the review period the group has attempted to bridge the gap between understanding of ribosome synthesis in yeast and human cells. This is an important exercise because these pathways are much better understood in yeast, whereas understanding of the human pathway is likely to be more informative for human development and disease.

They have focussed on the late pre-40S particles, which are the simplest and best-characterised particles, and on snoRNP assembly. The result is a series of well-constructed, useful and interesting reports. In addition, they have started to investigate links between ribosome synthesis factors and cell cycle progression, for which there is a lot of dispersed data, but limited real understanding.

The publications of the group have been steady and solid. The analyses of NAF1 have made a significant contribution to understanding of box H/ACA snoRNP assembly, the analyses of Prp43 make an important contribution to understanding 40S assembly and the recent findings on the apparent translation competence of the pre-40S particles raises a host of interesting questions. The review article was also well written and has been very useful to the field.

The PIs have successfully collaborated with other groups in France and abroad, leading to joint publications.

The group has given only two oral presentations at international meetings, although both were at the high-profile international meetings of the RNA Society, but has been active in poster presentation.

The group has attracted good PhD students and post-doctoral researchers.

The group has attracted limited national funding, in addition to a prestigious HFSPO fellows

The work has made significant contributions to understanding ribosome synthesis, which is likely to be of long-term importance in understanding human growth, development and disease.

Team members have participated in events aimed at communication of science to a general audience., and are active in local and national research committees.

- Appreciation on the project

The projects envisaged are a continuation of the type of work that has been ongoing during the review period. A series of well-defined projects aim to answer specific questions, with increasing emphasis on the analysis of human factors. The work on the late pre-40S makes good use of their successful biochemical analyses of factors interacting with the Prp43 helicase, functional analyses of the Rio kinase family and the unexpected observation that immature pre-40S particles apparently engage with the translation machinery. The other projects address functions of ribosome synthesis factors outside to context of ribosome synthesis, in particular on chromatin structure. There is evidence for numerous apparent examples of this, but very few cases have been characterised in detail and the work proposed has the possibility of opening important new avenues of research.

The work is innovative and novel and will advance the field of research. However, the techniques and approaches are not notably cutting edge.

– Summary

The research of the group has been sound and useful. The committee understand that it is anticipated that the current leader will step down, but the proposed leader should be well placed to take over this role.

– Strengths and opportunities

The solid work undertaken by the group over the review period should place them in a good position to carry forward the projects on Prp43, Rio and pre-40S. The analyses on the non-ribosomal functions of the ribosome synthesis may uncover unexpected and fruitful avenues for new investigation.

– Weaknesses and threats

The analyses proposed on the non-ribosomal functions of the ribosome synthesis factors is interesting but quite diverse. Some care may be needed to retain focus in the work.

– Recommendations

The group has been undertaking good work, and deserves continued supported.

Team 5 : Dynamic Nuclear Organization

Team leade r: Mr Olivier GADAL

- 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)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file) + 2.7 past	3	2
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)	1	-
N6: Number of Ph.D. students (Form 2.8 past – 2.7 future of the application file)	2	2
N7: Number of staff members with a HDR or a similar grade	2	3

- Appreciation on the results

The group leader joined the LBME on an ATIPE contract from the CNRS in 2006 when he started his own group. Overall, the project addresses the role of spatial organization in the control of gene expression, with a particular focus on early steps of ribosome biogenesis in the yeast nucleolus. A major aim is to understand how the cell coordinates RNA polymerase I, II and III transcription in order to achieve balanced production of ribosomal constituents and to what extent spatial organization contributes to this coordination. The project can be divided into three axes, all concerning ribosomal transcription. The first part tries to find partners of polymerase I, the second, not well defined, aims at understanding the degradation process associated with abnormal ribosome production, and the last part concerns spatial positioning of ribosomal transcription and the analysis of the nucleolus compartment at the ultrastructural level. Those are important questions corresponding to competitive and up-to date research problems.

Earlier work of the group leader focused on the development of bioimaging and statistical techniques to describe nuclear gene positioning in yeast, a study that led to the identification of gene territories smaller than the nucleus, which become remodelled upon transcription activation. These analyses also revealed that the nucleolus represents an important landmark in gene localization. More recently, genetic and biochemical approaches led this group to identify transcription factors involved in Pol I transcription as well as in RNA Pol II transcription of ribosomal protein genes regulated by TORC1, and therefore potentially involved in coordinating ribosome biogenesis. In addition, biochemical purifications of malformed RNPs allowed co-purification of factors potentially involved in ribosome assembly surveillance and whose functional analysis may reveal new quality control checkpoints along the pathway.

Five publications have been published, two from the group (one in collaboration with a lab in Paris). This may appear a bit low, but part of this project is also technically very challenging.

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

Since 2006, only one PhD student has graduated. The hiring of one or two more collaborators will allow to fully exploit the genetic and biochemical data collected so far, and to analyze new mutants for defects in assembly and gene localization.

The group leader has been invited twice to give a conference, and abstracts have been selected three times for a talk at meetings. Nothing is mentioned about the other members of the team.

Two PhD students are mentionned in the project. One post-doc is currently in the group, probably paid by the initial ATIP, but no publication from this person was mentioned. Two experienced scientists were hired in the team.

Funding is quite successful, a grant from ATIP, two participations in ANR grants and a subvention from FRM as a new team. Maybe one could have expected more grants as a coordinator. However, this again shows that this group is able to set up collaborations with other labs. This also shows that this project is of interest and competitive as compared to other national groups.

From the text and the interview, it appears that in addition to collaborations in France, the group leader has collaborations with international groups both in India and in Germany.

The organization is that of a classical team, except that the number of PhD students is quite low. One of the team members is assistant professor with an important teaching load, although she got extra research time from the CNRS. Besides this, there is no strong involvement in local university duties from the other members of the team.

- Appreciation on the project

The data obtained so far have set the basis for interesting future work, in which the group leader plans to extend the analysis of transcription factors functionally linked to both RNA Pol I and Pol II transcription of ribosomal protein genes, how these factors are regulated and how and when they are recruited to the transcribed genes. To correlate gene activity with spatial organization, these biochemical studies will be paralleled by the localization of genes implicated in ribosome biogenesis in the nucleus or the nucleolus, either by fluorescent tagging and live imaging or by cryofixation and electron microscopy. In this latter case, the establishment of the Miller spread technique in yeast combined with immunodetection of transcription and early assembly factors in wild-type and mutant backgrounds will provide additional important information on the dynamics of early co-transcriptional events.

– Summary

Overall, the proposed studies nicely complement the research of another group in the lab as both projects involve similar methodologies to study ribosome biogenesis in yeast, focusing on earlier co-transcriptional events underlying this process.

– Strengths and opportunities

The coordinated regulation and spatial organization of genes involved in ribosome biogenesis are important and timely questions. The approaches proposed by the group leader are new and original. They will further document the importance of nuclear architecture and gene positioning in gene regulation, emphasizing the role of the nucleolus and nucleolar localization in the coordinated expression of ribosomal genes.

– Weaknesses and threats

One comment on the results obtained so far is that only two publications came out from this group on its own the last three years, and both are from the same PhD student. Although the publication record of the group leader is not bad at all, there is no paper from postdocs since 2006. There is two PhD students in the team and this is really low if one considers the training duty of a lab.

– Recommendations

As mentioned above, this project is very broad and ambitious, which is a positive point. However, some approaches are also technically very challenging. The outcome of initial experiments may help restrain the goals and become more focused on some aspects of the project in the future.

4 • Appreciation team by team and/or project by project (to be pasted as many as needed)

Team 6 : - Dynamics and disorders of ribosome assembly

Team leader: Mr Pierre-Emmanuel GLEIZES

- 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)	3	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file) + 2.7 past	3	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	1 until 2013
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 2.8 past – 2.7 future of the application file)	1	0
N7: Number of staff members with a HDR or a similar grade	1	2

- Appreciation on the results

The background of the group is largely based on EM analyses of the nucleolus, which historically tended to be rather descriptive. During the evaluation period the focus of the work changed to more mechanismstic approaches, and this was a very positive development. The field of ribosome synthesis is large, and the group has wisely selected a specific subtopic for detailed investigation. The topic selected for greatest analysis, the role of the r-proteins in 40S maturation and export, is an appropriate choice. The late pre-40S particles are probably the most tractable pre-ribosomes, and there are interesting links to human genetic disease. Moreover, the r-proteins have the advantage over other ribosome synthesis factors in that their binding sites are frequently known, but they have not been extensively studied in Eukaryotes. The work shows a fair degree of novelty and has made several useful contributions to the field.

More specifically, the group has been using RNAi screens to deplete factors implicated in 18S rRNA formation. This approach allowed functions to be assigned to a number of ribosomal proteins either in early rRNA processing steps or in later assembly and export phases. The yeast S. cerevisiae has also been used to conduct genetic screens to identify new factors involved in 40S ribosome export. Interestingly, a synthetic lethal screen with Rps15, involved in ribosome export competency, identified mainly factors involved in rRNA modification emphasizing the potential importance of nucleotide modification in nuclear export.

This team has also been very productive in describing the molecular basis of Diamond-Blackfan anemia (DBA), a genetic disease leading to a strong deficiency in erythroblasts. The disease has been linked to the ribosomal protein Rps19 and the group leader was the first to show, using the yeast system, that Rps19 is required for 40S ribosome assembly. The crystal structure of yeast Rps19 established in collaboration allowed further characterization of the functional domains of this protein. Additional collaborative work revealed that DBA can be due to mutations in several other ribosomal proteins, all resulting in rRNA processing and maturation defects.

The publications are good for a junior PI with a modestly sized group. The PI has published 4 papers in respected international journals as senior author and a further paper as joint senior author over 4.5 years. Other papers have been published as collaborations, with groups from within France and internationally. Two PhD theses have been presented during the review period.

Several good papers have been co-authored with other groups, pointing to the ability of the PI to engage in productive international collaborations. The group also has joint national funding together with other members of LMBE and groups from elsewhere in France, indicating a strong degree of collaboration.

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

The group has successfully published with international partners. Group members have given 12 oral presentations – 10 at international meetings – over the review period. Most of the meetings have been relatively small, but this is still good evidence of international standing. No other awards are listed.

There is little evidence for recruiment of international researchers. However, the PI is relatively junior so this might not have been expected.

The group leader has had some success at raising research funding from within France, both as coordinator or participant of various collaborative interdisciplinary projects. No international funding is listed. The group has participated in joint grant applications and has successfully collaborated with international partners.

The work has yielded potentially important insights into the basis of a human genetic disease.

The PI has presented his work to a general audience and engages with other workers studying DBA.

The combination of different approaches that are brought together in the proposed analyses of pre-40S particles allows these projects to be described as cutting edge.

Team members participate in teaching at a local level.

- Appreciation on the project

Two major directions of research are proposed. The structural analysis of 40S subunit assembly, and detailed analyses of the links between the underlying defects and the apparent DBA disease. Both are well-founded and interesting proposals.

A great part of the project is dedicated to the study of 40S ribosome biogenesis at the structural and ultrastructural level using various electron microscopy techniques. The expertise of the group in EM, the acquisition of a new microscope, and the recent hiring of two experienced scientists should generate interesting new observations on the ribosome assembly pathway in increase molecular understanding of DBA.

For the analyses of 40S maturation, the combination of cryo-EM with structural and biochemical analyses is a potentially powerful combination. This is very timely and the group and its collaborators should be in good position to make major contibutions to understanding ribosome biogenesis. The work on DBA addresses important general questions on why mutations in widely expressed proteins give rise to specific diseases and phenotypes. It may also generate useful tools for future analyses by the group and other researchers in the field.

– Summary

The PI is relatively junior and is making steady progress in establishing a research niche and an international profile. The group has been performing good work and the directions proposed for future research are well chosen.

– Strengths and opportunities

The group has established a solid reputation and has access to excellent technology and collaborators that should allow rapid progress in the pre-40S structure projects.

– Weaknesses and threats

Several different approaches are proposed in the DBA projects. Care might be needed to ensure that the research effort is not dispersed, particularly as it appears that some of these approaches involve techniques not previously used by the group.

– Recommendations

The group has been undertaking good work, and deserves continued supported.

Team 7 and 8 : DNA motors and Chromatin Dynamics

Team leader: Mr Mikhail GRIGORIEV and Mr Emmanuel KÄS

- 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 7 8	3 1	4
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file) + 2.7 past	0	0
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)	-	-
N6: Number of Ph.D. students (Form 2.8 past 2.7 future of the 7 application file) 8	1 1	>1
N7: Number of staff members with a HDR or a similar grade	2	3

- Appreciation on the results

This is a new 4-persons team, which results from the recent merge (September 2009) of two separate groups. Both teams originally worked on DNA motor proteins, TIP49a/b and TopoII, involved in chromatin dynamics, structure and organisation. In collaboration with Pierre Fabre Research Institute, they characterized novel anti-cancer drugs directed against Topoisomerase II. Due to health problems that started in 2006-2007 for both team leaders, production, publications, financial and human resources of the two groups have been seriously limited. Therefore they decided to pool their resources into a single group that they are leading jointly. The core of the future project is largely determined by the combined accomplishment and expertise of the two pre-existing groups. As such they aim at studying the properties of the TIP49 orthologs, pontin and reptin, in drosophila and their link with replication, repair and genome compartmentalization. They will also combine their expertise to analyze DNA conformational changes in the presence of the DNA motor proteins reptin, pontin and topoisomerase II, by using a single- molecule magnetic-tweezer instrumentation (DyNaMate station) that is a nanobiotechnology applicable to single molecule studies.

Due to health problems, the number of publications is low (for the review period, one of the group leaders has two collaboration papers in Biochem. J. and EMBO J. and the other has two papers as last author in EMBO J. Curr Med Chem anti-cancer agents, plus a collaboration in another paper and a review), and almost inexistant since 2006. The same holds true for the participation to international meetings, and invited conferences were also cancelled.

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

Since 2006, the impact of the research activities of both groups has been too low to sustain their separate existence. This severely affected their attractiveness in terms of student recruitment, publications and invitations to international conferences. Therefore it is a good point that the two leaders took the decision to asociate and present a joint project.

It is important to note that the groups obtained in collaboration a significant ANR grant, which partially funds the DyNaMate station that has been wholly built at the LBME. The DynaMate magnetic-tweezer instrument seems to be able to create a unique (inter)national and competitive position for the combined group. Indeed, it provided opportunities for effective local collaborations within Toulouse.

Effective marketing of the DyNaMate instrument would be complicated by the small and specialized market for this type of instrumentation. Moreover, there is very significant competition in the field of magnetic tweezers and DNA dynamics and the group does not have a unique (international) position in this field of nanotechnology.

It is a good point that the two leaders took the decision to associate. However, the group is not in a very good position to compete unless teaming up with the other teams of the LBME with a clear biological focus. In other words, the combined group still appears too weak to survive at the current scale.

They should actively seek in-house applications of their experimental setup. Indeed, the molecular systems of the other groups in the Institute hold more promise in the field of chromatin dynamics. This might bring the newly formed group back at the cutting-edge of modern research.

- Appreciation on the project

The scientific output and quality of the group is below what should be expected from a group of this size and working in this environment. As an example, focusing on the activities and the regulation of the Tip49(Rvb1/2) proteins in isolation represents a too-limited view. Indeed, these proteins are subunits of much larger multi-protein complexes, which work on DNA in the context of nucleosomes and chromatin. Thus it seems more relevant to study the Tip49 proteins in the context of their respective complexes and substrates. The Prp43p work seems to hold more promise and the intra-institute collaboration with stronger groups ensures a better grounding than the Tip49-Rvb1/2 work. The work on TopoII resulted in a very limited scientific output. Discontinuation of this research line is justified.

– Summary

Due to health problems that started in 2006-2007 for the two team leaders, production, publications, financial and human resources of the two groups have been seriously limited. The merging will hopefully give new directions, and the committee recommends to give a chance to this new setting.

– Strengths and opportunities

Due to strong convergent scientific interests, the two teams obtained a joint ANR grant (2007-2009, extended until end of 2010), and merged in 2009.

The in house development of the DyNaMate platform provides local and in-house collaborations.

– Weaknesses and threats

The groups were clearly at crossroads and it is very good that they have been rethinking their strategy. It seems, however, that a further focusing on the strengths of the group is needed to become again competitive in obtaining funding and human resources. Indeed, despite the presence of two permanent researchers, increasing the size of the group will be necessary to reach the highest achievement standards.

– Recommendations

The combined group needs to rethink its strategy and allocation of resources. Two strategies can be followed. One is to integrate the groups according to the present plan and take advantage of the present expertise. However, it seems uncertain that the TIP49 system will give the group a leading edge. An alternative is to take further advantage of collaborations within and outside of the institute.

The group should become very active in recruiting PhD students as well as a technician to secure their research and in obtaining external funding : the financial supports of the team will be rather limited when the ANR grant expires and the team leaders should combine their efforts to apply for new grants.

Team 9 : Small regulatory RNAs

Team leader: Mr Tamas KISS

- 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	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file) + 2.7 past	2	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 2.8 past – 2.7 future of the application file)	3	3
N7: Number of staff members with a HDR or a similar grade	2	1-2

- Appreciation on the results

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

The group is headed by a senior scientist with an INSERM DR1 position. It includes 3 permanent staff scientists (1 CR1 and 1 CR2 CNRS) and a technical assistant (AI CNRS). The group studies small nuclear RNA with special emphasis on the function and dynamic of human box H/ACA small nucleolar and small Cajal-body-specific RNPs (snoRNPs and scaRNPs), human telomerase RNP and on the regulatory role of human 7SK snRNA. This is an internationally very competitive research area addressing basic questions related to the regulation of eukaryotic gene expression and structure of chromosomal telomeres. The results obtained by the group show that expression of human box C/D and box H/ACA intronic sno/scaRNPs follow distinct, splicing-dependent and transcription-dependent pathways respectively. They also identified additional complexes containing 7SK RNA, which appear to play a regulatory role in formation of the 7SK/HEXIM1/P-TEFb complex. Taken together, these results provided new insights into the regulation of human RNA polymerase II transcription. In unrelated sets of experiments, the group leader and associates discovered and characterized a novel U1 snRNP particle tightly associated with chromatin. In addition, they obtained important new information regarding intra-nuclear in vivo dynamics of human telomerase.. The committee considers that the group is among the best in the field, and is internationally competitive at a very high level.

This research group has regularly produced very significant contributions in the past. In the period 2006-2009, the group has produced 10 scientific papers, 7 of which with the group leader as senior corresponding author. The papers are of very high standard and appear in high impact peer-reviewed journals, such as Molecular Cell, EMBO Journal, Molecular Biology of the Cell and Molecular and Cellular biology.

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

The team is involved in a very timely, challenging and competitive research. It steadily produces highly original and important results, which provide major advances in the field. The group belongs to the to the worldwide top research groups active in the field of small RNPs. It is involved in many collaborative projects, both nationally and internationally. It also develops new methodologies which are of great impact for the local community

The group leader continues to contibute very original finding in the area of snoRNPs, 7SK RNA and telomerase RNP. He continues to invited to may interantional meeting as an invited speaker.

This group has recruited a young and talented scientist with a CNRS position in 2009. The very strong national and international visibility of the group should attract scientists from abroad. The group is of middle size but comprises very competent and productive people. So far, the group leader was very competitive to attract good PhD students: three PhDs were obtained in the past years and three PhD students will soon join the group.

The group manages to attact very generous funding from French sources which appear to be sufficient for supporting its research: this group has obtained several grants from national agencies (ANR, ANRS) and from charity associations.

The group participates in several national networks. It would be good if it also put more effort to join EC networks focused on research on RNA and RNPs.

No patents were submitted during the past period. However, it should be noted that past research on telomerase and current and planned research of regulation of pol II activity by the HIV TAT protein may have important medical implications.

The team is well managed and very productive.

Three students graduated with PhD theses during the review period. One additional student went through the 8-month long internship in the lab.

- Appreciation on the project

The proposed research project is both ambitious and very challenging, as several new techniques will have to be established within the laboratory or through collaborations. The vast broadening of the experimental approaches and the development of a novel technology called the SILAC will generate a large quantity of data and likely provide new research options for the identification and characterization of novel snRNP proteins. With the arrival of two young motivated scientists, the group will increase its potential of success.

The main projects rely on recent achievements. These projects address important questions on the understanding of the role of the newly discovered snRNP. Two new cutting edge projects will be developed: the regulation of host cell polymerase II activity by HIV TAT protein and the signalling factors regulating nuclear P-TEFb activity. Both projects could have biomedical impacts.

– Summary

In summary, the committee evaluates this group to be dynamic and vigorous, with a strong research program in an important research field and with good chances of future success.

– Strengths and opportunities

The group is among the best in the field and competitive at a very high level. The recruitment of two young scientists will reinforce the attractivity of the team and its potential to develop high-risk projects.

– Weaknesses and threats

This group needs to further develop its international profile to maintain its international visibility, for example by participating in more international networks.

– Recommendations

This is a very competitive team, publishing well and deserving the support they would need to reach a better standing at the international level. The committee encourages this team to follow its current work with continued enthusiasm.

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: CHROMATIN AND GENE EXPRESSION

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	NN	A

Team 2: C/D SMALL RNAs, micoRNAs AND GENOMIC IMPRINTING

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+	NN	A+

Team 3: CHROMATIN STRUCTURE AND CELL PROLIFERATION

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+	NN	A+	NN	A+

Team 4: RIBOSOMES AND TELOMERES

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	NN	A

Team 5: DYNAMIC NUCLEAR ORGANIZATION

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	NN	A+	NN	A

Team 6: DYNAMICS AND DISORDERS OF RIBOSOME ASSEMBLY

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+	NN	A+

Team 7 and 8: DNA MOTORS AND CHROMATIN 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
B	A	A	NN	B

Team 9: SMALL REGULATORY RNAs

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+	NN	A+

Université Paul Sabatier
TOULOUSE III

Direction de la Recherche

Toulouse, le 29 Mars 2010

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Le Président

au

Président du comité d'experts de l'AERES

Objet : Observations de portée générale sur le rapport d'évaluation
de l'unité **«Laboratoire de Biologie Moléculaire Eucaryote » LBME - UMR 5099**
portée par **Michèle CAIZERGUES-FERRER**

Monsieur le Président,

Je vous remercie pour l'évaluation du « Laboratoire de Biologie Moléculaire Eucaryote » - LBME - UMR CNRS/UPS 5099 dirigé par Michèle CAIZERGUES-FERRRER et rattaché à mon établissement.

Je me réjouis que le Comité d'Experts de l'AERES ait reconnu la grande qualité des recherches menées au LBME et son excellente intégration au sein de l'Université. Les points à améliorer seront discutés avec la Directrice de l'Unité dans un esprit constructif pour l'avenir de la recherche à l'Université.

Vous trouverez ci-dessous un message de la Directrice de l'Unité apportant quelques observations sur le Rapport d'Evaluation.

Je vous prie de croire, Monsieur le Président, à l'expression de ma meilleure considération.

UNIVERSITE PAUL SABATIER

Gilles FOURTANIER

Laboratoire de Biologie Moléculaire Eucaryote » - LBME - UMR 5099

We are grateful to the AERES Committee for its positive comments and constructive recommendations. All members of the Institute appreciated their exchanges with the experts during the evaluation. We can only welcome the Committee's comments on the very good productivity and attractiveness of the LBME, along with its strong connection with the Université Paul Sabatier. This review of our laboratory is a strong encouragement to pursue the development of high-profile research on RNA and chromatin biology.

As recommended, we will continue our ongoing efforts to broaden the international basis of the LBME. However, we wish to point out that, in 2010, LBME researchers represent as many as 12 nationalities, with three permanent researchers, half of the LBME post-doctoral fellows (4/8), one third of the PhD students (4/12) and 2 Master's students from foreign countries. Along the same lines, we take good note of the committee's recommendation to increase the visibility of our activities through participation in broad networks, especially at the European level. This will better highlight and formalize the numerous interactions that already exist between the LBME groups and international collaborators.

It has been our constant concern to give young starting groups the necessary means to develop ambitious projects, as exemplified by the group of Olivier Gadal. The group of Olivier Cuvier, which started in September 2009, has rapidly developed and is now on the same track. In this case, very rapid progress has been made possible in part by an intra-laboratory collaboration and the co-direction of a PhD student. We understand the Committee's remark on the necessity to keep research projects focused, especially for starting groups. Although risky projects should be balanced with more secure research, we believe that it is necessary to give a chance to ambitious programs with high potential outcomes. Indeed, these have enjoyed a considerable amount of grant support and start-up funds.

Finally, we can only agree with the committee's remark on insufficient technical staff support in our laboratory relative to the number of researchers, especially for some of the teams. We will work together with the Université Paul Sabatier and the CNRS in an effort to rapidly improve this situation, in agreement with the AERES recommendation, but note that the outcome we strongly hope for is largely beyond our control.

Michèle Caizergues-Ferrer et Pierre-Emmanuel Gleizes
Directrice du LBME, Directeur adjoint proposé pour 2011-2014