Expression génétique microbienne

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Microbial gene expression

Under the supervision of the following institutions and research bodies:

University Paris 7 - Denis Diderot

Centre National de la Recherche Scientifique

December 2012

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

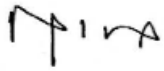
Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head



Pierre Glaudes

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

Grading

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

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

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

- Grading table of the unit: Microbial gene expression

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

- Grading table of the team: RNA helicases

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

- Grading table of the team: Translational control of gene expression in bacteria

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

- Grading table of the team: RNA maturation and degradation

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

- Grading table of the team: RNA control of gene expression

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

- Grading table of the team: Control of sporulation in *Bacilli*

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

- Grading table of the team: Anti microbial cytotoxins, translation mechanisms

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

- Grading table of the team: Transcriptional and post-transcriptional controls of gene expression

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

Evaluation report

Unit name:	Microbial gene expression
Unit acronym:	UPR9073
Label requested:	CNRS
Present no.:	
Name of Director (2012-2013):	Mr Marc DREYFUS
Name of Project Leader (2014-2018):	Mr Harald PUTZER/Mr Ciaran CONDON

Expert committee members

Chair: Mr Domenico LIBRI, CNRS, Gif sur Yvette

Experts:

Mr Frédéric BOCCARD, CNRS, Gif sur Yvette

Mr Bruno CHARPENTIER, University of Nancy (CNU representative)

Mr Benoit CHENAIS, University of Maine (CNRS representative)

Mr Colin KLEANTHOUS, University of Oxford, UK

Mr Ben F LUISI, University of Cambridge, UK

Mr Oliver MÜHLEMANN, University of Bern, Switzerland

Ms Béatrice PY, University of Aix Marseille

Mr Bertrand SERAPHIN, CNRS, Strasbourg

Mr Gerhardt WAGNER, University of Uppsala, Sweden (absent during the visit)

Scientific delegate representing the AERES:

Ms Sophie de BENTZMANN

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

Mr Marc BENEDETTI, Paris 7 University

Mr Gilbert DELÉAGE, CNRS

1 • Introduction

History and geographical location of the unit:

The unit is one of the five units located in the Institut de Biologie Physico-Chimique, in Paris.

Management team:

The director for the past period was Mr Marc DREYFUS with Mr Miklos de ZAMAROCZY as deputy director.

The proposed directors for the next term are Mr Harald PUTZER and Mr Ciaran CONDON as deputy director; it is agreed that at the mid-term Mr Harald PUTZER will resign and Mr Ciaran CONDON will be the director, with Mr Harald PUTZER as deputy director.

AERES nomenclature:

SVE1—LS1
SVE1—LS2

Unit workforce:

Unit workforce	**Number as at 30/06/2012**	**Number as at 01/01/2014**	2014-2018 **Number of project producers**
N1: Permanent professors and similar positions	1 (0,5)	2 (1)	1 (0,5)
N2: Permanent researchers from Institutions and similar positions	17 (16,4)	17 (16,4)	16 (16)
N3: Other permanent staff (without research duties)	12 (11,8)	12 (11,8)	8 (7,5)
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)			
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	4 (4)	4 (4)	4 (4)
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	34 (32,7)	35 (33,2)	29 (28)

Percentage of producers	***95,45 % (without N3)***

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	15	
Postdoctoral students having spent at least 12 months in the unit*	10	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	14	15

2 • Assessment of the unit

Strengths and opportunities:

The unit has a good visibility in the field of the biochemistry of gene expression in microorganisms (RNA in particular).

The productivity of the Unit is good overall

There is a good level of internal collaboration.

The unit is located in a very good scientific environment in the area.

The unit is characterized by a strong internal cohesion.

The unit will benefit from new funding available from a Labex programme

The unit will benefit from novel equipment available from an Equipex programme

Weaknesses and threats:

The scientific plan for the next five years is defined broadly and would benefit from more focus.

Having two different directors within the same five years term is a potential source of problems in sustaining a common scientific vision and direction .

The unit has attracted a low number of PhD students and Post-docs.

A thematic heterogeneity characterizes some teams, which is often reflected by the presence of two team leaders.

The relationship with the University is unclear.

Recommendations:

The unit should be headed by a single director over the five years period who will take responsibility for the scientific strategy, after seeking internal (and possibly external) advice.

An external Scientific Advisory Board should be appointed.

Teams should be headed by a single team leader and have reasonable internal thematic unity (avoid merging groups that maintain their scientific projects)

Efforts should be made to increase the critical mass on some lines of investigation

The unit should resume negociations with the University for the creation of an UMR

Efforts should be made to better define a scientific plan for the next term.

3 • Detailed assessments

Assessment of scientific quality and outputs:

The unit of Microbial Gene Expression (EGM) has a solid reputation in the field of RNA biochemistry and gene expression in microorganisms. Teams of the Unit have provided important contributions to the field of RNA degradation and polyadenylation in bacteria, in the field of translation and more recently, of small regulatory RNAs. Several additional aspects of gene regulation in bacteria (e.g. transcription) are also studied. The methodologies employed range from genetics to biochemistry and structural biology. Genome-wide approaches have been recently initiated, while proteomic approaches are not very developed. These are included in the projects of some teams. The unit appears to be well integrated in the scientific environment of the Montagne Sainte Geneviève, and there are numerous internal and external collaborations. The quality of the work produced in this term is good but uneven among the teams. Overall, the unit has a good publication record. A few papers are published in high visibility journals (NSMB, MolCell, EMBO J) and a majority of articles are published in more specialized journals (Mol Mic, NAR), which reflects to some extent the overall impact of the domain (fundamental research in microbiology). Although much has been done since the previous AERES visit, the parcelization of subjects is still present in the EGM leading to some dispersion of efforts and resources, and affecting the overall scientific performance of some teams. Additional efforts should be made in the direction of increasing the internal coherence of teams and the critical mass per subject.

Assessment of the unit's academic reputation and appeal:

The EGM has a good reputation nationally and internationally, and is regarded as one of the main research centers working on fundamental aspects of the biology of microorganisms in France. However, the committee found that the present scientific visibility of the unit is not as strong as expected based on its scientific history. With notable exceptions, the Unit does not appear to have recruited in the last few years a new generation of scientists to replace the many team leaders who are retiring. The unit has attracted a few permanent external scientists in the last term to compensate for retirements. The relatively low number of students and post-docs might also reflect poor appeal for young scientists (but see below). Attractiveness could be improved, for instance by organizing in house conferences focused on the leading subjects of the Unit. The recruitment of new groups will be, however, the main opportunity for increasing the visibility of the EGM.

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

N/A

Assessment of the unit's organisation and life:

The committee was favorably impressed by the strong internal unity and high community spirit of the EGM, which is in keeping with the tradition of the Unit. However, the contacts with researchers of the other Units of the Institute appear to be few and poorly developed. This could be improved with social/scientific initiatives such as scientific transversal projects or the institution of a journal club, which would be especially beneficial for the Masters and PhD students and postdoctoral researchers.

Several researchers are involved in scientific collaborations with groups in other Units of the Institute or external teams in the Montagne Sainte Geneviève campus. The unit also contributes teaching to the local or other Universities.

In agreement with the recommendation of the previous committee and the present Director's project, the distribution of funding has been modified, with a 20% internal overhead on contracts (excluding personnel resources), which guarantees a financial buffer for teams with temporary difficulties. This arrangement is approved by the teams and this committee.

The previous AERES committee was concerned by the excessive fragmentation of research subjects, leading to poor critical mass in some lines of investigation. Many efforts have been done in this direction under the present director's mandate. However, the present committee also feels that much still remains to be done. The committee understands the difficulty of the director facing the refusal of some researchers to abandon their favorite project, in spite of sometimes manifest difficulties and lack of competitiveness. However, the committee strongly feels that the teams should be defined based on scientific coherence and that individual researchers should generally comply with the scientific policy of their teams, the responsibility of which belongs to the team leader. This is important both for the career of the individual researchers (who could eventually find elsewhere a better environment for their research) and the visibility of the team leader, who is judged on the performance of his/her own projects.

The committee was surprised by the procedure adopted to propose a new director for the EGM, based on an equalitarian vote of all the members of the Unit. The choice of a Director implies the evaluation of specific attitudes (e.g. the attitude to influence and determine the scientific policy of the Unit taking into account the national and international research context), a judgement for which many members of the Unit may not have sufficient experience. Although the committee members certainly do not question the principle that all category of personel should participate to the vote, they think that this should more appropriately occur via the personnel delegates. The committee also feels that having two Directors in the next term is a source of potential problem, even if the two candidates declare to agree on many points. This might affect long term strategic choices in every instance where the two directors do not agree.

In many of the instances where decisions might be unpopular and conflict with established habits, a scientific advisory board would greatly help. The committee strongly urges the appointment of such a committee, that could eventually be consulted by email and meet once a year or whenever required.

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

The committee was somewhat surprised by the low number of students (presently 2) and post-docs (presently 5) in the Unit, which might reflect a problem of visibility of the Unit. The number of thesis defended in this term is however good (15 in the 5 years period), possibly indicating stochastic variation in the number of students. The total number of post-docs (overall 11 in the 5 years period) remains however low. New funding from the LABEX DYNAMO should help, by allowing the recruitment of 2-3 students and post-docs during the time frame of the project. Students could be attracted by increasing teaching and in any case by strengthening the relationships with the University.

Assessment of the five-year plan and strategy:

Critical to the plan of the unit appears to be the recruitment of two new groups for which laboratory space is presently available. Although the open call for these positions is rather large (microbial gene expression), the declared interest focuses on the introduction of new model bacteria in the Unit. For instance, groups working on cyanobateria and alpha-proteobacteria could be recruited with the support of LABEX funding. The scientific strategy undelying the introduction of new model systems is not always fully clear to this committee. Although the committee understands the "openness" to new model systems, the committee also feels that the introduction of new organisms cannot be a scope in itself and should be justified by an underlying rationale for new discoveries. Care should be taken to avoid strategies that might result in incremental advances or reveal merely descriptive accounts of similar molecular mechanisms in other systems. In the era of genomics, the unit may capitalize on bioinfomatic expertise to open new ways of research in the field "control of gene expression in microorganisms".

Generally, the committee could not identify a very clear and defined scientific plan for the five years period. This might be also due to the lack of specific resources that might enable Directors to directly determine the scientific policy of the Unit (e.g. starting grants for young PIs), but we feel that scientific directions should be identified in spite of these limitations. The committee strongly recommend the appointment of an external Scientific Advisory Board.

The committee supports the project to become UMR (University-CNRS mixed unit) because this will strengthen the connection with the Paris 7 University and might allow increased recruitment of students and permanent reearchers. The University will of course also benefit from quality teaching from renowned scientists.

4 • Team-by-team analysis

Team 1 : RNA helicases

Name of team leader: Mr Marc DREYFUS/Mr Kyle TANNER

Workforce

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

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

• Detailed assessments

Assessment of scientific quality and outputs:

The research theme of the group is focused on characterising the ATP-dependent RNA helicases of the DEAD-box sequence motif family. The DEAD box helicases play key roles in RNA metabolism and regulation, and understanding how they work will undoubtedly provide important biological insights and would therefore be of great interest to many researchers. The group has been studying representative helicases of bacteria and yeast, and their future work will build on their expertise and achievements with these systems. The outputs from the group, as seen in the publications, have been in good international journals (J Mol Biol (2), Mol.Cell.Biol. (1), NAR (1), Mol Mic (1), Biochemistry (1), PNAS (1) as major authors).

The work on helicases in cold adaptation has a compelling physicochemical basis and has lead to an interesting research direction. The publications have been insightful contributions to understanding the function and activity of these important groups of enzymes.

Assessment of the unit's academic reputation and appeal:

The team academic reputation and appeal are good, judging from the invitations to speak at meetings, but they have mostly been for the director of the previous term, who will retire in December. The future (from 2014 on) director has had fewer presentations at meetings to date.

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

One patent was taken within the term and two others were extended internationally.

Assessment of the unit's organisation and life:

The projects will sustain the momentum developed in studies of the DEAD box helicases. There appears to be good cohesion within the group, and the group has established very productive collaborations with the single molecule experts within the research campus. Overall there is a good level of external and internal collaboration.The group continues to attract funding.

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

This is good, with members affiliated with the university and involved in training PhD and summer students. The group has trained PhD students, master students and undergraduates.

Teaching was mainly performed by the past team Director, and we suggest that effort be made to improve this side of the team activity. This will expose the team scientific interests to a larger audience, thus favoring the recruitment of students.

Assessment of the five-year plan and strategy:

The team leader is retiring in December 2013, and the DR2 will become the new team leader. The research topic will remain in RNA helicases, with the aim of studying protein partners that affect helicase activity and specificity, and to study mechanism, principally through use of single molecule methods (optical and magnetic tweezers and FRET). Both these topics are highly competitive and there is tremendous international competition. In the report from the unit, there was mention of potentially fusing the team with team 6, which works on translational control in yeast.

The work on helicases in thermal adaptation is an interesting area, and may provide some insight into how helicases might have evolved to increase their mechanical power for duplex unwinding. The identification of RNA and protein partners is key to the future development of the helicase field. The report mentions preliminary results of experiments directed to the identification of partners of the yeast Ded1 helicase.

Aside from the expected interacting factors involved in translation initiation, novel factors were identified, some of which are involved in mRNA export, together with the nuclear Cap-binding complex, suggesting a possible nuclear function of Ded1p. This work should be continued and expanded, if possible with open ended approaches, as these could contribute to understanding a novel function of Ded1 in the nucleus. Several additional approaches are proposed to investigate a possible role of Ded1 in the remodeling of the mRNP, and the role of interacting co-factors in stimulating ATP hydrolysis and Ded1 function. A better understanding of the biological function of Ded1 will be essential to impact on the field and is likely to require the development of suitable in vitro assays.

Efforts at identifying RNA targets in vivo is also an important development of the current efforts to understand Ded1 function. In vivo crosslinking and immunoprecipitation approaches (CLIP) have been proposed but not discussed in depth in the oral presentation.

Several single molecule approaches have been proposed, in the framework of collaborative approaches, both for E. coli and the yeast helicase. While interesting and important, the power of this apporach will undoubtedly be much greater if it recapitulates a relevant in vivo system; so, perhaps the priority should be to identify partners and RNA substrates and then to return to the single molecule work to characterise these.

Conclusion:

- Strengths and opportunities:

The group has developed expertise with the helicases over the years and their future work can build on this experience. Another strength is the single molecule expertise and the available infrastructure to pursue this direction. The continued work on the yeast Ded1 protein to identify protein partners is also an exciting direction, and the use of CLIP to identify SrmB RNA targets. Perhaps there could be be opportunities to expand collaborations to identify the in vivo partners of the yeast helicase and to characterise the potential role in mRNP remodelling in yeast in vivo and in vitro. The results from such an effort might identify better targets for the in vitro single molecule work that will make the results more relevant to understanding helicase function and mechanism.

- Weaknesses and threats:

The DEAD box enzymes are clearly an important and topical research subject and they are being studied by many research studies internationally; the area is therefore very competitve. The single molecule studies are important but may lead to incremental advances without knowledge of the relevant protein partners and RNA targets. These studies are also quite challenging and might constitute a risky avenue. In the case of Ded1, its analysis may suffer from the fact that its biological function still remains poorly defined despite years of study (this of course could become an advantage if a significant scientific niche is discovered).

- Recommendations:

The research area is well developed internationally and, like most interesting problems, highly competitive, but the key remaining questions concern the identification of in vivo targets and partners of the DExD/H helicase - both RNA and protein. Identification approaches might include in vivo photocrosslinking and co-immunoprecipitation (CLIP) and related approaches, but there is little development of these approaches in the presentation on the proposed future work. The CLIP work and co-immunoprecipitation experiments might be considered as priorities.

The proposed fusion with another group may not optimise the complementarity of the researchers or serve a common research aims. Team 6 studies translational control in yeast , which might fit with the role of Ded1 in translation. However, common interests might only be apparent as the work of team 1 is focused more on the biochemistry of helicases than on translation itself. If a merger is required, its goal is to reinforce the overall scientific project of the team and it would be important to maintain (or create) an internal scientific coherence and avoid putting together scientists working on different (though related) subjects under the same label.

Team 2 : Translational control of gene expression in bacteria

Name of team leader: Mr Mathias SPRINGER

Workforce

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

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

• Detailed assessments

Assessment of scientific quality and outputs:

This team has experienced, in the recent past and present, deep alterations following the departure of several of the lab personnel (through both transfer and retirement) and the arrival of a young CR2. Some themes have disappeared at the beginning of the contract such as the project on transposable elements in yeast. This led to focus on the translational control of gene expression in E. coli. This general theme comes in three main complementary approaches: translational regulation and kinetics of RNA folding, translational control by sRNA and the role of ribosomal proteins.

Main results of the team include: i) the evidence that the efficiency of the translational control is dependent on mRNA folding kinetics; ii) the role of the transcriptional pausing in modulating mRNA folding, which in turn affects translation; iii) the study of the two component system PhoPQ (initiated by the newly recruited CR) and the role of small RNA (sRNA) MicA and Gcvb as negative regulators of PhoPQ ; iv) the study of a negative feedback loop involving the two component system EnvZ-OmpR, that regulates expression of two sRNAs, OmrA and OmrB, that in turn negatively regulate EnvZ-OmpR control. This feedback loop regulates the levels of OmrA and OmrB but surprisingly expression of other targets of OmpR, i.e. ompC and ompF, is not affected.

The overall scientific quality of the results is good with 7 publications in journals of good visibility (Plos Genet (1), J Mol Biol (1), Nucleic Acids Res (1), Mol Mic (1), J. Bact (1), MCB (1)), to which must be added four publications (also in good rank journals) from collaborations with other teams of the research unit and 5 participations to scientific books. Two additional publications (NAR and PLoS one) are signed by an emeritus research director hosted in the team until August 2012 but working independently on her own subject (HU regulon) and another one by a researcher who left the team at the beginning of the last contract to start her own group (September 2008, publication date 2008).

Assessment of the unit's academic reputation and appeal:

The team has a good visibility with several oral and poster presentations in international conferences. The team leader has a well-deserved reputation in the field of translation and RNA. Team members participated in 5 book chapters. The team leader was also a section editor for the American Society for Microbiology Press. International collaborations are also a positive sign of the high reputation of this team as well as the recruitment of (at least two) foreign postdocs (one funded by a Marie Curie fellowship and the other by an ANR grant). This is indicative of the scientific reputation and attractiveness of this team.

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

N/A

Assessment of the unit's organisation and life:

The team is generally well organized and with a good scientific coherence. The good quality of the scientific environment and the very good working conditions are apparent. The effectiveness of the interaction with other teams of the research unit and with other units in the campus is demonstrated by the collaborative publications. This was particularly the case of the single molecule experiments conducted in collaboration with people of team 1 and the Ecole Supérieure de Physique et Chimie Industrielle and which led to a PNAS publication. Internal collaborations also include projects on RNA helicases (team 1) and gene expression in bacteria (team 7). The team leader has had several administrative responsibilities until 2011.

The group will disappear in the next term. One member of the team has already started her own group in another Institute and another member is proposed to be co-leader of team 4. The committee welcomes the attitude of the group leader in promoting the career development of young promising scientists. The committee also agrees with the suggestion that the group leader join another team in the Unit, which will allow the independent scientific development of the “budding” team.

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

Three PhD students have defended their thesis in the term. The team has also trained three master 2 students and one master 1, which is more than satisfactory. One project leader has participated to a thematic course for PhD students in Strasbourg and one PhD student worked as a teaching assistant in Paris-7 University. The UPR status of this CNRS unit is certainly not in favor of greater involvement in this direction.

Assessment of the five-year plan and strategy:

N/A

Team 3 : RNA maturation and degradation

Name of team leader: Mr Ciaran CONDON

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions		1 (0.5)	
N2: Permanent EPST or EPIC researchers and similar positions	1 (1)	1 (1)	1 (1)
N3: Other permanent staff (without research duties)	2 (2)	2 (2)	2 (2)
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1 (1)	2 (2)	1 (1)
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	4	6 (5.5)	4

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students		
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	3

• Detailed assessments

Assessment of scientific quality and outputs:

While bacterial RNA processing and turnover has been the subject of numerous studies for several years, most analyses have been performed using *E. coli* or related species. Until recently, it was unclear whether results and dogmas derived from such work were widely applicable and how diverse the RNA decay process was in the microbial world. These issues were addressed by studying pathways of RNA maturation and degradation in *Bacillus subtilis*. In the last four years, this strategy revealed itself to be extremely fruitful. Key findings resulting from the work of this group include: i/the description of 5'-3' exonucleases in *Bacillus subtilis*. This observation was unexpected as such enzymes were thought to be absent in bacteria, II/ the identification and description of new enzymes involved in RNA decay and maturation in B. subtilis; iii/ the structural characterization of some of these factors; iv/the identification of an enzyme deprotecting the mRNA 5' end.

The group also developed assays for nuclease activities. It also analyzed nuclease regulation in yeast but the latter project is only distantly related to the main question addressed by the team.

Overall, the originality of the work developed by the group resides in the idea that microbial mRNA decay was more diverse than generally believed. By performing experiments of high technical quality while following rather classical strategies on new biological systems, this group obtained major results that shifted accepted paradigms and thus had a major impact on the field and beyond. The most visible results were published in top journals and are highly visible internationally (e.g. Cell, PLoS Genetics, Mol Cell, one article each), but the remainder of the group production is also of very high quality and was published in good journals (Mol Mic (5), RNA (2), J.Bact (1), PNAS (1), Structure (2)). Several reviews and methods articles have also been produced.

Assessment of the unit's academic reputation and appeal:

Due to the regular production of high quality research, the group has a well-established international reputation. While this is not demonstrated by international financial grants, the implication of the team leader in editorial board of important journals and the collaboration of the team with main international players in the field provide strong evidence for this statement. Further support from this conclusion derives from the invitation of the team leader to several international conferences and the funding that he obtained that includes several national grants of which he is coordinator. His internationally recognized position also allowed him to attract a foreign post-doctoral fellow.

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

One of the most important interactions of the group with the social and cultural environment was the presentation of "Ribonucleases" to young students at a local "lycée". On the economic side the group also developed a method to monitor nuclease activities, which served as basis for a scientific publication, but might be of interest at some point to industry even if it is apparently not patented

Assessment of the unit's organisation and life:

The group main objective is clear and well defined. Most of the various subprojects synergize to progress in this direction; the subproject on yeast nucleases will not be followed-up allowing the team to refocus on a single topic where it excels. The permanent researcher (CR1) in charge of the yeast project has left the UPR9073 in 2011 to form an independent group in the FRE3354 at the IBPC. This team is a very good example of successful compliance with the previous committee recommendation. The committee feels confident that this will be an important opportunity for the researcher working on Xrn1 while avoiding dispersion of energies in the EGM team.

When necessary, collaborations with internationally recognized experts are organized allowing the team to effectively implement new strategies and/or investigate new areas. The head has a clear leadership and group members appear to be productive. Altogether, this team appears to work very efficiently.

At the Institute level, several members of the team invested their time in governing committees and unit activities (e.g., safety responsibility). This underlines their involvement in the local organization and life. More broadly, the group is well integrated in the local research network:

- Its subjects fit in very well with the current projects of the Institute (IBPC);

- The group leader has established several fruitful collaborations inside the CNRS unit and with local groups in the Paris area;

- Several members of the group participate to teaching in local universities.

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

Several PhD students were trained in the group, one of who also performed her M2 practical training in the lab. Two PhD theses were defended in the last 4 years, each with a good publication record. Several post-doctoral trainees also benefited from working experience and training in the group. One PhD student of the team was involved in teaching as “Moniteur”. In addition, 3 team members have taught at local university while the group leader was in addition involved in teaching in a university abroad and in national summer school.

Assessment of the five-year plan and strategy:

The proposed project includes a follow-up of current studies as well as exploration of new areas. The study of the regulation of the yeast Xrn1 exonuclease, that was departing from the main stream of the team’s work, will not be pursued.

In particular, the team will invest in the identification of nucleases involved in steps of rRNA maturation for which no responsible factors are currently known. The detailed functional and structural characterization of some known but poorly understood nucleases will also be performed. Given the expertise of the group in this area, these experiments should provide interesting information. These studies will be extended by the characterization of the process of small RNA induced RNA degradation and the characterization of the factors mediating this process. This new area is of prime interest.

The group will also be joined by an emeritus research directorwho will develop his own project by investigating the regulation of magnesium concentration in *Bacillus subtilis*. This area is distantly related to the main project of the group. Nevertheless, interesting insights into the effect of internal divalent cation concentration on nuclease activities and/or RNA decay may arise from combination of this work with the main team’s project.

Overall, the group will address a topic of interest to increase our general knowledge. Application of such research to the economic world are not specifically anticipated and are naturally beyond the goal of this proposal, but may nevertheless occur.

Given the limited size of the group, the strong focus on areas of important interest in which the team has a leading expertise is a good choice. In this context, the strengthening of the group by an assistant professor (Maître de Conference) is welcome. Further support would facilitate the implication of the team leader in the direction of the institute. Continued funding support and facilitated access to PhD students may further favor the development of this highly productive group.

Conclusion:

- Strengths and opportunities:

Altogether, the team has produced high quality data during the review period, which led to publications in good to very good journals. The proposed project builds on the technical expertise and knowledge of the group as well as on the exploitation of an interesting niche. This situation provides interesting opportunities for the proposed project. Those should be exploited with the continuation of the functional and structural characterization of enzymes involved in rRNA processing while the study of small RNA-induced RNA decay provides occasions to expand the group's studies in a very interesting area.

- Weaknesses and threats:

Weaknesses that could threaten this group include its small size and limited possibilities to secure financial support.

- Recommendations:

The evaluation committee recommends that supervising bodies reinforce this group, e.g., by the allocation of PhD studentships, and, if applicable, financial support for post-doctoral trainees and/or lab running costs. This is especially important since the group leader will have major administrative tasks in managing the Unit (although only in the second term of the mandate if the current setting is approved) and will be able to dedicate considerably less time to his group.

Team 4 : RNA control of gene expression

Name of team leader: Ms Eliane HAJNSDORF/Ms Maude GUILLIER

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1 (0,5)	1 (0,5)	1 (0,5)
N2: Permanent EPST or EPIC researchers and similar positions	2 (2)	4 (4)	2 (2)
N3: Other permanent staff (without research duties)	1 (1)	2 (2)	1 (1)
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	4 (3,5)	7 (6,5)	4 (3,5)

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

• Detailed assessments

Assessment of scientific quality and outputs:

The scientific interest of this team has been centered on three major themes: i) the study of the impact of polyadenylation on mRNA stability ; ii) gene regulation by small RNAs and iii) structure and function of Hfq. In the first line of investigation the team has shown in a collaborative effort that RNase R is the exonuclease responsible for poly(A)-dependent degradation of *rps0* and *rpsT* mRNAs. Moreover the team has undertaken unbiased proteomic and transcriptomic analyses to identify genes affected positively or negatively by mutation of PAP I (poly(A) polymerase). They also revealed a role for polyadenylation in tRNA quality control. In the second line, they have studied the regulatory role of several small RNAs (GcvB, DsrA, SraG). Finally, they have studied the role of Hfq in favoring the interaction of sRNAs with their targets. This has led to a number of publications in good visibility journals (NAR (3), Cell Cycle (1), Mol Mic (1)) and more specialized journals (Biochimie (2), BMC Mol Biol (2), RNA biology (1), FEBS J. (1)). A few publications are also issued from collaborations and reviews/methods. Although without highlights, the publication outcome is relatively good for a small team.

Assessment of the unit's academic reputation and appeal:

After the retirement of the senior team leader, the visibility of the team appears to be restricted to the national community, with only one invitation to an international confererence.

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

N/A

Assessment of the unit's organisation and life:

The team has undergone significant turnover, with three team members with permanent positions being replaced. The senior team leader retired at the end of the previous term. Three team members from team 2 joined this team and a young CR2 from team 2 will share the direction. The CR2 researcher appears to be quite visible on the international scene and recently published an article in a high visibility journal (PLoS Genetics). The merge appears to be coherent scientifically, the two parties having shared interests in the sRNA field.

The senior team leader has been involved in teaching in the local University as part of his functions as a Professor. Teaching was also perfomed by other team members, always in the framework of their activities (assistant professors). Both team leaders had administrative duties.

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

One thesis has been defended in the term and two master students were trained.

Assessment of the five-year plan and strategy:

The proposed projects of the team are a logical follow up of the previous research of the two subgroups. The role of poly(A) polymerase will be studied in gene expression, RNA turnover and RNA based regulation. Regulation by sRNAs will be studied by both subgroups, each one focusing on different regulons. The Hfq interactome will also be analyzed. An additional project is proposed to be carried by a former team 2 member who will study the effect of RNA folding kinetics in translation.

As was presented, and in spite of scientific coherence, it does not appear that this merge will result on synergic effort on common projects. Rather, each subgroups will continue his own projects. Moreover, the project on RNA folding in translation, although interesting, represents a diversion in the otherwise coherent scientific context of this team. Given the small size of the team, the number of projects appear barely compatible with the competitive international context, choices should be made and synergy sought. This committee also feels that the young CR2 from former team 2 has the qualities and the visibility required for a young PI and should be supported. The interest of maintaining in this team the project on RNA folding and translation is highly questionable.

Conclusion:

- Strengths and opportunities:

The team is overall a coherent ensemble with "hot" subjects supported by a good expertise in sRNA field and RNA degradation.

- Weaknesses and threats:

The team has a small size and poor synergy exists among the team members on real common projects. The activity of the team might suffer from some thematic dispersion in a very competitive international context. The team does not appear to be very attractive for students and post docs.

- Recommendations:

The RNA folding and translation project should be relocated or terminated to avoid further dispersion. The young group leader should be supported. The team leaders should identify main projects and join efforts on these. Participation to international conferences should be increased. Teaching might help promoting team subjects.

Team 5 : Control of sporulation in *Bacilli*

Name of team leader: Mr Patrick STRAGIER

Workforce

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

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

• Detailed assessments

Assessment of scientific quality and outputs:

The research of the team focuses on the controls of sporulation in *B. subtilis*, in particular on the dual mechanism delaying synthesis and activity of the transcription factor SigG during the sporulation process.

This is a small team composed of a PI (DR1 CNRS) and an assistant-engineer (AI CNRS). In the last five years, the team has undertaken three projects concerning i) the identification and characterization of a protein inhibitor of the sigma factor SigG, ii) identification of the factor responsible for delaying SigG synthesis, iii) the identification of a small non-coding RNA synthesized in the forespore. These studies allowed publications in good specialty journals as main author (Molecular Microbiology, Journal of Molecular Biology, RNA Biology, one article each). For two of them, the work resulted from collaboration of the PI with other groups of the Unit. Two additional articles are issued from collaborations with external groups.

Assessment of the unit's academic reputation and appeal:

It has a very strong and prestigious historical background in the field of sporulation in *B. subtilis*. However, during 2007-2012, the PI was invited only once as a speaker to an international conference. Together with other internationally recognized sporulation experts, the PI participated to the debate on whether or not mycobacteria produce endospores, and this was published in PNAS.

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

N/A

Assessment of the unit's organisation and life:

The team has no external funding; the resources provided by the unit appear to be sufficient in respect of the size of the team and the approaches used.

The team has collaborated with other members of the unit (2 publications in common) and the PI has collaborations with three internationally recognized scientists.

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

The PI has supervised one thesis (giving rise to two papers as first and second author for the student) and two Master students.

Assessment of the five-year plan and strategy:

The proposed project aims to reveal one of the salient features of the transcriptional cascade occurring during the process of sporulation. It will consist of identifying the gene and the functional activity of the encoded product responsible for the inhibition of SigG synthesis. The ultimate goal of the project (before retirement of the PI in November 2015) is to comprehend how the negative control on SigG synthesis is reversed by the signal originating from the mother cell.

Conclusion:

- Strengths and opportunities:

The proposed scientific strategy has already given promising results and should be pursued to characterize this remarkable step of the sporulation process.

- Weaknesses and threats:

As the team has no external funding and no recruitment is envisioned for the two years, it will rely only on financial and human resources provided by the unit.

- Recommendations:

The merger with team 7 is fully artificial as it does not reflect scientific coherence and is not approved by the team leader. This committee does not see it as a necessity. Since the team leader is retiring on November 2015, the committee recommends that the PI remains a team leader for the first two years of the next term, which will allow maintaining his visibility. However, the relatively large space occupied by this small team should be reduced to a more appropriate size to comply with internal rules.

Team 6 : Anti microbial cytotoxins, translation mechanisms

Name of team leader: Ms Valérie HEURGUE-HAMARD/Mr Miklos de ZAMAROCZY

Workforce

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

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

• Detailed assessments

Assessment of scientific quality and outputs:

Team 6 is composed by 5 researchers that constitute two subgroups, called for simplicity groups 6a and 6b. The individual groups have little or no overlap in their research apart from a distant connection (group 6a works on methylation of the translation release factors in yeast, group 6b works on the cleavage of the *E. coli* ribosome or tRNAs by colicin). This situation is entirely historical and stems from both groups originally belonging to the same team, whose leader retired at the end of the previous term. Group 6a is composed by two CR1 researchers and a technician, group 6b by a DR2 and an engineer (IE1).

Group 6a: the publication record is acceptable (one NAR, one MCB, one Biochimie and one FEBS letters as corresponding author for the group leader), but outstanding innovative papers are missing. Consistent with this, the committee felt a missing ambition of the team leader to aim for publishing more comprehensive stories in journals with a higher impact. After having discovered (before this evaluation period) that the glutamine methylation of the GGQ motif also occurs in yeast eRF1, the team identified Mtq2:Trm112 as the required factors and started the structural (in collaboration with another group) and functional characterization of the Trm112:Mtq2 complex. However, contrary to bacteria, this methylation does not seem to affect either translation termination efficiency or nonsense-mediated mRNA decay (NMD). Purification of Trm112-containing complexes revealed Bud23 as an additional interaction partner. The Trm112:Bud23 complex functions in ribosome biogenesis by methylating 18S rRNA. Besides this main project, one team member persued a project that addressed mechanistic aspects of NMD using a tethering system as part of an international collaboration. This project resulted in one publication in Biochimie and an invited review in Nat Rev Struct Mol Biol with the post-doc laboratory. The committee finds this one-person-project in a highly competitive field problematic, because it deviates required resources from the main project and at the same time has relative small chances to succeed in this environment, where it is quite isolated.

Group 6b. The major focus of the group has been the mechanism of import of antibacterial colicins into *E. coli* cells, with a specific focus on the mode of entry of the group B colicin ColD and more recently that of the group A colicin ColE3, both RNase-type colicins. Nuclease colicins hijack endogenous cellular functions throughout the cell envelope, from the outer membrane through to the cytoplasm, and so studying their mode of entry gives insight in these functions as well as informing on the import process itself. The number and quality of outputs is good (two JBC papers) considering the level of personnel support engaged in this research. Both papers report new findings that are pertinent to the entry process; the first identified a novel contact between the colicin D central domain and the inner membrane protein TonB, which is implicated in the pmf-dependent import of the colicin across the outer membrane. The central (receptor-binding) domain also appears to affect immunity protein binding. The second solved a longstanding problem in the colicin field, that of how these molecules (ColD and ColE3) are processed on entry to the cytoplasm. Work from another lab had shown that the dislocating AAA+ ATPase/protease FtsH is required for group A and B nuclease colicin entry to the cytoplasm. Group 6b has now shown that FtsH is the protease responsible for the processing and that LepB, which they previously showed was involved in cytoplasmic entry, is most likely a co-factor for this process. These findings are important to the colicin field and may be more relevant to a wider audience if the molecular mechanism of FtsH-mediated import of colicins could eventually be established.

Assessment of the unit's academic reputation and appeal:

With the retirement of the previous group leader, the visibility of both groups can be said to be at the national level. The group had two grants during this period, an ANR jeune chercheur and a HFSP grant. Funding was limited to one grant (6a) and there was one invited international talk (6b), although a good deal of attendance at national and international meetings. Further grant funding and higher impact publications will be needed to increase visibility from which more international invitations will come and hence increase visibility. This should also increase the attractiveness of the lab to PhD students (two trained during this period).

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

N/A

Assessment of the unit's organisation and life:

Generally the two subgroups are well integrated in the unit. The 6b leader has served as the deputy director for the unit since 2009 through this period and has contributed to a number of administrative roles hence benefiting the wider community of the Unit. The team as a whole, however, has not been subject to any governance, rather the status quo has prevailed. The committee is concerned that neither group appears to have current external funding (6a leader is on the waiting list for an ANR grant) apart from the soon ending collaborative HFSP grant on the NMD project. It is somewhat surprising that, given the latter, a single person was working on this project.

There appears to be little added value in having teams with two co-leaders that run largely disconnected lines of research. Furthermore, in this instance the Committee felt that future research projects are too great for the number of team members (see below) especially if they are not successful in obtaining external grant support. The committee suggests they concentrate their activities on fewer projects in order to become more competitive.

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

Both subgroups have attracted PhD students (one each) during the period of assessment. Several Master students have benefitted from training in both labs. 6b leader has also been involved in teaching. There has been significant turnover of staff in this group principally through visits of Master students and two retirements. The last PhD student finished in September 2011 and the last Masters student left the lab in February 2011. The student that finished in September 2009 was co-supervised between the previous and current team (6a) leader.

Assessment of the five-year plan and strategy:

Team translation termination (6a): the team wants to identify Mtq2 targets responsible for several phenotypes observed in mtq2 mutant strains. In addition, identification of additional factors of the Trm112 interaction network and the regulation of this network is planned. Finally, the role of Bud23 in ribosome maturation shall be investigated. Overall, the proposed projects are feasible and represent a logical continuation of the current research. To pursue all proposed projects requires the CR1 researcher to abandon her NMD project and join forces with the co-leader of the team.

The strategy for the 6b group has four elements: (1) Defining the LepB-colicin D interaction. This will undoubtedly involve a good deal of biophysical characterisation of complexes and eventually their crystallization. This is an area where the group have a lead and, in large part, should be achievable. The committee encourages the group to adopt quantitative methods to, for example, define the Kd and stoichiometry for complex; (2) Reconstituting FtsH cleavage of colicins in vitro and analysis in vivo. Both goals are logical and important but will be very difficult to achieve given the limited resources available to the team; (3) Mechanism of ColD. ColD cleaves tRNAs and the group want to determine the mechanism of cleavage. While worthwhile, this is likely to have less impact than other elements of the programme (mechanisms of other colicin RNases have already been defined); (4) Role of FtsH in processing of DNase colicins. Some intriguing preliminary data relating to a large FtsH-derived proteolytic fragment for ColE2 was presented, suggesting this remains bound to the receptor BtuB. This looks interesting and may provide important new information on the import mechanism; it should be high priority. In summary, given the limited resources available to this group, the committee would suggest focusing on two of the four targets, which is also likely to lead to higher impact papers.

Upon 6b leader retirement in August 2016, a fusion of the yeast translation mechanism sub-team with team 1 will be considered, depending on the evaluation of the scientific and financial situation at that time. The committee supports the careful evaluation of this option at the given time.

Conclusion:

- Strengths and opportunities:

There are potentially interesting developments in both projects.

- Weaknesses and threats:

These are very small teams working on distinct projects leading to dispersion of energies.

The lack of external funding is critical

- Recommendations:

This committee strongly discourages the merger with team 1 unless a robust scientific coherence is found. The rationale for the proposed fusion is fully opaque to this committee. Again, we need to remind that increased critical mass relates to coherent scientific projects, and in no instance can be considered as the sum of researchers working in the same physical space or on the same organism.

Team 7 : Transcriptional and post-transcriptional controls of gene expression

Name of team leader: Mr Harald PUTZER/Ms Jacqueline PLUMBRIDGE

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	4 (3,4)	5 (5)	3 (3)
N3: Other permanent staff (without research duties)	2 (1,5)	3 (2,5)	2 (1,5)
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	6 (4,9)	8 (7,5)	5 (4,5)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1 from 1/12/12	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	3

• Detailed assessments

Assessment of scientific quality and outputs:

The team was constituted in 2002 around two PIs interested in how bacteria adapt gene expression to environmental changes. Each PI conducted parallel and independent research generating de facto two subgroups, one on regulation mechanisms acting on RNA at the co- and post-transcriptional level (subgroup #1), the other on transcriptional adaptations implicating trans acting factors NagC and Mlc controlling use of amino sugars (subgroup #2). Each PI is recognized in its own field and significant contributions were made during the past five years. The team is lacking scientific coherence and the scientific reason why the two subgroups are not considered two independent teams is unclear to this committee. As in other teams of the Unit, the increase in critical mass is only apparent. The two subgroups are therefore analyzed separately.

Subgroup #1. The project to study gene regulation in gram positive (*Bacillus subtilis*) using as a reference the gram negative *Escherichia coli*, which diverged ~2 billions years ago, is relevant. Such comparative approach confirmed that regulation systems could evolve convergently towards the same function. Importantly, the studies in *Bacillus* allowed identification of 2 new RNases (RNase Y and J) and among them one with an unexpected 5->3' exonuclease activity for a bacterial RNase. This paved the way for a fruitful work and collaborations on the structure-function analysis of this enzyme. The scientific quality is very good. In total, subgroup #1 has produced or co-produced over its research theme 10 original articles and 1 review published in: i) journals with high impact (1 *Nat. Struct. Mol. Biol.*, 1 *EMBO J*, 2 *Nucleic Acids Res*earch) and for all of them except one *Nucleic Acids Research* by insuring the leadership in the work presented, ii) good journals of specialty (3 *Mol. Microbiol.*, 2 *Microbiology*, 1 *Structure*).

Subgroup #2. The NagC and Mlc transcriptional regulators are key players for carbohydrates and amino sugars catabolism. The work based on a structure-function analysis helped to decipher the molecular bases of their respective specificity towards *cis*-acting DNA sequences. In addition, the NagC regulon was enlarged to two unexpected genes, and progress were made in the comprehension of peptidoglycan recycling in *E. coli* and *B. subtilis*. The productivity together with the scientific quality of this subgroup is good in regard of its very small size with 10 original articles and 1 book chapter published in good microbiology journals (4 *Mol Microbiol*; 1 *J. Biol Chem*; 3 *J. Bacteriol.*, 1 BBA, 1 *J. Mol. Microbiol. Biotechnol*). No data were presented in high impact journals of broad audience.

Assessment of the unit's academic reputation and appeal:

The team received major fundings with 2 ANR "Blanc" (one of such contract for each subgroup), supplemented by 1 cooperation programm of CNRS-Mexico (subgroup #2) and 1 in the frame of an interdisiciplinary CNRS program (subgroup #1). Both subgroups of the team have developped fruitful international and national collaborations. However, there is a lack of invited conferences.

Subgroup #1 attracts PhD students despite the absence of faculty staff in the team and the absence of any implication in local teaching activities. Through a colaboration with one UMR of the IBPC, the subgroup was the corner stone to set up task "Gene expression from bacteria to organelles" in the labex project "DYNAMO".

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

N/A

Assessment of the unit's organisation and life:

In spite of the lack of scientific coherence in the team, there appears to be good cohesion between the two subgroups.

There is fruitful cross interaction between subgroup #1 and team 3 about RNases structure-function study.

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

Among the 7 teams of the Unit, team 7 trained the largest number of theses (5 have been defended during the contract period). The PI conducting the work on post-transcriptional regulation (subgroup #1) had a high level of training in theses as well as Master degree, including supervision and co-supervision of 4 theses. Some of the students were from universities outside Paris. Nevertheless, the team does not show a strong international attraction at the post-doctoral level. Subgroup #2 contributed to the training and graduation as CNAM Engineer of one non-permanent staff member.

Assessment of the five-year plan and strategy:

The project, still organized in two separate axes, is in continuum and development of the previous works performed by each subgroup.

For subgroup #1, project is strong and will move to concentrate on gene regulations implicating the RNases J and Y in B. subtilis which is seen as well focused and relevant. It is planned to implement a multidisciplinary strategy on combining molecular and cellular approaches for structure-function studies on RNase Y, and to study expression control of genes encoding RNases J1/J2 and Y. Moreover, in the context of the labex DYNAMO, the project includes the study of the chloroplastic RNase J in Chlamydomonas.

For subgroup #2, the project is deliberately conservative in the perspective of retirement of its PI during the upcoming contract period. It aims at completing the ongoing projects on the bacterial regulation of amino sugar usage. Nevertheless, it should be more focused to be completed by a single working person.

Conclusion:

- Strengths and opportunities:

The team was able to implement relevant collaborations within and outside the Unit that helped to publish their data in high-ranking journals. Scientific production is leading in a competitive field. Both team leaders have also demonstrated their strong ability to secure fundings and develop fruitful collaborations.

- Weaknesses and threats:

The proposed strategy to include another PI working on another unrelated project, e.g. control of sporulation in Bacillus has not convinced the committee. This merging is not seen as necessary to allow the sporulation project to go to an end before the retirement of the PI conducting this work. The perception on the specialty of team 7, which is already dichotomous, will be more blurred.

- Recommendations:

The scientific output and the project of the two subgroups forming this team are both good. Retirement of one of the PI (subgroup #2) during the upcoming contract period will improve the scientific coherence of the subgroup working on RNA as a team. So the committee recommand the team not to create an additional complexity by including a new PI with another unrelated subject.

5 • Conduct of the visit

Visit dates:

Start: Thursday 6 december 2012 at 9:00

End: Friday 7 december 2012 at 15:00

Visit site(s): Intitute of Physico-chemical Biology

Conduct or programme of visit:

Day one – 6 december 2012

9:00 Welcome (closed-door) Visiting committee with the AERES Scientific advisor
9:15 AERES representative: the role and procedures of AERES
9:30 Direction of the unit: Presentation of the past activities and projects

10:30 Coffee break

10:45 Team RNA helicases
Name of the team leaders Mr Marc DREYFUS/Mr Kyle TANNER
11:40 Team Control of sporulation in *Bacilli*
Name of the team leader Mr Patrick STRAGIER

12:10 Team Transcriptional and post-transcriptional controls of gene expression
Name of the team leader Mr Harald PUTZER/Ms Jacqueline PLUMBRIDGE

13:10 Lunch

14:00 Parallel meetings with personnel:
Discussions with engineers, technicians, administrative
Discussions with staff scientists
Discussions with students and post-docs

15:30 Team RNA maturation and degradation
Name of the team leader Mr Ciaran CONDON

16:25 Coffee break

17:00 Team Anti microbial cytotoxins, translation mechanisms
Name of the team leader Ms Valerie HEURGUÉ-HAMARD/ Mr Miklos de ZAMAROCZY

18:00 Debriefing on the team presentations

Day two: 7 december 2012

8:30 Team Translational control of gene expression in bacteria
Name of the team leader Mr Mathias Springer

9:00 Team RNA control of gene expression
Name of the team leader Ms Eliane HAJNSDORF/Ms Maude GUILLIER

9:55 *Coffee break*

10:10 Discussion with the representatives of the managing bodies

10:35-11:20 Discussion with the heads of the unit (past director and future directors)

11:20-15:00 Private meeting of the visiting committee (in presence of the AERES scientific advisor) including lunch

15:00 End of the visit

Specific points to be mentioned:

Due to meteorological conditions, Mr Gerhardt WAGNER, University of Uppsala, Sweden, could not join the committee for the on site visit.

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

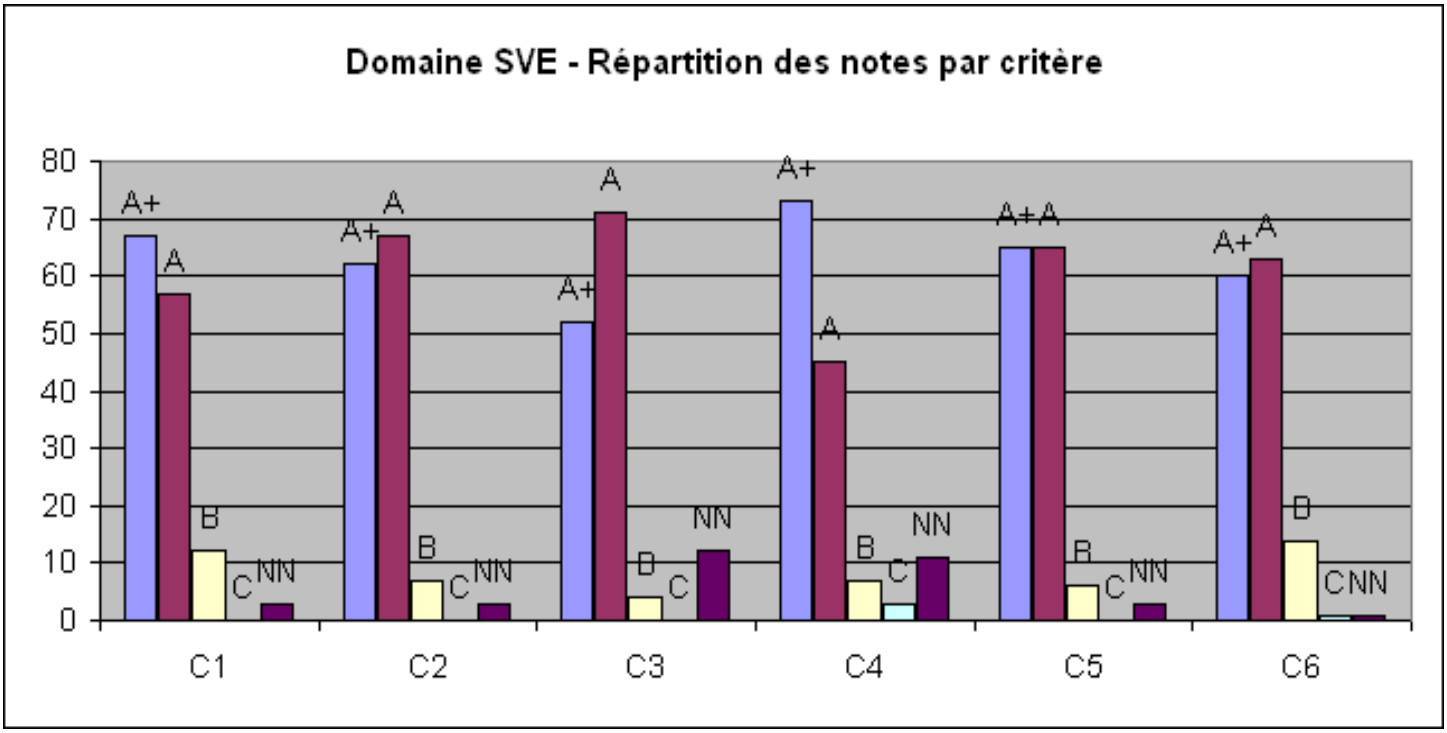
Grades

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

Percentages

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

Histogram



7 • Supervising bodies' general comments

université PARIS DIDEROT PARIS 7

Le Président

P/VB/NC/YM – 2013 - 119
Paris, le 26 avril 2013

M. Pierre Glaudes
Directeur de la section des unités de l'AERES
20 rue Vivienne
75002 PARIS

S2PUR140006433 - Expression Génétique Microbienne - 0751723R

Monsieur le Directeur,

Je vous remercie, ainsi que les membres du comité de visite, pour l'envoi du rapport d'évaluation concernant le laboratoire «Expression génétique microbienne», rapport qui souligne le bon niveau scientifique de l'unité dans l'ensemble, mais également l'implication de son l'équipe dans le labex « DYNAMO » et l'IDEX.

Je me réjouis également des commentaires soulignant les efforts faits par l'équipe pour réduire la parcellisation des sujets de recherche, et donc une meilleure redistribution des chercheurs sur les sujets les plus innovants de l'unité.

Enfin, comme le comité le mentionne, le projet de devenir UMR (CNRS-Université unité mixte) visant à renforcer le lien avec l'Université Paris Diderot et permettre une augmentation du recrutement des étudiants et de chercheurs permanents, doit être un projet réfléchi par l'établissement et les tutelles du laboratoire, en tenant compte des moyens disponibles de chacun.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de toute ma considération.

Vincent Berger

Tél +33 (0) 1 57 27 55 10
Fax +33 (0) 1 57 27 55 11
secretariat.president@univ-paris-diderot.fr
www.univ-paris-diderot.fr

Adresse Postale
Présidence
Grands Moulins
75205 Paris Cedex 13

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General comment
on the AERES report on UPR9073 (Expression Génétique Microbienne)

On behalf of all members of the Unit, I would like to thank the Committee members for their time and efforts in evaluating our Unit and suggestions for improvements in governance. In general, we found the evaluation very professional and useful. However, there are a few points that we feel deserve further comment, some of which concern the whole Unit and, in one case, an individual team.

Assessment of the Unit as a whole.
The choice of the new directors. The Committee was "surprised" by the way Harald Putzer and Ciaran Condon, the new directors for the EGM, were nominated. We want to emphasise that, although atypical, the procedure used was the only applicable one in this particular case and that at each step it was fully supported by the CNRS administration. The two candidates were equally supported by the vote, and therefore they decided to share the charge, one being the deputy-director of the other, with an exchange of roles at mid-term. This agreement to two 2.5-year terms rather than successive 5-year terms (as suggested by the evaluation Committee) was warmly supported by the directeur scientifique adjoint (DSA) in charge of our laboratory, Mr. J-C Michalski, as well as by our lab council.

Relations with other Units of the Institut de Biologie Physico-Chimique (IBPC). We confess that we were puzzled by the statement that "contacts with researchers of the other Units of the Institute appear to be few and poorly developed". Indeed, the EGM has been a major driving force in the elaboration of the Labex "DYNAMO", which establishes collaborative links between all the IBPC Units and has a total budget of 10 M€ for the next 8 years. We feel that this achievement might have deserved a positive comment.

General style of the report. We appreciate the very neutral, factual wording of the report. Nevertheless, a small dose of encouragement might have been appropriate, particularly for those who invested their time in the managing of the Unit during the last term or those who prepared the evaluation documents, a considerable effort for a large fraction of the year 2012.

Assessment of group 6a.
We feel that group 6a has been harshly evaluated, based in part on a couple of factual errors. One key publication in NAR, with the group leader as co-corresponding author was missed; one grant (either ANR Jeune Chercheur or Human Frontier Science Program) was not

counted. These errors for group 6a, coupled with a recent PhD student that was missed in group 6b, give the impression of a mediocre publication record or lack of recent attractiveness that we feel is quite unjustified and potentially damaging to the group's future prospects.

Written in Paris, April the 11th 2013

Marc DREYFUS
Directeur CNRS UPR 9073