ARN - Architecture et réactivité de l'ARN

Rapport Hcéres

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

Research Units Department

AERES report on Unit:

Architecture et Réactivité de l'ARN

ARN

Under the supervision of the following institutions and research bodies:

Université de Strasbourg

CNRS

November 2011

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

Unit

Name of unit:	Architecture et Réactivité de l'ARN
Acronym of unit:	ARN
Label requested:	UPR
Present no.:	9002
Name of Director (2009-2012):	Mr Eric WESTHOF
Name of project leader (2013-2017):	Mr Eric WESTHOF (Director) Ms Pascale ROMBY (Adj-Director)

Members of the committee of experts

Chair:	Mr Agamemnon CARPOUSIS, Toulouse
Experts:	Mr Yves HENRY, Toulouse
	Ms Dagmar KLOSTERMEIER, Münster, Germany
	Mr Daniel KOLAKOFSKY, Genève, Switzerland
	Mr Ben LUISI, Cambridge, United Kingdom
	Ms Anita MARCHFELDER, Ulm, Germany
	Mr Pierre PLATEAU, Palaiseau (Représentant CoNRS)
	Ms Anne-Catherine PRATS, Toulouse
	Mr Peter SCHÜSTER, Vienna, Austria
	Mr Markus WAHL, Berlin, Germany

Representatives present during the visit

Scientific Delegate representing AERES:

Mr Yves GAUDIN

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

Mr Gilbert DELÉAGE, CNRS

Mr Wais HOSSEINI, University of Strasbourg

Report

1 • Introduction

Date and conduct of visit:

The visit took place from November 28th to 30th, 2011 under good conditions. The experts convened on the evening of the 27th to organise the work and share impressions on the paper documents. The next two days were devoted to hearing presentations by team leaders and to formal discussions with various staff groups (students and postdocs, staff scientists, technical staff, and group leaders) and with representatives of the institutions. Finally, a private meeting with the director and the deputy director allowed the management team to clarify a few points. The last day was devoted to a closed-door reunion of the committee to discuss its evaluations and prepare an initial draft of this report.

History and geographical location of the unit, and overall description of its field and activities:

The UPR9002 was first created in 2005. It is one of the three units constituting the Institute of Molecular and Cellular Biology of the CNRS (FRC 1589). The research unit investigates posttranscriptional regulation of gene expression and structure-function relationships of the translation machinery in viruses, bacteria, and eukaryotes. RNA and its numerous roles in biological regulation are the central theme unifying the research of the UPR.

Management team:

Eric WESTHOF (leader of team 11) directs the research unit. He is assisted by deputy a director, Pascale ROMBY (leader of team 10), who is proposed to take the direction when Eric WESTHOF retires (January 2015).

Unit workforce:

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	11	13	13
N2: EPST or EPIC researchers	27	26	26
N3: Other professors and researchers	1	2	2
N4: Engineers, technicians and administrative staff ***on a permanent position**	20 (19)	21 (20)	
N5: Engineers, technicians and administrative staff * on a non-permanent position	5		
N6: Postdoctoral students having spent at least 12 months in the unit	13		
N7: Doctoral students	25		
N8: PhD defended	23		
N9: Number of Habilitations to Direct Research (HDR) defended	5		
N10: People habilitated to direct research or similar	34	34	
TOTAL N1 to N7	**102**	**62**	**41**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.
Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

2 • Assessment of the unit

Overall opinion on the unit:

An excellent research unit that is highly focused on a central theme: RNA structure and function, and its numerous roles in biological regulation. The research unit has very strong forward momentum based on 1) the recruitment of several new young and dynamic group leaders, 2) the recent award of significant long-term funding (LABEX), and 3) leadership of the deputy director who will take charge when the current director retires.

Strengths and opportunities:

The research unit is built on several well-established teams that have national and international recognition for their scientific contributions. Combined with the establishment of several new teams that have already had significant scientific impact and that are expected to continue making leading contributions in the future, the success of the unit appears to be assured for the next 5 to 10 years.

Weaknesses and risks:

The research unit has no significant weaknesses except for the pending retirement of the current director. Nevertheless, the transition in leadership is well organized.

Recommendations:

The recruitment of a scientific advisory board (SAB) to review the scientific projects of the teams is a good practice that should be continued. The purview of the SAB should be extended to include the creation of groups that emerge from personnel within the unit.

Given the very ambitious scope of the next 5-year project, a smooth transition in leadership will be essential when the current director retires. It is in the best interest of all members of the unit to support fully the future director during this transition.

3 • Detailed assessments

Assessment of scientific quality and production:

The unit published 205 articles in peer-reviewed journals and 42 non-reviewed works (primarily book chapters).

Approximately 15% of the peer-reviewed articles were published in high impact journals (IF >9) including 3 *Angew Chem Int Ed Engl*, 1 *Cell*, 2 *EMBO J*, 3 *Genes Dev*, 1 *Genome Res*, 1 *J Cell Biol*, 1 *Microbiol Mol Biol Rev*, 2 *Mol Cell*, 1 *Nature*, 1 *Nat Genet*, 3 *Nat Methods*, 5 *PLoS Pathogen*, 5 *Proc Natl Acad Sci*, 2 *Science*. About half of these publications come directly from the work of the unit and the other half are collaborative efforts often involving international research consortia.

Of the remaining work published by the unit about half of it is in good journals (IF 5-9) such as *FASEB J*, *Mol Microbiol*, *Nucl Acids Res*, *RNA*, and *Structure*; the other half of the work was published in specialised journals.

The overall scientific production of the unit is excellent.

Assessment of the unit's integration into its environment:

The unit filed 9 patents (see Teams 1, 7, and 8), and it has multiple industrial collaborations (see Teams 1, 6, and 9).

The unit has been very successful in obtaining external funding from national (ANR, ANRS, CNRS ATIP, FRM) and international (EU) sources.

Team 9 was recently awarded an ERC starting grant.

Total external funding for the period under review was 7018 k€.

Four teams are part of a consortium that recently won LABEX funding (Teams 4, 9, 10, and 11).

The unit's integration into its environment, as judged by industrial collaboration and external funding, is excellent.

Assessment of the research unit's reputation and drawing power:

As indicated in the reports on the individual teams:

> Several of the team leaders are well known internationally for their contributions to the fields of posttranscriptional regulation of genetic expression and structure-function relationships of the translation machinery in viruses, bacteria, and eukaryotes.
>
> Members of the unit have won regional and national prizes. The director of the unit was recently elected as a member of the French Academy of Sciences.
>
> Members of the unit are frequently invited to present their work at national and international scientific conferences. They have participated in the organization of numerous regional, national and international scientific events.
>
> Many of the teams are part of national and/or international research consortia.

During the period under review, a total 55 PhD students and 22 postdocs were part of the unit. A significant proportion of these personnel were non-French including students and postdocs from European countries other than France, the Middle East, Japan and China.

Considering the above-mentioned indicators, the unit clearly has an excellent reputation and strong drawing power both at the national and international level.

Assessment of the unit's governance and life:

The governance of the unit is typical of a CNRS laboratory in the life sciences. The unit's structure is based on the research teams. The team leaders together with the director of the unit form a 'directorate' that deals with the day-to-day decisions as well as medium and long-tem planning of scientific projects. The unit has a

council (CDL) that is representative of all members of the unit. The CDL provides a forum for the dissemination of information and discussion.

The unit has an expert Scientific Advisory Board with international membership, and they provided a critical evaluation of the research projects in a 3-day review in December 2010. This exercise was undoubtedly an asset in preparing the unit for the evaluation by the AERES.

The unit has undergone successful restructuring in which four new teams were created during the period under review and two new teams are proposed in the project presented to the AERES committee. These changes have involved the recruitment of several young and dynamic new group leaders.

During their visit to the unit, it became evident to the AERES committee that the director of the unit had a leading role in the renewal and invigoration of the unit.

As the director of the unit will retire during the next mandate, it is planned that the deputy director will take over the direction. The deputy director is an internationally recognized scientist with an outstanding record of achievement. The choice of the future director has the strong support of the members of the laboratory. In addition, the AERES committee is confident that the future director has the management skills that will be needed to lead the research unit.

The university personnel in the unit have an active role in educational activities beyond their normal teaching duties. For example, the director of the unit is Vice President of the University of Strasbourg in charge of research and PhD studies; the leader of Team 3 is head of the Life Sciences PhD School.

The researchers in the unit have active roles in regional and national management and evaluation of research. For example, three members of the current unit are part of the National Committee section that evaluates CNRS researchers in the area of structural biology and biochemistry.

The unit has a policy of actively encouraging participation in national and international organizations such as the French Biochemistry and Molecular Biology Society (SFBBM) and the RNA Society.

The successful restructuring of the unit is a strong indicator that the unit is well governed. The members of the unit are involved in a variety of scientific and educational activities that demonstrate a high level of commitment to creating and maintaining a dynamic and stimulating research environment.

Assessment of the strategy and 5-year project:

The 5-year project of the research unit is based partly on the projects of the individual teams. The AERES committee has made detailed comments on these projects in the reports on the individual teams. In addition to the research projects of the teams, the unit is affiliated with two other research units in Strasbourg as part of the NetRNA LABEX project, which is coordinated by the director of the unit.

The 5-year project is very well structured. The proposed research is original and ambitious. The unit, as it is currently structured, is well positioned to manage this project.

The AERES committee was impressed with the global coherence of the research project.

Assessment of the unit's involvement in training:

The research unit has strong ties to the university and it attracts highly motivated Master's and PhD students.

During the period under review, 23 PhD theses were defended and 6 members of the unit were habilitated to direct PhD students (HDR) demonstrating a strong capacity for providing high quality training of doctoral students.

Each team in the unit routinely trains several Master's students every year.

The visiting committee interviewed the PhD students and postdoctoral researchers. All of the PhD students had salary support for 4 years of PhD training (the 4th year being sometimes partly paid by the research unit on its own funds). The students and postdocs all have opportunities to attend national and international scientific conferences. The Life Sciences PhD School has a program to monitor the progress of students in which there is a formal interview during the second year in the absence of the thesis supervisor.

Overall, the students and postdocs are well integrated, and participate actively in the research unit. They are pleased with their working environment and showed remarkable communal identity.

4 • Team-by-team analysis

Team 1: Biophysics and Structural Biology

Team leader: Mr Philippe DUMAS

Workforce

Workforce	Number on 06/30/2011	Number on 01/01/2013	2013-2017 Number of producers**
N1: Professors or assistant professors	0	0	0
N2: EPST or EPIC researchers	4	4	4
N3: Other professors and researchers	0	0	0
N4: Engineers, technicians and administrative staff * on a permanent position	1,5	1,5	
N5: Engineers, technicians and administrative staff * on a non-permanent position	1		
N6: Postdoctoral students having spent at least 12 months in the unit	2		
N7: Doctoral students	2		
N8: PhD defended	1		
N9: Number of Habilitations to Direct Research (HDR) defended	0		
N10: People habilitated to direct research or similar	4	4	
TOTAL N1 to N7	**10,5**	**5,5**	**4**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The team, which includes a DR1, DR2 and two CR1s, has a critical mass of expertise in crystallography and biophysics. The team members are capable and careful experimentalists.

The key topics of investigation are the HIV reverse transcriptase, the multi-functional HIV Vif protein, and the structure of complex RNA, such as the HIV dimerisation element. These are studied using X-ray crystallography and other biophysical tools. The team is also involved in method development to study RNA folding and kinetics of RNA-ligand interactions.

The research work represents important topics; in particular, the studies on the interaction of the HIV reverse transcriptase with primer/template and nucleotide substrates and on the novel inhibitor mechanism of that enzyme may help to identify new lead compounds for therapy. There are very effective interactions of this team with other groups within the unit on HIV to study the Vif/cytosine deaminase interaction structurally. This is a high risk but important project.

The group has published 29 articles in peer-reviewed journals, 16 of which come directly from their work. Their output is solid, and their strongest contributions are in *Angew Chem Int Ed Engl* (2), *J Mol Biol* (1), *Mol Microbiol* (1), *Nucleic Acids Res* (2), and *RNA* (2). The Faculty of 1000 has highlighted two of these articles. The group has developed a novel kinetic approach with calorimetry, and this work has recently been published in *J Am Chem Soc* (2011). Note that *Angew Chem Int Ed Engl* (IF=12.7) and *J Am Chem Soc* (IF=9.0) are first-rate international journals in chemistry and multidisciplinary sciences.

The team has filed three patents and has collaborations with two companies (pharmaceuticals and biophysical equipment).

Assessment of the research team's integration into its environment:

The research topics studied by this group fit well to the remit of the unit. The group is well integrated into the unit, as judged by inter-team publications as well as by the support they provide for other groups in applying biophysical techniques.

The work has potential biomedical importance for treatment of HIV infection. Indeed, the work has lead to patents relevant to treatment of HIV.

The team has been successful in obtaining support from the ANRS (2 grants, 180 k€) and ANR (3 grants, 2 as coordinator, 433 k€).

Assessment of the research team's reputation and drawing power:

Invitations to international meetings are satisfactory. The proportion of non-permanent staff (two postdocs, 2 PhD students) to permanent staff is small and could be improved. The team has good international collaborations (Italy, Holland and Austria). Some of their collaborations are within France, where they are part of a collaborative network of groups that have worked on HIV for many years.

Assessment of the strategy and 5-year project:

The proposed research project has four identified aims: 1) to determine the structure of the human cytosine deaminase APOBEC3G alone or in complex with Vif, 2) to continue their crystallographic work on HIV1 reverse transcriptase, 3) to study the kinetics of riboswitch folding, and 4) to continue the development and application of kinetic analyses using isothermal titration calorimetry (ITC).

The crystal structure of AQPOBEC3G will hopefully help to elucidate how this deaminase acts selectively during viral infection. For this, they will have to diversify approaches to express the protein and to identify suitable crystallization targets. This should be a priority of their efforts and the team needs to strengthen their strategies. In particular, they should exploit in house expertise with eukaryotic expression systems to explore the preparation of recombinant materials.

Some of the subsidiary future aims to develop methods in crystallography and calorimetry are valuable scientifically, but it must be insured that these methods can be widely disseminated (for example, with user-friendly graphics interfaces).

The group proposes to implement single molecule methods, such as FRET. This makes sense as a complementary technique. Although the technique per se is well developed, its application to co-translational RNA folding is challenging. The team needs to consider carefully the risk vs. benefits of implementing this approach.

Conclusion:

Overall opinion on the team:

The members of the team are highly experienced structural biologists, and they are working on important and challenging research problems.

Strengths and opportunities:

The work on the HIV RNA, reverse transcriptase, and the inhibitors of the innate immunity response has potential for strong synergy with other research groups in the institute and in France.

The collaborative work on the HIV reverse transcriptase might be well suited for fragment based drug discovery, but it is appreciated that this activity entails a commitment of time and resources, and it may not be within the remit of the research group.

Weaknesses and risks:

The team works on diverse topics, and there should be more effort to consolidate the diverse lines of research.

Recommendations:

The team should reinforce internal collaborations with the teams working on APOBEC3G and RNA regulatory mechanisms.

The expertise to probe RNA structure in a time resolved manner has potential for collaborations within the institute. In this regard, it would be ideal if they could pursue the planned collaboration with Team 10 to study, by time-resolved probing experiments, interactions of the translation initiation complex with folded mRNA species.

The commitment of the team to develop platforms and tools for the whole institute is appreciated, but it does represent a burden to their own research. The appointment of a research manager to run the ITC as a service might alleviate this.

The team should increase the proportion of student and postdocs to permanent personnel.

Team 2: Evolution of translation initiation systems in eucaryotes

Team leader: Mr Gilbert ERIANI

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	0	1	1
N2: EPST or EPIC researchers	2	3	3
N3: Other professors and researchers	0	0	0
N4: Engineers, technicians and administrative staff * on a permanent position	0,5	1	
N5: Engineers, technicians and administrative staff * on a non-permanent position	0		
N6: Postdoctoral students having spent at least 12 months in the unit	1		
N7: Doctoral students	3		
N8: PhD defended	1		
N9: Number of Habilitations to Direct Research (HDR) defended	0		
N10: People habilitated to direct research or similar	1	2	
TOTAL N1 to N7	**6,5**	**5**	**4**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

This small team, created in 2007, has performed a very elegant and innovative study of histone H4 mRNA translation initiation. They have uncovered a novel mechanism of translation initiation that is different from both the canonical scanning mechanism and the IRES-dependent internal initiation mechanism. They provided detailed mechanistic insights into this novel and unexpected translation initiation mechanism. This important finding has recently been published in *Mol Cell* (2011).

The team has also continued working on the editing reactions catalyzed by aminoacyl-tRNA synthetases, the former main research topic of the team. They have been very active in this area as evidenced by the publication of 7 research articles in good journals (1 *Biochem J*, 2 *J Biol Chem*, 3 *Nucl Acids Res*, 1 *RNA*). This work is the fruit of collaboration with a team in China that has had the leading role in the research.

Altogether, the work performed is excellent; in particular, the *Mol Cell* paper is an important contribution to the translation field, which has opened up a new mechanism of translational initiation. The team is well placed to explore the generality of this mechanism.

Assessment of the research team's integration into its environment:

The team's research fits well with longstanding interests of the research unit.

Given the rather small size of the team, the funding secured by the team is excellent (2 ANRs coordinated by the team leader, 450 k€; 1 ARC, 50 k€).

Assessment of the research team's reputation and drawing power:

The team has a long-standing collaboration on editing reactions catalyzed by aminoacyl-tRNA synthetases with a Chinese group. This collaboration is very active (seminars, student exchange) and productive, as evidenced by the number of publications. The 'drawing power' of the team is expected to increase with the striking finding published in *Mol Cell*, which was featured on the cover with an accompanying commentary.

Assessment of the strategy and 5-year project:

The research of the group will be almost entirely focused on the study of non-canonical processes of translation initiation in eukaryotes. The work on aminoacyl-tRNA synthetases will become a side project, and may come to a close in the long run. This decision to focus on translation initiation is a reasonable strategic move.

Three main avenues of research are envisaged: 1) continuation of the work on histone H4 mRNA and its extension to other mRNAs, 2) genome wide screen for mRNAs able to interact with eIF4E in a cap-independent fashion and 3) investigation of translation initiation mechanisms of selenoprotein mRNAs. This project includes research that is a logical follow-up to the work described in the *Mol Cell* paper (accurate mapping of the cap-binding pocket on the H4 mRNA; high-resolution study of the eIF4E/4E-SE interaction), and should yield results in the short to medium term.

Also already well advanced and highly interesting is the cryo-EM study of 80S ribosomes stalled on H4 mRNAs. Other aspects of the planned research are more risky (crystallographic study of the cap-binding pocket, investigation of the cryo-EM structure of 48S and eIF4F complexes bound to H4 mRNA, genome wide screen) but could lead to high impact results.

A researcher from another team will join Team 2, bringing along the discovery that selenoprotein mRNAs carry a trimethyl cap. The new research theme fits well with the team's ability to elucidate the functional consequences of the presence of this unusual cap on mRNAs. The project on selenoprotein mRNAs also features studies on UGA Sec recoding, cryo-EM studies of ribosome bound selenoprotein mRNAs and nucleo-cytoplasmic export of selenoprotein mRNAs.

The project involves collaborations with a team in Poland and two outstanding structural biology teams in Strasbourg, which should strengthen the national and international connections of the team. The overall project is highly ambitious given the size of the team.

Conclusion:

Overall opinion on the team:

A small team that has produced excellent work in the translation field and that has a very strong potential. It is expected that its international visibility will increase significantly in the coming years.

Strengths and opportunities:

The project reflects a good balance of more secure projects that are the logical follow up of the recent work of the team and ambitious projects that could lead to high impact results.

The collaborations envisaged with excellent groups with complementary expertise to that of the team are appropriate and should widen the national and international connections of the team.

Weaknesses and risks:

This team has no significant weakness although its small size means that the leader needs to be especially careful to keep the team well focused.

Recommendations:

Some aspects of the project concerning selenoprotein mRNAs may need to be more focused, taking into account the size of the team.

The manner in which all the histone mRNAs are co-ordinately translated is an attractive topic of investigation, for which the group is well qualified.

Team 3: Mitochondrial translation and disorders

Team leader: Ms Catherine FLORENTZ

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	2	2	2
N2: EPST or EPIC researchers	3	3	3
N3: Other professors and researchers	0	0	0
N4: Engineers, technicians and administrative staff * on a permanent position	1	1	
N5: Engineers, technicians and administrative staff * on a non-permanent position	0		
N6: Postdoctoral students having spent at least 12 months in the unit	3		
N7: Doctoral students	5		
N8: PhD defended	3		
N9: Number of Habilitations to Direct Research (HDR) defended	2		
N10: People habilitated to direct research or similar	4	4	
TOTAL N1 to N7	**14**	**6**	**5**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

This team is the result of a fusion in 2009 with the team of a retired group leader.

The focus of the team is on the mitochondrial (mt) translation machinery, in particular on mt aaRSs, tRNAs and RNase P. One main line of research is concerned with the evolution of the mt aaRS/tRNA systems. Another line deals with the structure-function relationships of these molecules and with the molecular mechanisms of diseases associated with mutations in the mt tRNAs and aaRSs. The problems are being tackled with biochemical, biophysical, bioinformatics and structural techniques.

Since the merger with an emeritus group, there are also strong activities in the development of crystallization techniques and instrumentation. This part of the research program is more applied and promises to improve throughput of biomacromolecular crystallization. The usefulness of the methods developed is documented, for example, by the successful X-ray structure analysis of a virus particle.

Major achievements include the delineation of unusual structural properties in mt tRNAs, the determination of the first two crystal structures of mt aaRSs and the discovery of unexpected translation start sites in mt aaRS. A major joint publication in *Nature Genetics* with another group, for which the team provided functional analyses, revealed mutations in an aaRS as a newly understood cause for neurodegeneration.

Several key results now open the way to new research questions. For example, the discovery of unexpected N-terminal ends in mt aaRSs may pave the way to their successful overproduction. The discovery of disease-linked mutations in nuclear encoded aaRS expands the spectrum of factors involved in mt-linked pathologies and indirectly suggests novel functions for mt aaRS, which can now be explored.

The group has been very productive with 25 original publications, 20 of which come directly from their work, and 4 reviews/book chapters. The publications include two invited reviews. The majority of publications are in good journals including *Biochem J* (1), *Cryst Growth Des* (5), *FEBS Lett* (2), *Lab Chip* (1), *Nucl Acids Res* (2), and *RNA* (2).

Assessment of the research team's integration into its environment:

The work is of fundamental molecular biological interest as well as of relevance for human health.

The team fits well with the remit of the unit. The research program makes optimal use of expertise and technologies provided by other teams of the unit (e.g. molecular modelling, biophysical analyses) and in turn provides novel methodologies beneficial for the unit (vaccinia virus-based protein expression, crystallization techniques and tools) and beyond (tRNA databases and annotation tools).

Most team members are heavily involved in teaching. Furthermore, the team leader is director of the PhD school "Health and Life Sciences", the largest graduate school on campus. The keen interest of the team in education is also documented by two contributions to the journal *Biochemistry and Molecular Biology Education* and by the production of a French/English movie on the molecules of life.

The team has been successful in obtaining external funding (3 ANR grants, 1 as a coordinator, 356 k€ total).

Assessment of the research team's reputation and drawing power:

The team is visible both nationally and internationally. The head of the team is a leading figure in her area of expertise. Members of the team are frequently invited to international seminars and conferences (10 invited seminars, 24 invited lectures at national or international conferences). Team members have organised two meetings.

A PhD student from the team was awarded the "Prix de Thèse" of the Société de Biologie de Strasbourg (2009).

The team has been successful in recruiting researchers on all levels. The group has strong ties to the University of Leipzig, Germany, from where a number of PhD students and postdocs have been recruited.

The team established, maintains and curates a number of databases on tRNAs that are used by researchers worldwide and thus contribute significantly to their international visibility.

The group is collaborating with a number of other groups nationally and internationally in the areas of pathologies linked to the mitochondrial translational apparatus and in the development of new crystallization techniques and instrumentation.

Assessment of the strategy and 5-year project:

The project is hypothesis-driven and original. It is soundly based on good preliminary results.

The proposal presents an integrated approach with the following aims: 1) to decipher structure-function relationships in components of the mt translational apparatus, 2) to investigate their evolutionary relationships in particular to the bacterial counterparts and the molecular basis for adaptations to the special needs of mitochondria, 3) to uncover putative new cellular functions of these components, and 4) to elucidate the molecular basis for disease-causing mutations in these factors.

The methods to be applied are suitable to tackle the research problems. The program is well structured and coordinated and the goals are feasible. There are both medium and long-term prospects; for example, stepwise structural analysis of individual aaRS will eventually lead to an encompassing view on the structural repertoire of mt aaRS. In the future, the program can be expanded by including other components of the mt translational machinery.

Conclusion:

Overall opinion on the team:

The team is well focused. Different members provide complementary expertise and work together constructively and efficiently.

Strengths and opportunities:

The team mutually profits from and contributes to key technologies within the unit.

Weaknesses and risks:

This team has no significant weaknesses.

Recommendations:

Presently, the evidence for novel functions of mt aaRS is circumstantial. Although it is probably worthwhile to explore this possibility, the team needs to manage the time and effort invested in this project.

If results are obtained using fractionation approaches, the investigation of the sub-mt localization of aaRS, tRNAs or other components of the mt translation apparatus should be taken to a higher level.

The team should include difficult to express proteins from other teams in the unit as a test for their vaccinia virus-based expression system to assess the potential of this system as a technology for the entire unit.

The team should be encouraged to tackle somewhat more risky lines of investigation such as including more complex assemblies in the structural analyses, or embarking on a quest for new ncRNA-based regulation in the mt translation machinery.

Team 4: Aminoacylation of eukaryotic tRNAs : control and pathogenicity

Team leader: Ms Magali FRUGIER

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	0	0	0
N2: EPST or EPIC researchers	3 (2,3)	2 (1,8)	2
N3: Other professors and researchers			
N4: Engineers, technicians and administrative staff * on a permanent position	2 (1,6)	2 (1,6)	
N5: Engineers, technicians and administrative staff * on a non-permanent position	0		
N6: Postdoctoral students having spent at least 12 months in the unit	2 (1,5)		
N7: Doctoral students	3		
N8: PhD defended	2		
N9: Number of Habilitations to Direct Research (HDR) defended	0		
N10: People habilitated to direct research or similar	2	2	
TOTAL N1 to N7	**10 (8,4)**	**4 (3,4)**	**2**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

This team, created in 2007, concentrates on two projects: 1) Investigations concerning the incorporation of host tRNAs in *Plasmodium* and 2) analysis of human tRNA synthetases potentially involved in novel functions and diseases.

The first project led to the discovery of a tRBP (transfer RNA binding protein), which is involved in the import of host tRNAs into the *Plasmodium* cell. This is an attractive project with additional interesting results to be expected.

The second project dealing with human tRNA synthetases also yielded interesting results. The team showed that the human AspRS is regulated by binding of tRNAAsp7 to the 3´ UTR of the mRNA. This work resulted in a *PNAS* publication that was highlighted by an accompanying commentary.

The team published 9 articles and 1 book chapter. Five of the articles come directly from their own work (*FEBS Lett*, *J Biol Chem*, *PNAS*, *RNA*, *Structure*).

Assessment of the research team's integration into its environment:

The research is fundamental and could have important medical applications.

The team is part of a consortium that recenty won LABEX funding.

The team has obtained competitive funding from charities (La Ligue Contre le Cancer, AFM), the ANR (1 project coordinated by the team leader, 245 k€) and the European Commission (consortium of 8 laboratories, 288 k€ to Team 4).

Assessment of the research team's reputation and drawing power:

The team fits well with the remit of the unit.

The team leader obtained a regional prize of the FRM and co-organised an international meeting.

This project is well integrated into European research networks. The team has collaborated with three foreign groups (Australia, Spain and Uruguay).

Assessment of the strategy and 5-year project:

The group will continue to analyse the likely import into the parasite of host tRNAs, and the fates and roles of these imported host tRNAs on the differentiation of the parasite. It is essential for the group to clearly demonstrate the import of the host tRNAs into the parasite.

The group will attempt to determine the crystal structure of tRBP and its role in vivo. They will investigate the localization and processing of internalized host tRNAs and the proteome of sporozoites containing host tRNAs. This part of the project is a logical continuation of the research already carried out in the team.

In addition to unravelling the structure of tRBP the team will study the potential additional roles of the host tRNAs in the *Plasmodium* cell in particular in light of the fact that tRNA derived fragments might be involved in gene regulation. Furthermore, they want to optimise bacteria for expressing *Plasmodium* proteins.

The second project consists of the study of the structure of the 5' UTR of the GlyRS mRNA, which accumulates in neuron cells. Future studies will involve the analysis of tissue specific expression of GlyRS and its involvement in disease.

Conclusion:

Overall opinion on the team:

The team has produced interesting and original research on important topics from both fundamental and medical points of view.

Strengths and opportunities:

The team is working on an attractive and original hypothesis and has already gathered important experimental evidence to support it. They have an important and atypical complementary expertise in the tRNA field and *P. falciparum* biology.

Weaknesses and risks:

The attractive hypothesis of host tRNA import requires further validation.

Recommendations:

The team should not delay any longer publication of their interesting results on tRBP.

Team 5: Evolution of non-coding RNAs in yeasts

Team leader: Mr Fabrice JOSSINET

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors		3	3
N2: EPST or EPIC researchers		0	0
N3: Other professors and researchers		0	0
N4: Engineers, technicians and administrative staff * on a permanent position		0,5	
N5: Engineers, technicians and administrative staff * on a non-permanent position			
N6: Postdoctoral students having spent at least 12 months in the unit			
N7: Doctoral students			
N8: PhD defended			
N9: Number of Habilitations to Direct Research (HDR) defended			
N10: People habilitated to direct research or similar		3	
TOTAL N1 to N7		**3,5**	**3**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

This new team will be composed of three university lecturers.

The team leader has in recent years focused on the development and use of bioinformatics tools designed to model RNA 3d structures. In particular, he has developed the S2S graphical tool allowing the structural alignment of an RNA sequence of unknown structure with a related RNA, for which the tertiary structure has been solved. He has interconnected the S2S graphical tool with an RNA 3D viewer and modeller termed "Assemble". "Assemble" allows the improvements of 3D models obtained using S2S. Importantly, these tools have been tested and used to model 3D structures of eukaryotic ribosomal RNAs, using the constraints of cryo-EM data provided by a group in Germany.

The bioinformatics tools developed by the team leader are proving of great use to the RNA structure community. He has a good publication record, with a well-balanced mix of articles in good journals and collaborative articles in high impact journals (2 *PNAS*, 2 *Nat Methods* and 1 *Science*). The collaborative work on eukaryotic ribosome structure has attracted wide international attention.

Two university lecturers from another research unit having experience with yeast molecular genetics will join the team leader. Together, during the period under review, the three university lecturers who will constitute the new team have contributed to 13 articles of which 4 were signed first author including articles in *Bioinformatics* and *Cur Opin Microbiol.* The team leader signed a review in *New Biotechnology* as last author.

Assessment of the research team's integration into its environment:

The bioinformatics tools developed by the team leader are now publicly available through web services hosted by the server of the unit. Furthermore, his work is part of an international effort to improve the archiving and visualization of RNA data.

Assessment of the research team's reputation and drawing power:

The team leader has been involved in several high profile collaborations. Furthermore, he and another member of the team have been invited to give talks at international meetings.

Assessment of the strategy and 5-year project:

The three university lecturers forming the new team have complementary expertise: the team leader is an expert in bioinformatics and RNA structure prediction, while the other two members have experience in yeast genome analysis and yeast genetics. Together, they aim to exhaustively retrieve and analyse ncRNAs from the genomes of some 75 yeast species published by the Genolevures and Dikaryome projects. This will be performed using comparative bioinformatics combined with deep-sequencing approaches. They will start with the identification of "house-keeping" ncRNAs (tRNAs, rRNAs, UsnRNAs, snoRNAs, RNase P, etc.) to study their mode of evolution. There is little doubt that this part of the project will be successful.

In parallel, they will identify and compare the ncARNs expressed from pathogenic and non-pathogenic yeast species of the genus Candida, to select those that are specific to the pathogenic species. By mutational analyses, they will investigate the roles of the pathogen-specific ncRNAs in the establishment and maintenance of regulatory networks associated with virulence. This part of the project is largely a fishing expedition whose outcome cannot be predicted.

Altogether, this ambitious and interesting project should significantly increase our understanding of gene regulation networks involving ncRNAs. In spite of the small size of the team, the initial aims of the project are realistic, for the following reasons. The team can rely on the help of two unit members specifically recruited to analyse deep-sequencing data (in the framework of the NetRNA LabEx). They will also greatly benefit from an already initiated close collaboration with experts in Candida genetics.

Conclusion:

Overall opinion on the team:

The work of the team leader on RNA 3D structure modelling is excellent and has led to top-level publications in collaboration with foreign groups.

Strengths and opportunities:

The team has complementary expertise in bioinformatics, RNA 3D structure modelling, and yeast genome analysis and genetics.

The project, which constitutes a strategic investment for the future of the unit, is strongly supported by the head of the unit.

Weaknesses and risks:

The project is very ambitious for a small team composed of only three University lecturers. The project is overly dependent on techniques that have yet to demonstrate their reliability.

There is no independent funding for this group.

Recommendations:

More emphasis should be placed on simpler techniques that do not require heavy investments and which will yield the preliminary results needed to secure financing of the project.

Team 6: Post-transcriptional regulations and nutrition

Team leader: Mr Alain LESCURE

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	0	0	0
N2: EPST or EPIC researchers	0	2	2
N3: Other professors and researchers		0	0
N4: Engineers, technicians and administrative staff * on a permanent position		0,5	
N5: Engineers, technicians and administrative staff * on a non-permanent position			
N6: Postdoctoral students having spent at least 12 months in the unit			
N7: Doctoral students			
N8: PhD defended			
N9: Number of Habilitations to Direct Research (HDR) defended			
N10: People habilitated to direct research or similar		2,5	
TOTAL N1 to N7			**2**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

This new team will be composed of two CNRS researchers and a PhD student.

The future leader was previously working in the former "Expression and assembly of eukaryotic regulatory RNAs" team, where he was studying the function of selenoproteins in mammalian cells. In the recent years, he has analyzed the functional consequences in whole animal models of loss of SelN, a selenium containing protein of unknown function. Mutations in the gene encoding SelN causes congenital muscular dystrophy in humans. Disruption of the gene encoding SelN causes muscle architecture disorganization during zebrafish embryogenesis. Mice in which both alleles of the gene encoding SelN have been knocked out display muscle stem cell deficiency and impaired muscle regeneration following injury. When subjected to forced swimming tests, these mice develop body rigidity, progressive curvature of the spine and alteration of paravertebral muscles. Hence, the mouse model recapitulates many of the symptoms of patients suffering from SelN-related myopathy.

This work has been published in journals with good impact factors. For the period under review, the future team leader has signed 3 research articles as last author (*Experimental Cell Res*, *Nucl Acids Res*, and *PLOS One*), contributed to 4 other articles (*Human Mol Gen*, *Biochemistry*, *BMC Dev Biol*, and *PNAS*), and two reviews (*Chem Biodivers* and *BBA*).

Assessment of the research team's integration into its environment:

These studies have medical relevance since mutations in the gene encoding SelN cause congenital muscular dystrophy in humans.

The research project will benefit from a partnership with two companies interested in human and livestock nutrition: research contracts (20 k€/year for three years, 2011-2013) and funding for a doctoral position (CIFRE).

For the period under review, the team leader had support from the 'Association Française contre les Myopathies' (10 k€, 2009-2010).

Assessment of the research team's reputation and drawing power:

The team leader has already established a network of collaboration with several French and foreign laboratories (Institut de Myologie in Paris, Tokyo University, Karolinska Institute in Sweden, University Charity in Berlin).

A researcher from the Ecole Supérieure de Biotechnologie de Strasbourg (ESBS), with experience in biochemistry and molecular biology, will join the team in January 2013.

Assessment of the strategy and 5-year project:

The project includes: 1) attempts to determine the crystal structure of the SelN protein and biochemical assays to search for its potential enzymatic activity, 2) an in-depth characterization through biochemical, cytological and physiological analyses of the redox status in the mouse model in which both alleles of the gene encoding SelN have been knocked out, 3) studies of how different anti-oxidant compounds (selenium and vitamin E) modulate the oxidative stress response in this mouse model, 4) the search of specific markers of the oxidative stress defence pathways, in particular, by deep-sequencing of the transcriptome of knockout mice fed with different anti-oxidant diets. Aims 1) and 2) are a logical continuation of the previous work of the team leader that should further our understanding of the role and mode of action of SelN. Aim 3) is an interesting more applied aspect allowing for a collaboration with two companies. Aim 4) addresses a large and important question.

Conclusion:

Overall opinion on the team:

The leader of the new team has performed interesting work on the consequences of SelN deficiency using animal models. The team is well placed to unravel the molecular role of this protein, which could have important medical consequences.

Strengths and opportunities:

The team leader has experience with the SelN knockout mice as well as with selenoprotein biology. Collaborations with academic partners have already been established. The project involves an interesting applied aspect, involving collaborations with two companies.

Weaknesses and risks:

The research on the physiological function of SelN is distinct from the activities of the other teams of the unit. The size of the team is small and, on a subject as large as the role of nutrition in the oxidative homeostasis, future success will depend on the capacity of the team leader to define a clear line of investigation.

Recommendations:

Given the small size of the team, the committee encourages the team leader to focus the efforts of his group on a few clearly identified questions. Care must also be taken to maintain coherence between the activity of the team and that of the other teams of the unit.

Team 7: Retroviruses and RNA viruses

Team leaders: Mr Roland MARQUET and Jean-Christophe PAILLART

Workforce

Workforce	Number on 06/30/2011	Number on 01/01/2013	2013-2017 Number of producers**
N1: Professors or assistant professors	0	0	0
N2: EPST or EPIC researchers	5 (4,2)	5 (4,4)	5
N3: Other professors and researchers	0	0	0
N4: Engineers, technicians and administrative staff * on a permanent position	1 (0,9)	1	
N5: Engineers, technicians and administrative staff * on a non-permanent position	0		
N6: Postdoctoral students having spent at least 12 months in the unit	2		
N7: Doctoral students	9		
N8: PhD defended	6		
N9: Number of Habilitations to Direct Research (HDR) defended	0		
N10: People habilitated to direct research or similar	4	4	
TOTAL N1 to N7	**17 (16,1)**	**6 (4,4)**	**5**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The work done in this team is of excellent quality, and until recently, almost entirely centered on HIV-1 reverse transcription (RNA:RNA and RNA:protein interactions that occur during HIV-1 replication), and its Vif protein. During the period under review, this team has reported on:

1) The discovery of another activity of the HIV-1 Vif protein (genome RNA chaperone), which is important in dimer genome packaging.

2) HIV-1 Vif binding to the 5' UTR of APOBEC-3G mRNA and inhibition of its translation.

3) HIV-1 Vif oligomerisation is crucial for specific binding to nucleic acids.

4) Design, synthesis, and evaluation of nucleoside analogues inhibiting HIV-1 replication by lethal mutagenesis.

5) More recently, the identification of influenza A genomic RNAs forming a network of RNA interactions mediated by packaging signals, which is central to how this virus packages one each of its 8 genome segments.

This is all excellent quality work that has been published in good journals. Its quantity of publications is reasonable. This group is well positioned between, and well regarded by the virology and RNA communities.

The team has published 19 articles in peer-reviewed journals including 3 reviews, as well as 1 abstract from an international meeting and 1 book chapter. Eleven of the peer-reviewed articles come directly from the work of the team (1 Appl Microbiol Biotechnol, 1 J Biol Chem, 1 J Med Chem, 1 Microbiol Mol Biol Rev, 3 Nucl Acids Res, 2 Nucleosides Nucleotides Nucleic Acids, 1 Viruses, 1 RNA). In addition, the team has filed 4 patents.

Assessment of the research team's integration into its environment:

The team fits well within the remit of the research unit. This work is highly relevant.

Although the treatment of HIV-1 infections are now manageable when sufficient resources are available, their costs are still enormous and beyond the reach of many countries. Any insight into how to better deal with this scourge is important and will have global impact. The submission of 4 patents is testimony to the potential of this research for real application to therapy.

The team continues to attract adequate funding: ANRS (130 k€, 56 k€, 75 k€), Sidaction (79 k€, 68 k€) and United Arab Emirates Union National Research Foundation (34 k€)

Assessment of the research team's reputation and drawing power:

The team recruited 4 PhD students and 2 postdocs during the period under review, of which 4 were non-French (Ireland (2), Egypt, Ecuador). The members of the team frequently talk at national and international scientific meetings (24 talks, of which 2 were invited). Members of the team participated in the organization of 6 scientific meetings and chaired 3 sessions in scientific meetings. The senior team leader did a sabatical at the Burnet Institute, Melbourne, Australia (2008).

Assessment of the strategy and 5-year project:

The group intends dropping its work on "Design, synthesis, and evaluation of nucleoside analogues inhibiting HIV-1 replication by lethal mutagenesis", to better concentrate its efforts on other and newer subjects, like the packaging of one each of the 8 flu genome segments which is seen by the visiting committee as a wise decision. The remaining work on HIV-1 falls into 2 categories;

1) How HIV-1 packages only the gRNA dimer. This has turned out to be a very difficult problem, but one that is really central to virus replication. This investigation will require several new approaches, but the risk is well worthwhile.

2) More care should be taken about how "HIV-1 Vif binds to APOBEC-3G mRNA and inhibits its translation", as this falls into a different category of interest. Almost every virus has its own approach to this problem, and the simplest possibility is that Vif may interfere with formation of the A3G ribosomal initiation complex.

Conclusion:

Overall opinion on the team:

This is a strong team doing truly original work.

Strengths and opportunities:

The proposed study of the interaction and localization of Vif/ARNm/A3G complexes is both timely and a neglected aspect of HIV replication.

The move into flu genome-segment packaging is also timely and welcome, and can be expanded; for example, it is important to determine whether the positions of the NP proteins relative to the genome sequences are fixed (or not),i.e. getting more detail of what the flu RNPs being selectively packaged actually look like. This team's expertise is well suited to this problem.

Weaknesses and risks:

The committee believes that the question of how Vif inhibits APOBEC-3G mRNA translation is likely to be a detail of HIV molecular biology that will not have broad impact in the field of fundamental virology.

Recommendations:

In addition to flu genome-segment packaging, possibly other viruses should be considered, such as HCV, a positive-strand RNA virus where intra-genome RNA interactions are not complicated by the presence of nucleoprotein.

Team 8: Retrovirus and Molecular Evolution

Team leader: Mr Matteo NEGRONI

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	1(0,8)	1(0,8)	1
N2: EPST or EPIC researchers	1	1	1
N3: Other professors and researchers	0	0	0
N4: Engineers, technicians and administrative staff * on a permanent position	1(0,74)	1(0,8)	
N5: Engineers, technicians and administrative staff * on a non-permanent position	0		
N6: Postdoctoral students having spent at least 12 months in the unit	1		
N7: Doctoral students	2		
N8: PhD defended	1		
N9: Number of Habilitations to Direct Research (HDR) defended	0		
N10: People habilitated to direct research or similar	1	1	
TOTAL N1 to N7	**6 (5,54)**	**3 (2,6)**	**2**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

This new team was created in December 2007 when the team leader moved from the Pasteur Institute with ATIP funding.

The team has mostly been interested in the evolution of the HIV-1 *env* gene, both naturally (within patients, where selection is important) and in cell culture without selection. Genetic recombination plays an important role in this evolution, and this group has found that this recombination is non-random even without selection. Rather, recombination is guided by structures found in the RNA genome architecture (recombination hotspots). These authors have inferred that these RNA structures also function to guide recombination toward gene junctions, with the intriguing implication that the architectural organization of the HIV-1 genome modulates recombination in such a manner that it tends to shuffle entire genes or sub-gene fragments that encode autonomously folding protein domains (there is "method in this madness").

They have also developed a new lentiviral vector system for gene evolution, naturally driven by the lentivirus replication. The advantage here is that a mutant library can be generated directly within any animal cells using VSV G-pseudotyped lentivirions. They have tested this system by identifying super-active mutants in a host gene (dCK) that convert an anti-cancer pro-drug into its active form. The idea is to target the tumor cells with a vector that also includes a siRNA against the insufficiently active endogenous dCK, and thereby hope to improve the selective toxicity of this drug treatment. This approach looks interesting and will now be tested in an animal tumor model. One of the unanticipated advantages of this method was that mutants were generated in the absence of selection, which would never have been discovered if selection had been applied. This methodology has now been patented and this team is well positioned to cooperate with commercial concerns.

All the above is clearly interesting work of high quality.

The team has published 6 articles in peer-reviewed journals inducing 2 reviews as well as 1 book chapter. Four of the articles come directly from the work of the team (*J Virol*, *PLoS Pathog*, *RNA Biol*, *Virus Res*). The team has also filed 2 patents that cover about half of the research during the period under review. This work should lead to further research publications now that the patents have been filed.

Assessment of the research team's integration into its environment:

The team fits well with the remit of the research unit.

The team is highly successful in obtaining external financing (393 k€ total). The team was established with ATIP financing from the CNRS and has additional funding from sources including the ANRS, Ligue Contre le Cancer and ERC.

Assessment of the research team's reputation and drawing power:

The team has numerous collaborations and hosts PhD students from the collaborating labs. The team has established 6 international collaborations (2 USA, 1 Canada, 1 South Africa, 1 UK, 1 Switzerland). The team leader was an invited speaker at two international seminars.

Assessment of the strategy and 5-year project:

The proposed research is innovative and highly original.

Work on the new lentiviral vector system for gene evolution (dubbed Retrovolution) will continue in an obvious direction, but will no longer be as "intellectually challenging"; whether in the end it will have practical application is much less likely to depend on the skills and knowledge of the investigator. Other target host genes for directed or undirected retrovolution will be examined (proof of principle to be expanded).

The work on the evolution of the HIV-1 env gene will continue along the lines that "inter- and intra-gene interactions define a coevolution network essential for the functionality of proteins and, more in general, genomes". The work will be expanded to include the RTase and integrase genes, which because they are more highly conserved, may behave differently from env during natural and unselected evolution.

Conclusion:

Overall opinion on the team:

This is an excellent young team, which has strengths that do not overlap, and which nicely complement those of the other groups within the unit.

Strengths and opportunities:

The team leader is clearly well established in his field.

Weaknesses and risks:

The team has no significant weakness.

Recommendations:

The team needs to maintain a judicious balance between the cooperation with commercial concerns interested in the Retrovolution technology and with the more fundamental aspects of the project involving retroviral molecular evolution.

Team 9: Non-coding RNAs and viral infections

Team leader: Mr Sébastien PFEFFER

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	0	0	0
N2: EPST or EPIC researchers	1	1	1
N3: Other professors and researchers	0	0	0
N4: Engineers, technicians and administrative staff * on a permanent position	0	2	
N5: Engineers, technicians and administrative staff * on a non-permanent position	3		
N6: Postdoctoral students having spent at least 12 months in the unit	6		
N7: Doctoral students	2		
N8: PhD defended	1		
N9: Number of Habilitations to Direct Research (HDR) defended	1		
N10: People habilitated to direct research or similar	1	1	
TOTAL N1 to N7	**12**	**3**	**1**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

This small team, created in 2009, has been interested in the role and regulation of RNA silencing related pathways in the context of viral infections in mammalian cells. Three main projects plus one "side-project" were studied.

Project 1, focused on identification of cellular targets of viral miRNAs, led to evidence that Kaposi's sarcoma herpes virus microRNAs participate in oncogenesis by targeting caspase 3 and inhibiting cell death. Another key result is the discovery that the chemokine CXCL16, reported to guide migration of activated Th1, Tc1 cells and NK cells, is a target of mouse cytomegalovirus (MCMV) miRNA miR-M23-2.

Project 2 addressed the importance of viral miRNAs during infection and provided compelling evidence that MCMV miR-M23-2 plays a crucial role in countering the innate immune response and in enabling virus accumulation in different tissues.

Project 3 searched for the regulation of cellular miRNAs in viral infection, revealing that miR-27A expression is completely abrogated in MCMV infected cells.

The side project was on the role of miRNA in rheumatoid arthritis, in collaboration with a local laboratory.

The team has published 15 articles in peer-reviewed journals since 2009, including 7 reviews. Five of the research articles come directly from their own work (1 *J Immunol*, 1 *J Virol*, 2 *PLoS Pathog*, 1 *RNA*).

The group masters a broad range of state-of-the-art methods. Outstanding productivity by a young team leader of novel results that have had a large impact in the field.

Assessment of the research team's integration into its environment:

This team's reseach is fundamental with a strong impact in the field of viral infection.

The team's research fits well with the remit of the unit. This team will soon benefit of a permanent engineer, reflecting the support of the direction of the unit.

The team is part of a consortium that recenty won LABEX funding.

The team has been very successful in obtaining support including an ATIP (180 k€), an ERC Starting grant (1470 k€), contracts from INCA (550 k€), ANR (380 k€, 390 k€), Ligue Contre le Cancer (70 k€).

Assessment of the research team's reputation and drawing power:

ERC Starting grant in 2010. Claude Paoletti prize in 2009.

Ten invited conferences (7 international) and 13 oral communications in international (11) or national meetings. Fifteen seminars. Organization of the European Congress of Virology in 2010.

The team has recruited 7 postdocs and 2 PhD students.

The team has several international collaborations (Munich, Edinburgh, Basel), 1 national collaboration (Villejuif) and 1 local collaboration. One collaboration is with a big pharma (Basel).

Assessment of the strategy and 5-year project:

The project for the next 5 years focuses on 5 lines of research:

1) Importance of RNA silencing pathways during RNA viruses infection. The aim is to reexplore the nature of viral small RNAs generated from several RNA viruses (SINV, VSV, HCV and togothovirus), and to assess the impact of viral infection on cellular miRNAs.

2) Identification of factors involved in miRNA decay, in particular in the case of miR-27 that is degraded during MCMV infection.

3) Regulation of viral miRNAs processing.

4) Global role of the host miRNA machinery in MCMV infection, in particular the role of DICER.

5) Viral and cellular miRNAs variations in lymphproliferative disorders: the participation of miRNAs in the lymphomagenesis process initiated by Epstein-Barr virus.

Taken together, this research focuses on the cross talk of viral infection and miRNAs, with the purpose of deciphering the mechanisms at the molecular level.

This is a strong and original research program with mature perspective. The field of viral miRNAs and role of viral infection on cell miRNA expression is very competitive area in which the team has established a position of leadership. The strategy for the future is clear, ambitious and feasible with a group of this size and the important funding obtained.

Conclusion:

Overall opinion on the team:

Outstanding young team with tremendous potential to continue leading edge research.

Strengths and opportunities:

The team is a leader in the viral noncoding RNA field.

Exceptionally good funding for the next 5 years.

The team has a strong potential to develop interactions with other groups in the unit, with the platforms in the unit and in the FRC 1589, and with other groups that are part of the Labex NetRNA grant.

The collaboration with a private company reveals a valorisation strategy.

Weaknesses and risks:

This team has no significant weakness.

Recommendations:

The leader needs to maintain the clear and ambitous strategy upon which the team was founded.

Team 10: mRNA and regulatory RNAs in bacteria

Team leader: Ms Pascale ROMBY

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	1	1	1
N2: EPST or EPIC researchers	3	3	3
N3: Other professors and researchers			
N4: Engineers, technicians and administrative staff * on a permanent position	1	1	
N5: Engineers, technicians and administrative staff * on a non-permanent position	1		
N6: Postdoctoral students having spent at least 12 months in the unit	4		
N7: Doctoral students)	2		
N8: PhD defended	1		
N9: Number of Habilitations to Direct Research (HDR) defended			
N10: People habilitated to direct research or similar	1	1	
TOTAL N1 to N7	**12**	**5**	**4**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

This group is internationally recognized for its detailed mechanistic studies of RNA-dependent regulation in bacteria. The topics that have been studied during the period of evaluation include 1) the control of translation initiation by the *Pseudomonas putida* Crc protein and by the *Escherichia coli* S15 protein, 2) determination of the secondary structure of a cold-activated mRNA in which low temperature favours a conformation that promotes translation initiation, and 3) the identification and characterization of small RNAs involved in the control of virulence in the Gram-positive pathogen *Staphylococcus aureus*.

Research on translation initiation and its control by regulatory proteins and RNA secondary structure is part of the core activity upon which the group has established its reputation over the past 15 years. In collaboration with structural biologists in Strasbourg, the group continues to make important contributions involving the dynamics of the 30S translation initiation complex (*Cell* and *Nature*). Over the past decade, it has become apparent that RNA can act as a 'thermosensor' by changing conformation in response to changes in temperature. The group has made an important contribution to our understanding of the regulation of the *cspA* mRNA, which encodes the major cold-shock protein in *E. coli* (*Mol Cell*). Their work suggests that the co-transcriptional folding of the *cspA* mRNA at low temperature results in a structure that promotes efficient translation initiation.

In a new line of work, the group has made significant contributions to our understanding of the post-transcription regulation of gene expression in *S. aureus* by regulatory RNA (*PLoS Pathogen* and *Genes & Dev).* This research involves the characterization of the RNAIII regulator, which has a leading role in controlling the virulence of *S. aureus*, and the identification and characterization of small regulatory RNAs involved in the post-transcriptional control of gene expression.

The team has an outstanding scientific production: 25 articles published in peer-reviewed journals including 10 reviews and methods articles as well as 6 book chapters and 2 educational contributions. Six research articles come directly from the work of the team (1 *Biol Chem*, 1 *Genes Dev*, 1 *Mol Cell*, 1 *Nucl Acids Res*, 2 *PloS Pathog*) and the team made significant contributions to collaborative work published in *Cell* and *Nature*.

Assessment of the research team's integration into its environment:

Although the principal focus of the group is primarily fundamental, the work has potentially important medical applications involving the virulence of bacteria and viruses.

The group is very well integated into the area of research of the CNRS laboratory.

The team is part of a consortium that recenty won LABEX funding.

For the period of the review, the group has been highly successful in attracting external funding with multiple grant awards at the national and international level: European contracts (356 k€, 281 k€), ANR (91 k€, 155 k€, 160 k€, 182 k€), Labex NetRNA (40 k€/year).

Assessment of the research team's reputation and drawing power:

The group's attractiveness is attested to by recruitment of 3 Ph.D. students and 6 postdoctoral researchers during the period of evaluation.

The members of the group have participated in numerous national and international research conferences including 28 invited talks (21 by the group leader). The members of the group have been involved in the organization of 1 national conference for young scientists, 2 European Conferences and 2 International Conferences.

The members of the group have received local and national awards including the recent attribution of the Langevin prize (French Academy of Sciences) to the group leader.

Assessment of the strategy and 5-year project:

The project involves two main areas of research: 1) dynamics of translation initiation involving structured or regulated mRNAs in bacteria, and 2) regulatory RNAs in *S. aureus* and their involvement in regulatory circuits. The team has demonstrated competence in these areas of research, the projects are relevant and feasible, and the committee anticipates that the scientific output should be considerable in terms of both quantity and quality.

Conclusion:

Overall opinion on the team:

This is an outstanding team producing interesting and original research on RNA-dependent regulation in bacteria. The team leader is internationally recognized as a leader in this field of research.

Strengths and opportunities:

The teams strength is based on the marriage between competence in the structural and molecular biology of RNA and proteins that interact with RNA, and the choice of timely and relevant research topics such as the dynamics of the 30S translation initiation complex, the mechanistic basis of regulation involving RNA thermosensors, and the characterization of regulatory RNAs involved in the control of virulence in *S. aureus*.

Weaknesses and risks:

The scientific project of the team has no significant weakness. The team leader will be the deputy director of the unit, and will become director in 2015. This represents significant additional administrative responsibilities that need to be carefully balanced with the responsibilities of leading the team.

Recommendations:

The proposed work on the role of regulatory RNA in networks controlling the virulence of *S. aureus* is ambitious. In the context of the LABEX project, there is no doubt that the team will have the capacity to generate large data sets involving gene expression under a variety of conditions. The success of the project, however, will depend on the recruitment in the context of the LABEX project of scientists with the necessary expertise to model regulatory networks. The team leader therefore needs to be vigilant that this expertise is recruited in a timely manner.

Team 11: Networks of biomolecular recognition

Team leader: Mr Eric WESTHOF

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	3	5	5
N2: EPST or EPIC researchers	2	1	1
N3: Other professors and researchers	0	0	0
N4: Engineers, technicians and administrative staff * on a permanent position	0,5	1	
N5: Engineers, technicians and administrative staff * on a non-permanent position	1		
N6: Postdoctoral students having spent at least 12 months in the unit	2		
N7: Doctoral students	7		
N8: PhD defended	5		
N9: Number of Habilitations to Direct Research (HDR) defended	1		
N10: People habilitated to direct research or similar	3	5	
TOTAL N1 to N7	**15,5**	**7**	**6**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The team leader is a worldwide renowned expert in the principles of RNA structure and structure prediction. The team is very well structured, has several highly promising young researchers and has been very productive in four different areas during 2007-2011:

1) *Molecular dynamics simulations of solvated nucleic acids.* RNA structure and function strongly dependent on solvation dominated by water structure and interaction with ions, in particular Mg^{2+}. The specific contribution of the team is the usage of molecular dynamics (MD) in structure prediction. The determined structures are compared with available empirical data and the force fields underlying the MD calculations have been substantially improved.

2) *Alignment and modelling tools.* The group leader and his group are worldwide number one in the prediction of three-dimensional structures of RNA molecules. Two contributions of the Strasbourg group were and are outstanding: (1) the classification of base pairs and other dominant interactions in nucleic acids and (2) the identification of 3D structural motifs or modules that can be ascribed to sequence patterns. Many alignment and structure modelling tools are currently available. The specific contribution of team 11 is the usage of 3D-structures rather than the commonly applied secondary structures. In structure modelling the team is top worldwide.

3) *Modelling, biochemical and crystallographic studies on RNA.* Strength of the team is the strong cooperation with crystallographers. The recent studies aim at an exploration of the mechanism of GIR1 ribozyme and the structure determination of eukaryotic ribosome. Two findings on GIR1 are of general interest: (1) GIR-1 structure suggests its descent from a group-I ribozyme and (2) the branching reaction leading to inactivation of the mRNA in one branch is very likely due to an RNA-switch.

4) *Search for and structure of non-coding RNAs.* The search for non-coding RNAs is done in many bioinformatics groups worldwide. The major problem in the genome wide search for functional RNAs with conserved structures and compatible sequences is the enormously large number of false positives. Again, the specific contribution of the group is the usage of 3D-structure that allows reducing the false positives substantially.

The team has an outstanding scientific productivity with 42 publications in peer-reviewed journals including 6 reviews. Twenty of the publications come directly from the work of the team including 2 *Bioinformatics*, 1 *Cell* (review), 1 *EMBO J*, 1 *Genome Biol*, 1 *Mol Biol Evol*, 1 *Nat Methods*, 2 *Nucl Acids Res*, and 1 *RNA*. In addition, the group has an impressive list of 16 book chapters with a member of the team as first or last author.

Assessment of the research team's integration into its environment:

The research of the team is essentially fundamental in nature with possible applications in bioinformatics and biotechnology.

The team has been well funded as evidenced by the participation in 3 contracts ANR (160 k€, 1200 k€, 136 k€), and 1 European contract (252 k€).

The team is part of a consortium that recenty won LABEX funding. Team leader is coordinator of this project, which will support 3 other teams in the unit as well as several teams in in neighboring research units (NetRNA, 900 k€ per year, 10 years).

Assessment of the research team's reputation and drawing power:

The long-time experience of the renowned team leader in RNA structure and properties together with his worldwide visibility is the basis of a great variety of international co-operations and contacts. The expertise on RNA 3D-structure prediction is unique worldwide.

The team leader was been awarded the Charles-Léopold MAYER prize from the French Academy of Sciences (2007) and the Feodor Lynen Medal, Gesellschaft für Biochemie und Molekularebiologie, Mosbach, Germany (2011). The team leader has recently been elected member of the French Academy of Sciences (2011).

Assessment of the strategy and 5-year project:

The projects of the team are excellent and have a great perspective. At the same time, they are quite ambitious and will require substantial manpower and equipment in order to be carried out successfully.

1) *Consideration of weak interactions in nucleic acid structures.* The idea is to include weak interactions by means of molecular dynamics simulations based on potentials that are to be determined by high accuracy quantum chemical calculations and empirical data. The project is ranked with high priority since prediction of accurate 3D structures of RNA and DNA is of primary importance in present day molecular genetics. It is a high-risk project at the same time since it is unclear how structure specific cooperative networks of a large number of very weak interactions can be modeled properly. Pioneering work on non-covalent interactions in liquids is required. The ultimate goal of the work is the development of an automatic tool for RNA model building that is urgently required at present and in case of success could revolutionize RNA bioinformatics.

2) *Modeling of bacterial regulators networks involving regulatory RNAs.* Thius is a powerful proposal that can be successfully carried out with the expertise in the group and the planned cooperation with Institut Pasteur. New algorithms will be developed that can handle the various non-coding RNAs -for example sRNAs and riboswitches - within conventional genetic regulatory networks. Eventually, the work will show light on the subtle interplay between epigenetics and genetics for bacteria grown under different environmental conditions. There is an open question whether or not such an approach can be successful in full.

3) *Microfluidics and single cell studies of non-coding RNA network dynamics.* This is a very promising approach for which no expertise exists at IBMC. Expert knowledge will be brought into the group by a new person. The consideration of stochasticity in populations of cells is a very important complementation of current knowledge that is almost entirely based on population averaged data and consensus sequences. It is a large project and has more the character of a whole program rather than a stand-alone project - both RNA-specific experimental developments is needed together with a novel theoretical approach based on the mathematics of stochastic processes.

4) *Transcriptional and post-transcriptional networks regulations in human cells.* A more conventional strong proposal that is aiming at the detection of new RNA species involved in regulation. The proposal is based on plenty of previous work within IBMC and outside. The researchers were recently transferred from another group closed because of retirement.

Conclusion:

Overall opinion on the team:

This is an outstanding team producing interesting and original research. The team leader is internationally renowned as the leader in bioinformatics approaches to predict RNA 3D structure.

Strengths and opportunities:

The new projects are highly original, innovative and of high actuality, and have the capacity to provide a strong perspective for the research unit in the forthcoming years.

Weaknesses and risks:

The retirement of the team leader within the next five-year period will pose challenges in terms of leadership of the project.

Projects 1) and 3) require high manpower and expensive equipment to be invested into new methodology and theoretical approaches towards the common goal of deciphering RNA structure and function. These approaches will be rather expensive, and might tie up a large fraction of the unit's resources.

Recommendations:

The excellent and ambitious projects of the team will require careful management of manpower and equipment in order to be carried out successfully.

5 • Grading

Once the visits for the 2011-2012 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 four criteria defined by the AERES and was given along with an overall assessment.

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

Overall assessment of the unit "Architecture et Réactivité de l'ARN":

Excellente unité à tous points de vue.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A+	**A+**	**A+**	**A+**

Overall assessment of the team 1 "Biophysics and Structural Biology" (WESTHOF-DUMAS):

Équipe dont la production et le projet sont très bons. Le rayonnement est bon mais pourrait être amélioré.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	B	-	A

Overall assessment of the team 2 "Evolution of translation initiation systems in eucaryotes" (WESTHOF-ERIANI):

Équipe dont la production et le projet sont excellents. Le rayonnement est très bon.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A+	A	-	A+

Overall assessment of the team 3 “Mitochondrial translation and disorders” (WESTHOF-FLORENTZ):

Équipe dont la production, le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	A	-	A

Overall assessment of the team 4 “Aminoacylation of eukaryotic tRNAs : control and pathogenicity” (WESTHOF-FRUGIER):

Équipe dont la production, le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	A	-	A

Overall assessment of the team 5 “Evolution of non-coding RNAs in yeasts” (WESTHOF-JOSSINET):

Équipe non notée pour la production et le rayonnement et dont le projet est bon.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
NN	NN	-	B

Overall assessment of the team 6 “Post-transcriptional regulations and nutrition” (WESTHOF-LESCURE):

Équipe non notée pour la production et le rayonnement et dont le projet est très bon.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
NN	NN	-	A

Overall assessment of the team 7 “Retroviruses and RNA viruses” (WESTHOF-MARQUET-PAILLART):

Équipe dont la production, le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	A	-	A

Overall assessment of the team 8 “Retrovirus and Molecular Evolution” (WESTHOF-NEGRONI):

Équipe dont la production et le rayonnement sont très bons. Le projet est excellent.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	A	-	A+

Overall assessment of the team 9 “Non-coding RNAs and viral infections” (WESTHOF-PFEFFER):

Excellente équipe à tous points de vue.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A+	A+	-	A+

Overall assessment of the team 10 “mRNA and regulatory RNAs in bacteria” (WESTHOF-ROMBY):

Excellente équipe à tous points de vue.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A+	A+	-	A+

Overall assessment of the team 11 “Networks of biomolecular recognition” (WESTHOF-WESTHOF):

Excellente équipe à tous points de vue.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A+	A+	-	A+

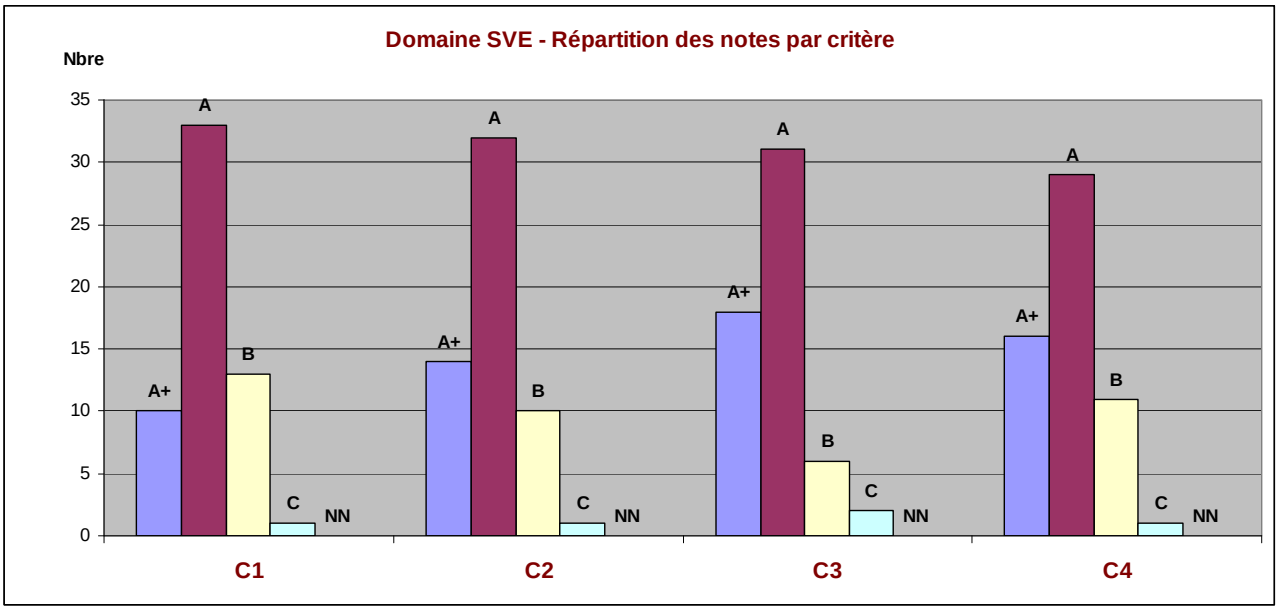
6 • Statistics per field

Notes

Critères	C1	C2	C3	C4
	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Gouvernance et vie du laboratoire	Stratégie et projet scientifique
A+	10	14	18	16
A	33	32	31	29
B	13	10	6	11
C	1	1	2	1
Non noté	-	-	-	-

Pourcentages

Critères	C1	C2	C3	C4
	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Gouvernance et vie du laboratoire	Stratégie et projet scientifique
A+	18%	25%	32%	28%
A	58%	56%	54%	51%
B	23%	18%	11%	19%
C	2%	2%	4%	2%
Non noté	-	-	-	-



7 • Supervising bodies' general comments

UNIVERSITÉ DE STRASBOURG

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Alain BERETZ
Président

Strasbourg, le 16 février 2012

Objet : Rapport d'évaluation de l'UPR 9002 (réf. S2PUR130004490)
Réf. : AB/EW/N° 2012-59

Direction de la Recherche

Cher collègue,

Je vous remercie pour l'évaluation de l'unité de recherche « Architecture de Réactivité de l'ARN » (ARN – UPR 9002) dirigée par Monsieur Eric Westhof.

Vous trouverez ci-joint les réponses du directeur d'unité de recherche concernant les erreurs factuelles.
Il n'y a pas d'observations de portée générale de la part du directeur de l'unité de recherche sur le rapport d'évaluation.

Je vous prie d'agréer, Cher Collègue, l'expression de mes sentiments distingués.

Alain BERETZ
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- **Une partie corrigeant les erreurs factuelles**