IBITEC-S - SBIGeM - Service de biologie intégrative et génétique moléculaire

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

SBIGeM

From the

CEA

May 2010

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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

May 2010

Research Unit

Name of the research unit: SBIGeM

Requested label

N° in the case of renewal

Name of the director: Mr. Christophe CARLES

Members of the review committee

Committee chairman:

Mr. Alain NICOLAS, Institut Curie

Other committee members

Mr. Enrique HERRERO, Universitat de Lleida, Spain

Mr. Jean-François COLLET, Université Catholique de Louvain, Belgium

Mr. Michael GLICKMAN, Technion-Israël Institute of Technology, Israel

Mr. Tom Owen-Hughes, University of Dundee, United-Kingdom

Mr. Jesper SVEJSTRUP, Cancer Research UK London Research Institute, United-Kingdom

Mr. Bertrand SERAPHIN, IGBMC

Mr. Fabrizio d'ADDA DI FAGAGNA, IFOM-IEO Campus, Italy

Mr. Frédéric SAUDOU, Université Paris-Sud 11

Mr. Evelyne HEYER, Musée de l'Homme

Mr. Herman VAN TILBEURGH, Université Paris-Sud 11

Observers

AERES scientific advisor

Ms. Michelle DEBATISSE

University, School and Research Organization representatives

Mr. Jacques NEYTON

Report

1 • Introduction

- Date and execution of the visit

The committee visited the Unit on March 22-23, 2010. The committee appreciated the overall organisation, the friendship of the reception, and the diligence with which the Director provided additional information on the spot! The written document was informative and sent well in advance. The presentation of the activities started from the general presentation of the unit director, followed by the presentations of the individual teams (11 teams). The intermediate organisation of the unit into 6 « laboratories » constituted of 1-4 teams was not specifically emphasized and evaluated. Only members of the team were present during these oral presentations.

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

The SBIGeM Unit belongs to the CEA Life science (DSV) division. It is one of the 5 Units of the Institute of Biology and Technology-Saclay (iBiTec-S). The overall interest of the iBiTec-Saclay is genetics and molecular physiology, physics of biological systems and life chemistry, technologies for health and innovative molecules for health. The SBIGeM unit was recently created (2007). It mainly resulted from the fusion of two units: the SBGM (Biochemistry and Molecular Genetics) and the SBMS (Systemic Molecular Biology Unit), The animal facilities headed by one team leader of the present Unit was attached to the SBIGeM.

- Management team

The committee thus evaluated a fairly recently formed unit. It has not been made aware of previous scientific evaluations and conclusions. Thus, the capacity of the unit to implement external recommendations could not be mesured. However, the committee perceived that the overall unit has matured over the recent years, and is on good ground of excellence and expansion under the management of the current director.

- Staff members

Total number of teams: 11; Total number of lab members: 109

N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	27
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	39
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	20
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	18
N7: Number of staff members with a HDR or a similar grade	17

2 • Overall appreciation on the research unit

- Summary

Globally, this is a mid-size unit, balanced in terms of staff categories, e.g. permanent and non-permanent researchers and staff members. The unit currently hosts 11 teams of various sizes.

The research carried out is essentially fundamental and is organized around two major axes: understanding the mechanisms governing genome integrity maintenance and transcription, and the mechanisms and regulation of cell responses to genotoxic and oxidative stresses. A large spectrum of experimental approaches is employed: genetics, genomics, molecular biology, cell biology, biochemistry, bioinformatics, mathematical modelling, and physics. The organisms studied are diverse: cyanobacteria, yeast, mouse and human cells, mouse models and even extinct bears.

- Strenghts and opportunities

- A clear strength of the SBIGeM over the past years has been the ability of all the teams, to conduct a high level of competitive research;

- Several teams have international impact in the area of transcription, DNA damage and oxidative stress responses, indicated by high impact publications;

- Several teams were successful to conduct innovative and risky projects with long-term vision;

- Ability to attract a relatively large number of good PhD and postdoctoral researchers.

- Weaknesses and threats

- Complete loss of institutional funding in 2010. The increased uncertainty of funding should be closely taken into account by the Unit policy since this will significantly impact the ability of the teams and the unit as a whole to compete on the national and international scene;

- The multiplicity of projects in some teams, leading to one project per permanent researcher;

- Limited funding and integration into European networks;

- Limited resources in bioinformatics.

- Recommendations to the head of the research unit

- Defend and support competitive projects in the predominant and highly competitive areas of research, e.g. gene expression and regulation, in particular transcription, and cellular and molecular responses to various stresses (genomic and oxidative);

- Reinforce the historical expertise of the Unit in biochemistry;

- Encourage original and emerging fields of research, such as done for chromatin organization, ancient DNA and cyanobacteria;

- Recruit new teams able to bring complementary scientific and technological expertise and resources. The option of bringing in teams interested in the fields of epigenetics and chromatin appears as a good choice;

- Elaborate a common bioinformatics platform to foster the sharing of already existing competence and the likely further development of the functional genomics research activity.

- Production results

A1: Number of permanent researchers with or without teaching duties (recorded in N1 and N2) who are active in research	27
A2: Number of other researchers (recorded in N3, N4 and N5) who are active in research	ND
A3: Ratio of members who are active in research among permanent researchers [(A1)/(N1 + N2)]	100%
A4: Number of HDR granted during the past 4 years	ND
A5: Number of PhD granted during the past 4 years	25

3 • Specific comments

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

Interactions between the researchers exist in various ways, mostly through seminars at the level of the teams, laboratories and the whole Unit, including regular invitation of external speakers. Research collaborations within the Unit are validated by some common co-author publications but are not extensive. It can be reinforced.

With 11 teams, the Unit has a sufficient critical mass and profile of competence to pursue the proposed projects, but since additional laboratory space is available, a significant expansion of the Unit is an interesting opportunity to increase its strength. Indeed, during the visit, the committee was informed of the wish of the Unit to increase the number of teams. This can be linked to the natural evolution of the scientific emphasis, the internal emergence of potential new group leaders, as well as the arrival of new teams. Since these issues were not addressed in the document and not formally presented during the presentations, the committee considered that it was not sufficiently informed to evaluate these future evolutions. To get advice and implement a strong scientific strategy, the committee strongly recommends the organization of an international scientific advisory board that will assist the Unit director in preparing, evaluating and implementing the future teams. The possibility that the expansion of the Unit could be accompanied by the creation of an UMR Unit with the CNRS seems also an interesting possibility that should be considered.

Director.

The present director started his mandate about one year ago. Considering the high quality of his scientific track record, the support of the Unit members, and his knowledge of the CEA organization, the committee recommends the Director to pursue his mandate.

Permanent researchers.

Four representatives of the committee met with 17 permanent scientists of the SBIGeM that are not group leaders. The SBIGeM members had prepared a short presentation which served as a basis for an open and lively discussion. The participants concluded in indicating that they generally appreciated the working conditions at the SBIGeM but raised two issues of the utmost importance:

The limited options for mobility are seen as a major problem for promotion and career development (e.g., change of research topic).

The mechanisms for promotion to group leader appear to be ill-defined. The committee strongly encourages the establishment of a clear competitive procedure, open to internal and external candidates, so that the promotion to group leader and as a consequence the creation of novel teams, occur via a transparent and fair process, including external referees.

Technicians and administrative personnel.

The meeting was well prepared and the representative of the technical staff communicated to us the conclusions of a previous internal discussion.

Each technician is clearly associated with a team; thus, technicians are not grouped into technical platforms. This organisation seems particularly appreciated, as it enables the follow-up of scientific projects from the start. This enhances motivation and maintains long-term knowledge, particularly in small teams. Technicians have an annual meeting with their team leader, which seems to be appreciated.

The institute has a good organization as regards the daily tasks such as the washing of material, preparation of buffer solutions and culture medium. One person per building is in charge of security.

The technical staff can follow courses and training formations, although administrative heaviness in the procedures is sometimes a hindrance. In particular, qualifying formations are difficult to follow, since the technicians must integrate into another team after these formations. Furthermore, mobility is extremely difficult inside CEA, since there is no more replacement of staff for the posts left vacant.

Students and postdocs.

They stated explicitly that they are happy working here at CEA. Reasons for that are good salaries, nicely equipped laboratories with good technical support and good training. However, a number of issues were raised:

Working hours: Students and postdocs ask to be able to work more. As working hours are not flexible, it is advised that at least transportation to and from CEA is facilitated by the addition of extra bus rides or pushing the existing ones to later hours. Similarly, access during the weekend should be relaxed. Overall this will boost the productivity of the scientists of CEA allowing them to be more competitive, also in terms of grant applications, an invaluable asset in this period of dramatic budget cuts.

The limit of 3 years for PhD and 2 years for postdoctoral period is a limitation to achieve international competitive science, particularly if working hours during this short period are also restricted. A solution may be the association with other research organizations (CNRS) and/or the establishment of collaborations with non-CEA teams. In this way, research may be planned for longer periods, therefore avoiding the premature abortion of potential promising research lines because of administrative working contract regulations. However, it has been mentioned that these restrictions do not apply to postdocs with their own fellowships such as EU Marie Curie, etc: this should be confirmed and the information passed to all.

Access to CEA courses: not all PhD students can attend some (much appreciated) courses (on patenting, biotech start-up, etc). It is demanded to open the attendance to all PhD students in CEA trainings. Other students mentioned they might have attended external courses (such as those mentioned below) if attendance at CEA courses had not been compulsory.

Information about "modules d'Ecole Doctorale" in the Ile-de-France that could be of interest for the PhD students and postdocs seems insufficient and needs to be improved. This will enhance the formation [education??] of PhD students in their own field of research and can potentially open them to other scientific fields.

In contrast to the general usage in all the "Ecoles Doctorales", it seems that none of the PhD student working in the Unit have a "Thesis committee" that follows their work on an annual basis. The creation of such thesis committees is strongly suggested. This will also increase communication about research direction in a unit with several teams of overlapping scientific interest.

In summary, it appears that the atmosphere and conditions in the Unit is satisfactory and reflects motivation and adhesion of the personnel to the present organisation and management.

Resources and infrastructures

Financial resources. Historically, the research teams of the CEA have been supported by significant, stable intra-mural funding, waves of permanent researcher and technician recruitment, and postdoctoral fellowships. Over the last four years, these resources have significantly eroded and this was reduced to Zero, in 2010! The committee thinks that the present situation is unsustainable. Teams have successfully raised their own funding through competitive national and international grants and should be commended for this. This external funding provides a level of independence for the teams, but is also associated with the following e disadvantages: (i) it yields

heterogeneous funding level between teams, (ii) it is a source of internal tension and selfish attitudes, (iii) it generates unpredictable fragility for recruitment, (iv) bias in research choices and, as a growth factor, (v) it prevents any strategic management by the Unit. As in all research institutions in France, at the very least a minimal core of institutional funding needs to be established and guaranteed to support the infrastructure of the Unit. In addition a means of recovering overheads form external grants needs to be established. These income streams could be supplemented with additional external funding providing the unit with a means of maintaining its long term vision and competitivness.

in addition to the external funding and in the present funding climate a new formalized way of recovering overheads from CEA and teams' external grants is needed.

Infrastructures. The teams are located in two nearby buildings. This didn't appear to cause problems. However, it increases the unit expenses which must include some operating building running costs (for example security devices). All teams have sufficient lab space and space remains available for the installation of new teams.

4 • Appreciation team by team

Title of the team : Mechanisms of DNA checkpoints

Team leader : Marie-Claude Marsolier-Kergoat

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	4
N3: Number of other researchers including post-doctoral fellows (Form 2.2, 2.4 and 2.7 of the application file)	2	2
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3	3
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	2
N7: Number of staff members with a HDR or a similar grade	3	3

- Appreciation on the results

This medium size team (11 members), composed of a number of young researchers, is very active. The main focus is the study of DNA checkpoints, which are biological response pathways activated by spontaneous and induced DNA damage, and especially the role of the checkpoint kinase Rad53 in yeast and its mammalian homolog Chk2. Important contributions have been made to understand the inactivation of Rad53 after the DNA lesions are repaired and the modes of regulation of this kinase. For instance, contributions uncovered: (1) the role of Wip1/Ptc2 phosphatase in inhibiting Rad53; An interesting twist is the proposal that Wip1 itself is also subject to down regulation, (2) the links between the DNA and the spindle assembly checkpoints. Convincingly, an original direction was taken in searching for genetic suppressors of a conditional mutant of Rad53 (rad53-DL is an hyperactive dominant lethal allele of RAD53). Phenotypic and epistasis analyses uncovered new regulators of the DNA damage response pathways and, in particular, led to the discovery of the role of proteasome assembly factors. After great successes

using the yeast model system, the team is now putting a larger effort to tackle the mammalian system, as well as including some bioinformatical/theoretical approaches. Thus, this team has conducted a timely and fruitful contribution in the field of DNA damage response that jusitifies continuation. However, the committee noted that this line of research has been dispersed with additional interests on the regulation of DNA replication dynamics and the analyses of the genome-composition elements of meiotic DNA double-strand breaks sites in yeast meiosis.

Members of the current team have published 18 papers in the period 2005-2009. Two ground breaking and internationally acclaimed papers (Molecular Cell 2007, 2009) originated from the proteasome study. Additional papers on the other topics were published in high quality journals such as MCB, PLOS one and Oncogene.

Most of the work is done in-house by members of the team and productive collaborations are also conducted.

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

The team has convincing contributions on the DNA damage response field but, surprisingly, participations and invitations to seminars, international conferences and links to international networks are limited. Nevertheless, the team should be attractive due to its original work. Indeed, it was able to recruit talented graduate students and postdocs. The research led to two awards to a graduate student and a permanent researcher. Financially, the team has been well funded by ANR grants.

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

The management style is a somewhat dispersed, with each researcher working on a separate project. Not mentionned in the document, the team leader recently spent a one-year sabbatical stay abroad (USA) focusing on new grounds, namely theoretical studies. Apparently, the team didn't suffer from such personnal initiative but the committee becomes concerned about future dispersion of scientific interests, priorities and allocation of ressources. Rooted on good ground, to reach the expected level of excellence, the major challenge of the team in the coming years will be the scientific strategy and the management of the team.

Initiative aiming at scientific animation as well as contribution to teaching and structuration of the research at the local level are limited.

- Appreciation on the project

The team plans to continue on multiple directions, those embarked on earlier, and new ones. All research projects related to DNA checkpoints are on potential cutting edge but highly competitive, with numerous other groups worldwide working on similar topics. Therefore, without pooling efforts and working together, some of the recent achievements and successes may not be repeated so easily. The team has however significant human resources and a good mix of permanent staff scientists and technicians, as well as post-docs and graduate students.

- Conclusion

  – Summary

The team production on the role and regulation of Rad53/Chk2 in DNA damage response and the proteasome chaperones has been fruitful and of excellent prospective for the next years. In contrast, the new projects on regulation of DNA replication, polo-kinases, chromatin structure and meiotic recombination using experimental and theoretical modeling approaches appears as a dispersion factor to be avoided. The isolation of permanent researchers activities on such isolated projects is risky.

  – Strengths and opportunities

- Expertise and rigorous research on inactivation of the DNA damage checkpoints exploring interfaces between several key biological processes;

- Power to use the yeast model system and extend the work to mammalian cells;

- Interest and capacity to acquire novel technological developments ;

- Capacity to uncover novel questions, for example the role of proteasome;

- Quality of the publications;

- In summary, the committee feels that this team has done well, in recent years, by targeting original work.

– Weaknesses and threats

The team seems to favor the multiplicity of individual and experimentally diverse projects. The threat is the risk of dispersion, since the permanent research scientists is to develop independent projects without the necessary human resources and technical support. While the team leader is personally interested in the development of theoretical approaches, an effort to maintain a strong and collaborative attitude in the team should be emphasized.

– Recommendations

The team should focus on two major topics (1) The role and regulation of Rad53/Chk2 in DNA damage response and repair, headed by the present team leader and (2) The proteasome chaperones. It should be considered that the current sub-team on proteasome assembly and the relationship of proteasomes to DNA damage response becomes independent but the synergy with the parent team should be maintained within the laboratory structure.

In both cases, after the successes using the yeast model system, it is recommended that a large effort be made in tackling the mammalian system as well.

Title of the team : Mechanistics and Regulation of RNA polymerases

Team leaders : Mr. Christophe Carles and Mr. Michel Riva

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including post-doctoral fellows (Form 2.2, 2.4 and 2.7 of the application file)	1	0
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	0
N7: Number of staff members with a HDR or a similar grade	2	2

- Appreciation on the results

This is a team of modest size working in the field of transcription, in particular on yeast (*S. cerevisiae*) eukaryotic RNA polymerases (RNAPs). RNAPs are evolutionary conserved from budding yeast to human. Indeed, many of the genes encoding human RNAP subunits can functionally replace their yeast counterparts. Therefore, lessons learnt from yeast are more than likely to apply in multicellular organisms.

The work done by this team is of very high quality and original, taking advantage of the unique possibilities afforded by yeast research. Arguably, the main effort in the period has been the finding that the transcription activity of RNA polymerase I (RNAP-I) can fundamentally affect RNAP-II transcription: when RNAP-I activity is globally up-regulated, mRNAs encoding ribosome proteins are as well. This fundament finding was made via the clever

construction of a strain that is constitutively activated for RNAP-I transcription, since it has a the Rrn3 regulatory subunit fused to one of the integral RNAP-I subunits so that it cannot dissociate. The team has also performed important work on the structure-function relationship of RNAP-III, again using experimental approaches afforded by yeast. In this project, advantage was taken of the fact that deletion of the genes encoding certain non-essential subunits leads to dissociation of other subunits, some of which are encoded by essential genes. By back-addition of the recombinant subunits, alone or in combination, the importance of these subunits for different RNAP-III functions could be assessed. The results shed new light on the molecular function of RNAP-III and its individual subunits. A final project, deserving a specific mention, involved work on the transcriptional fidelity of RNAP-III, and the function of the C11 subunit (enabling transcript cleavage) in this process. This well-controlled and carefully conducted research has an internationally high profile.

The team has published 10 papers in the period 2005-2009. These are almost without exception in journals of significant impact (Genes & Dev., EMBO J, PNAS*)*. This is complemented by a couple of reviews, theses, and communications at scientific meetings. Considering the modest size of the team, this is very good productivity.

The two team leaders shared responsibility of the team research seems to be working very well; this is a very stable, long-term working relationship which allows to run the team, while maintaining senior administrative positions.

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

The staff members have given talks at prestigious meetings in the field. Possibly, there has not been quite as much activity as one would ideally like, but the yeast transcription field, and especially the field of RNAP-I and RNAP-III research, is not one of many meetings.

In the description of past staff, a good mix of postdocs and students are listed. In the latter part of the period, the recruitment activity seems to have decreased; this is probably in part due to the lack of in house-funding for such positions but also to the involvement of the team leaders in time-consuming administrative duties. Going forward, only a research Engineer and a Technician are listed, for the same reason. Because both team leaders are scientific heads of Unit and Institute, they have found it difficult to award themselves the necessary positions. This should ideally be rectified.

The team has had good funding in the past, with several grants from the ANR. They would probably benefit from establishing scientific clusters or grouping with others outside the institute, but because the unit already has some of the best teams working on RNA polymerases in Europe, this may not previously have seemed necessary. The new funding situation makes such groupings much more interesting going forward.

The team has several national and international collaborations. One of these is on the structure of RNAP-III, resulting in an excellent publication in Molecular Cell on which the two team leaders are both co-authors. However, the laboratory does not necessarily need lots of collaboration partners to fulfil its goals, which can be considered a strength.

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

This is a well-managed, well-functioning team. Its members only have taken teaching responsibilities, and are closely involved in the running of research at the local level.

- Appreciation on the project

The project is both original and cutting edge, which will likely make it possible for the team to continue successfully. There is a very good mixture of safe continuations of existing programs, and much more high-risk projects, such as that on cytoplasmic RNAPII. The latter project is somewhat speculative. However, the initial experiments to evaluate whether the project should in fact be pursued vigorously can be easily done. In a broader perspective, there is a need to maintain biochemistry as a strong focus in this team in further in the Unit. This group with their history of excellence in RNAPI-I research are in an ideal position to contribute to this effort.

- Conclusion

– Summary

This is a a very strong team, performing original, unique research of substantial impact. The research is highly regarded internationally, and is of great value for our understanding of the fundamental mechanisms of transcription.

– Strengths and opportunities

The team is one of the relatively few on the international scene to make such great use of the advantages of yeast, combining genetics, chromatin-immunoprecipitation and protein biochemistry in a very impressive manner. It is in a unique position to expand its work on reconstituted transcription, and given the relative lack of good biochemists in basic research today, their skills in this area should be taken advantage of. It is a great strength that the team have two senior scientists and two permanent technician positions, which allow them to take on a mixture of safe and long-term, high-risk projects.

– Weaknesses and threats

This is a team with several interesting projects to pursue. However, the size of the team is too small. The team contains two of the Unit and Institute administrators with the heaviest work-load.

– Recommendations

This is a very important scientific project and team, which is in a situation that requires strong support. It is recommended that the team rapidly recruits an experienced staff researcher (level: post-doctoral return) in order to reinforce the team, facilitate the recruitment of postdocs and graduate students and help drive the many interesting projects forward for the next four years and beyond.

Title of the team : Nuclear regulation and Stress

Team leaders : C. Conesa, O. Lefebvre

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including post-doctoral fellows (Form 2.2, 2.4 and 2.7 of the application file)	1	0
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	0
N7: Number of staff members with a HDR or a similar grade	2	2

- Appreciation on the results

This is a rather small team. A system for reconstitution of TFIIIC has been developed. This represents an important step in the establishment of a minimal system for Pol III transcription. The system was sucessfully applied to structural studies that resulted in high resolution structural information for two subunits of TFIIIC, in collaboration with the group of C. Muller. This provides a framework for understanding how TFIIIC acts to regulate Pol III transcription.

Thoughrough characterisation of the Pol III regulator Maf1 has been carried out. A combination of genomics and biochemical studies were used to show that Maf1 acts as a negative regulator of Pol III transcription. Furthermore, it was found that Maf1 is dephosphorylated by protein phosphatase 2A, allowing it to enter the nucleus and repress pol III transcription in response to nutrient limitation. Maf1 is conserved from yeast through to human, and is likely to represent an important means by which Pol III transcription is regulated.

A protein that was previously found to act as a repressor of Pol II transcription, Sub1, was found to be associated with a subset of pol III genes. Characterisation of the role of this protein *in vitro* showed that it assisted both initiation and re-initiation of transcription. This raises the intriging possibility that it acts to transfer pol III from the terminator to the transcriptional start site.

The team published 22 papers over the period of assessment. These include a number of high quality publications (*Mol. Cell*, *EMBO J.*, *PNAS*, *Gene and Dev.*, *MCB.*, *J. Mol. Biol.*, *J. Biol. Chem.*) that have been cited highly.

Numerous interactions between team members, between different teams and with external collaborators have been established.

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

The team attended national and international conferences. It successfully applied for external research funding and have been awarded grants amounting to 400,000 euros over the period surveyed.

- Appreciation on the project

The project involves a combination of projects that differ in their natures and risks. The continuation of ongoing research projects is likely to be informative and is of relatively low risk. Amongst these is the proposal for further structural studies and investigations into the function of Maf1 and Sub1 proteins.

Preliminary data suggest that chromatin modifying enzymes are recruited to Pol III genes. This novel line of research is attractive.

It is also proposed to apply a novel technique to identify all proteins involved in Pol III regulation. Although, not yet successful in all trials, two factors act to significantly increase the chance of success. Firstly, a collaborative interaction with the researcher that originally developed this approach. Secondly, Pol III genes are repeated; this should improve yields. Considering the stable resources of the team and the specificity of the target sequence, it is worth to try while alternative strategies should be considered.

The resources allocated are not sufficient to complete all the projects proposed. External funding together with recruitments will be required to improve staffing.

The proposal provides a good blend of feasible research expanding upon exisiting projects with more ambitious, cutting-edge, research.

- Conclusion

  - Summary

This team has an history of providing innovative new insights into the regulation of RNA Pol III transcription. The research over the recent period is no exception, with important progress reported in a significant number of quality publications acknowkedged by the international community. The proposal for research to be undertaken in the next 4 years is well considered and innovative.

  - Strengths and opportunities

- The research activity builds from a strong expertise in the field;

- Projects are solid and innovative;

- Good synergy between members of the team.

  - Weaknesses and threats

- High risk associated with the development of some aspects of the project;

- The departure of two PhD students in 2010 and the retirement of one research staff in 2011 will leave the group short handed.

  - Recommendations

- Overall, the proposal is very strong. New recruitments will be beneficials. Considering the presence of several staff scientists, the wish to recruit a PhD student in the near future is highly supported by the committee.

Title of the team : Transcriptional regulation of genomes

Team leaders : Mr. Pierre Thuriaux and Mr. Michel Werner

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	2
N3: Number of other researchers including post-doctoral fellows (Form 2.2, 2.4 and 2.7 of the application file)	1.6	4
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	2.4	1
N7: Number of staff members with a HDR or a similar grade	3	2

- Appreciation on the results

This is a strong medium-size team equilibrated with permanent researchers, postdocs, graduate students and technicians. The team addresses questions pertaining to the role of defined transcription factors and to their distribution at the genome scale using the yeast S. cerevisiae as a model organism. The work produced in the 2005-2009 period is of high quality and impact. The finding that TFIIS is involved not only in helping RNAPII during transcriptional elongation, but also independently as an initiation factor required, with the so-called Mediator complex, for normal promoter recruitment of RNA polymerase II (RNAP-II) is an intriguing discovery. This led to the proposal of new models for the role of this central transcription factor. Likewise, the finding that TFIIS appears to be involved in RNAP-II, but also RNAP-III transcription, is very important. Finally, the work on Mediator-mediated recruitment of the basic transcription factor TFIIH gave unexpected results showing that general transcription factors can be recruited by Mediator independently of RNAPII. Even if some of these results still await biochemical confirmation, the overall work performed by this team is of the highest profile. The development of parallel research on mammalian systems is well advanced and appropriated.

The team listed 18 publications for the assessed period, some of which appeared in prime journals. Highlight papers originating from within the team itself include papers in Molecular Cell, Genes and Dev., PNAS and MCB. Internationally, the team is clearly visible in its field as a result of the publications for which they are the main contributors. Some of the publications are originated from collaboration, in which the members of the team appear as minor contributors.

Several members of the team were invited to give oral presentations to the best international conferences. In addition, the team produced 4 PhD theses and 1 HDR. The team is certainly one of the influent actors in this crowded and highly competitive field.

The team had two complementary group leaders, specialized in molecular and genetical approaches, respectively. They have been collaborating for 20 years, so this has been a very stable, long-term and productive working relationship. With the team leader's retirement, there will undoubtedly be some loss of expertise and changes, but this should not impact too strongly on the productivity of the team or the general quality of the research. The team established solid connection with the CEA genomic center in Evry as well as with international partners in an EU network. Financially, the overall activity and future is secured by specific grants. In summary, the team has solid scientific and networking bases.

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

The staff members gave talks at some of the major meetings in their field. Members of the team were invited to 7 international events as well as to 5 meetings in France. One PhD student received a honour prize. Overall, the team visibility is excellent in its field.

The team had excellent recruitment capacities (e.g., 5 PhD students). Going forward, two staff technicians are listed and the team has funding for two postdoctoral researchers from the EU, positions which should be attractive and fairly straight-forward to fill.

The team is well connected at the national and European levels. It raised a significant number of grants from national (2 ANR "blanc", 1 local grant, 2 from charities) and international (EU) sources.

The team appears to have established solid connections with some partners. As mentioned above, this includes internationally recognized teams with whom some important publications have been co-signed.

The scientific production of the team is internationally recognized (publications/new knowledge). There are no specific activities besides basic research.

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

- Management, assessed during the visit, appears to be very good.

- The team has been a pioneer in the implementation of ChIP-on-chip approaches in Europe and is still well positioned in such genowide approaches, now including ChIP-SEQ. The current team leader has been involved for two years in the management of the SBIGeM Unit before engaging his efforts to develop CEA activities on genomic

approaches in Evry. Upon the departure of his life science scientific director, this was not concluded. Now, the team leader is encouraged by this committee to invest part of his time and expertise into the establishment of a local group supporting bioinformatics analyses for the whole Unit.

- The team seems to have some, but limited, connections to teaching.

- Appreciation on the project

The project is very interesting, well designed and feasible. Generally, the prioritization of the project on Mediator analysis (at the expense of the TFIIS analysis) is supported by the committee as well as their decision to apply their expertise on genome-wide exploration of mammalian, in particular mouse ES cell. This is a big shift which is likely to bend the focus of the lab in the long run. The team leader is encouraged not to neglect biochemical approaches which will be unavoidable to understand the mechanism of action of the factors under study. The team and colleagues in the Unit have a strong expertise on biochemistry, so the general scientific environment is highly favourable and indeed should be exploited.

The projects are both interesting and important. The lab has built up an array of expertises and methodologies that make it easy to move forward, both in yeast and mammalian cells. Their research questions are of wide interest and they have the tools and ability to solve them.

The project on the Mediator is particularly strong. Likewise, the possibility to collaborate on the analysis of the genome-wide localization of some transcription factors in mouse cells offers the group an opportunity to contribute to transcription research in more complex systems. The team leader is strongly encouraged to continue to go beyond descriptive work and invest into functional and mechanistic studies, as successfully achieved in the past years.

- Conclusion

– Summary

This is certainly one of the leading teams of this unit. They perform original and cutting-edge research of constant impact in the highly competitive field of transcription.

– Strengths and opportunities

- It is a very strong team with excellent expertise in genetics, molecular biology, and genomic approaches. They make great use of the advantages of yeast, combining genetics and ChIP in an impressive manner. Their moving into mammalian cells as well is a well-taken development;

- Excellent connection through the EUROTRANS program, including leading european teams in the field.

– Weaknesses and threats

- The retirement of one of the past joined group leaders is an important loss.

- With now a single staff researcher in addition to the group leader, the team is not so large and relies on postdoctoral fellows and graduate students. The size of the team should not shrink.

- The use of biochemical approaches, surprisingly limited given the context and topic, should be reinforced.

– Recommendations

- This solid and well spirited group should pursue its effort to gain increasing output;

- The team should maintain its diversity of approaches and concentrate on the most promising question;

- Increase international visibility beyond the borders of the field through their high profile collaboration in the EU network ;

- Maintain and possibly increase high profile publications;

- Gather strong bioinformatics support;

- The committee recommends that, with no delay, this team leader take direct responsibility in the establishment of a local support service in bioinformatics so that the SBIGeM Unit can maintain, and further expand, its competitiveness in genome-wide analyses.

Title of the team : Epigenetic regulation and cancer

Team leader : Mr. Matthieu Gerard

- Staff members

	Past	Present
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including post-doctoral fellows (Form 2.2, 2.4 and 2.7 of the application file)	4	1
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	4	2
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	1
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

Over the last years, the team conducted 4 research projects. The first involved depleting the histone chaperone complex CAF-1 in mouse ES cells. In itself, this is not trivial and a new shRNA vector was developed specifically for this purpose. Depletion of CAF-1 was found to dramatically disrupt the spatial organisation of heterochromatin domains within nuclei. These observations indicate the importance of a histone chaperone in the maintenance of chromatin marks. The second project, involves investigating chromatin structure at the Prader-Willi syndrome chromosomal locus. The third project concerned the contribution of Histone deacetylase 2 to tumour formation. These last two projects, approaching the stage of publication, provides valuable insights with relevance to humans.

Completion of these projects may have been hindered through involvement with the fourth, long-term project. This truly extraordinary undertaking involved the generation of a series of knock-in ES cell lines in which 15 chromatin remodelling enzymes have been tagged with tandem affinity tags. Care has been taken to select tags most appropriate for use in immunoprecipitation of chromatin fragments. A procedure for isolating DNA fragments with which they associate has been developed and the sequences are currently identified. Analysis of the preliminary data shows that the team has access to the bioinfomatics tools required to interpret the data. Several members of the review committee were impressed with the potential information these datasets could provide. While it has been possible to use related approaches to investigate the locations with which modified histones interact with DNA, ATP-dependent chromatin remodelling enzymes associate with DNA transiently and several research groups have had difficulty performing chromatin immunoprecipitation assays to define their locations. This explains why genome-wide location data are only available for a few of these enzymes in yeast. Generation of data for 15 chromatin-remodelling enzymes in ES cells has the potential to provide insight beyond anything accomplished since this family of enzymes was identified. For many of these enzymes, very little is known about their biological functions. Being able to visualise the locations they occupy in an annotated genome and compare this to other genome-wide datasets such as RNA and histone modifications will be truly informative.

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

Remarkably, all experimental researches are conducted in-house and complemented by a productive collaboration for the bioinformatics analyses in Strasbourg. The impact of the genome-wide analyses of the transcriptional regulatory networks controlled by chromatin remodelling factors in mouse ES cells is ground breaking. Once published, the visibility and the attractiveness of the team will extend. A high demand of collaboration is to be expected and ability to raise funds, increased. The team having a small size, they will have the ability to recruit diversified and high levels scientists.

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

While pursuing excellent classical research, this team developed a remarkable strategy, cleverly starting 3 years ago its ambituous and long-term chromatin remodeling project; They are now rich of a substantial amount of data.

- Appreciation on the project

Naturally, continuation of this high profile and ambitious chromatin remodeling project dominates the plans for the next 4 years of research. Although the team demonstrated that they have access to the tools required to analyse data, this will be time consuming due to the scale of the project. Furthermore, the team can add greatly by characterising the effect of knocking down each enzyme in ES cells using the technology they have developed in house. Finally, the ES cell system provides a means of studying how the role of chromatin remodelling enzymes alters as the ES cells are differentiated. It is widely anticipated that these enzymes will contribute to the reconfiguration of chromatin during the course of differentiation, but systems to study this have not been available. This project provides the first means of achieving it. The team has gained access to informatics expertise relevant to the analysis of high throughput sequencing datasets. As the scale of the data is, to some extent, overwhelming, though decisions will need to be made regarding how long to pursue the analysis (which could be continued for numerous years).

- Conclusion

  – Summary

- This scientific success illustrates the power of risk-taking, anticipation and long-term vision.

  – Strengths and opportunities

- The project is clearly defined and has a strong impact;

- Team with a strong expertise in the chromatin field and in the use of mouse ES cells

- Originality of the chromatin remodeling project;

- Substantial and very promising aquired data;

- Collaboration with dedicated bioinformaticians ;

  – Weaknesses and threats

- Still unpublished data;

- Handling potential competition upon publication of current data.

  – Recommendations

- Rapidly publishes a first wave of data concerning the chromatin remodeling project;

- Improve the output (publications);

- Maintain and if possible increase the size of the group;

- Gain international recognition and enhance networking to raise grants funding and attract talented graduate students and postdocs.

Title of the team : Neurotranscriptomes and Paleogenetics

Team leader : Mr. Jean-Marc Elalouf

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including post-doctoral fellows (Form 2.2, 2.4 and 2.7 of the application file)	1	0
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	0,5
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	2
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

The research of this team focuses on two completely different topics (Neurobiology and Paleogenetics). Both involve genomic approaches that are at the center and the basis of this team.

The neurobiology project is on the transcriptomics of different regions of the brain with the goal of deciphering the transcriptomic identity of specific regions involved in neurodegenerative disorders. Through this approach, the team has identified many different proteins that are specifically enriched in the striatum, one of the region degenerating in Huntington disease. They first reported Capucin, a gene of still unknown function. Another candidate is agpat4, a protein involved in catecholamine metabolism. This work led to a long list of proteins of interest that could be of relevance for neurodegenerative disorders. This work has therefore an impact by the identification of potential modifiers of neurodegenerative disorders such as Huntington's disease. Also, another work is the identification, by proteomics, of peptides selectively released in the striatum. Authors validated the relevance of the discovered peptides in rats.

The Paleogenetics project is part of a more global CEA project on the Chauvet-Pont d'Arc and the nearby Deux-Ouvertures caves in France; Initiated few years ago, it was successful, leading to the report of the complete mitochondrial genome and phylogeny from the extinct cave bear.

Indeed, although unrelated, both projects reflect the high competency and strong interest of the team in genomic technology.

The team had 12 publications within the last 4 years and one Ph.D. defence.

Brain transcriptomics: The number and quality of publications is very good (*Genomics*, *Physiol. Genomics*, *Mol. Cell Proteomics*) but not outstanding and in specialized journals. However, this is serious work using unbiased approaches on transcriptomics and proteomics of brain regions.

Paleogenetic**:** Although the project only gave one publication over the evaluated period, this work published in *PNAS* contributes to solidify the new era of ancient DNA studies and, very importantly, is of unusual high quality in this domain. It is considered as highly significant in the field.

Given the expertise of this team in the analysis of rare samples, an important aspect is that the team is collaborating with experts on the questions/studies they are focusing on. This is the case for the neurodegenerescence project with a strong and long-term collaboration with E. Brouillet (CEA, Fontenay-aux-Roses).

In the paleogenetics project, the team is in charge of molecular studies and efficiently collaborates with different experts in archaeology and in sample datation.

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

This is a small team: at present, 2 researchers, 1 technician and 2 PhD students (one per project). A postdoc present in the lab between 2005-2009, has now left. The expertise of the team and its privileged access to the caves and rare samples should be attractive.

One european grant and several national grants (Ministry of Culture, Genoscope for genotyping).

The team is involved in a national network on paleogenetics. This strong network led to a very significant publication on the phylogeny of paleolithic bears. No awards reported but the team leader has been invited to two conferences.

Concrete results involve the complete mitochondrial genome and phylogeny from the extinct cave bear that was published in *PNAS* and the maps of secreted peptides in the brain as well as transcriptomic identity of brain regions that are of importance as a resource.

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

The team is of limited size with two students and two researchers.

It has a cutting-edge expertise and ability in analyzing DNA from difficult and limited sources.

The team leader is reviewer for some journals and is involved in Ph.D. committees. No formal teaching activity are reported. Every year, the team trains one M2 student.

- Appreciation on the project

Both the paleogenetic studies and the study of the transcriptomic identity of brain specific regions are original, and strong projects to be continued. For paleogenetics, the most cutting edge project, preliminary analysis demonstrates technical feasibility. Getting long piece of ancient DNA and assembly are difficult tasks but progresses are being made. Considering the extraordinary reward, efforts and persistence are justified.

- Conclusion

  - Summary

This team has made important contributions on two different projects but that are based on the "omics" analysis of difficult materials, namely, transcriptomic analysis of specific regions of the brain, identification of specific peptides secreted from the striatum as well as the complete sequence and assembly of the mitochondrial genome from an extinct cave bear. All this work has a strong impact.

  - Strengths and opportunities

- Strength to tackle challenging genomic analyses.

- Priority access to the caves and ancient samples.

- Real advantage and expertise of this team over other research groups world-wide.

  - Weaknesses and threats

- Brain project: Expertise is essentially on the "omics" approach, and focus could be strengthened on the biological questions with the omics as the tool to answer the specific question.

- Paleogenomics: bioinformatics needs to be strenghten.

– Recommendations

- The committee is recommending the splitting of the team, acccording to the different areas of research:

- The Paleogenomics project should be pursued with J.M. Elalouf as the team leader. Priority should be given to recruiting postdocs and students to strengthen the team. Preliminary results look outstanding, thus recruitment should be implemented soon and strongly supported by the CEA.

- The Neurobiology project can be pursued given his interests in brain transcriptomics. Since this project is isolated in the Unit main area of research and is already conducted in collaboration with CEA scientists at Mircen, the commitee suggests that it would benefit to move to MIRCEN, at the Fontenay-aux-Roses site, in order to join a more appropriate intellectual and technological environment.

Title of the team : Biomolecules study by magnetic resonance

Team leader : Mr. Yves Boulard

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including post-doctoral fellows (Form 2.2, 2.4 and 2.7 of the application file)	0.7	0
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	0.7	1
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

The team has conducted two divergent projects. One concerns the study of DNA dynamics and the influence of protein interactions by electron paramagnetic resonance (EPR). In the second project, was developed caged hyperpolarized Xe compounds with the purpose to use these for magnetic resonance imaging (MRI). These two projects progressed significantly, leading to 11 publications, some of them in high ranked chemical journals (*Angew. Chemie* and *J. Amer. Chem. Soc.* for the Xe project). The papers are well cited. The EPR work, performed in collaboration with groups in Grenoble, resulted in 4 *Nucleic Acids Research* papers.

Reflecting expertise and originality, the team obtained 3 ANR grants, one of which as the principal investigator.

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

The team attracted two post-doctoral fellows and one PhD student finishing his thesis. Despite apparently fruitful interactions, the group seems somewhat isolated within the Institute. This is not related to the quality of the research but rather to the very limited size of the group. Collaborations with teams from the CEA Physics department and with groups from Grenoble have been very fruitful and of good quality, leading to common publications.

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

The size of the team has always been small and dedicated to technological developments at various distances to potential users. Strategically, the visibility of the team could have been more pro-active within the Unit and outside.

- Appreciation on the project

Despite his relative isolation, the team leader wishes to continue both projects. He has the knowledge and technical capabilities to do so. In the past, numerous technical problems were solved, and achievements are ready to be exploited.

One project is to apply spin labeling to study DNA interactions with repair enzymes and, in parallel, to develop modeling tools for protein-DNA interactions. Although these approaches are valuable, it is not entirely clear what this work really will lead to.

The second project is to use the caged Xe compounds for the imaging of transferring receptors and for the study of solid tumors. Extensions to develop novel biosensors for measurement of pH or detection of oxidative stress (presence of H202) in cells, and experiments on small animals in collaboration with the NEUROSPIN laboratories (CEA), are planned.

The imaging work should find practical applications and therefore should be able to attract fundings.

Although in continuation of a previous work, these cutting-edge technological developments are original and worth pursuing. New results are reasonably expected and applications, in perpective.

- Conclusion

– Summary

The team conducted two very divergent projects at the frontier of biophysics and structural biology. This applied to the study of DNA conformation deformation and the design of biosensors. It led to excellent publications and promises of interesting developments.

– Strengths and opportunities

The projects are technically challenging with, for one of them, possibilities for practical applications. Despite the small size of the group, collaborations will be established with the new high fetched research center NEUROSPIN.

– Weaknesses and threats

- The final objectives of the EPR work are insufficiently defined.

- The size of the team is too small. Without recruitments, it will be very difficult to continue both projects in a meaningful way.

– Recommendations

The committee appreciated the rare and multi-disciplinary expertise, the scientific output and the enthousiasm of the team leader. However, it recommends that, in order to increase the visibility of its research activities and improve its impact in biology, this isolated team integrates a larger group. This group could either be in the same Unit based on common biological interest (for example team 1) or move to the CEA Physics department with whom collaborative work has been successful, and thus reinforces Biology/Physics/Technology interfaces. During the visit, these options were discussed and agreed with the team leader. They are opened either way.

Title of the team : Plasticity of cellular functions and interactions

Team leaders : F. Chauvat, C. Cassier-Chauvat

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including post-doctoral fellows (Form 2.2, 2.4 and 2.7 of the application file)	2	3
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0.2	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	2
N7: Number of staff members with a HDR or a similar grade	2	2

- Appreciation on the results

This team investigates the metabolism and molecular responses to stresses generated by reactive oxygen species and metal pollutants of the cyanobacterium *Synechocystis*. Cyanobacteria are very abundant photosynthetic microorganisms. Despite their potential biotechnological interest, they are poorly characterized. The team focused on cross-talks between pathways, such as metabolism, cell division and stress responses. They have (i) studied the cellular response to cadmium, (ii) started the characterization of the thioredoxins and glutaredoxins and (iii) characterized the cell division machinery of this bacterium. The quality of the research performed in this team is good, although not outstanding. They have obtained some very interesting results which have had a wide impact. For instance, they have found that monothiol glutaredoxins from *Synechocistis* but also from other organisms form dimeric complexes bridged by an iron-sulfur. This was one of the first indications that monothiol glutaredoxins are involved somehow in the control of iron homeostasis. Their observation has been confirmed by others and contributed to the development of a new field. The team members are recognized experts of *Synechocystis* and they have developed genetic and molecular tools that they have distributed to numerous researchers around the world. They have established several collaborations, mostly with labs located within the CEA or elsewhere in France.

The scientific productivity is very constant, with 11 papers published in very good microbiology journals such as *Mol. Microbiol*. and *J. Bacteriol.* For almost all of these articles, most of the work had been performed in their laboratory. Four of the 11 papers resulted from collaborations. Two of their articles have been cited in *The Faculty of 1000*.

The team members have also supervised 5 theses, which represents an average of one per year.

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

This team has an obvious impact on the cyanobacteria community: they have sent their plasmids for mutant construction to more than 50 groups working on cyanobacteria.

French PhD students and foreign post-docs, mostly from Asia, were attracted.

The team leaders have been invited to give three lectures over the past 5 years at international meetings, one of them was organized in Spain (a meeting on cyanobacteria), and 2 in France. The team was involved in the organization of an international symposium in France. They have also been invited to give 12 talks at national

meetings and in various institutions. However, the international connections of the group are rather low. Internationally, leading scientists working on cyanobacteria are located in Germany, Asia or in America and they do not seem to interact much with them.

The quality of the research has been recognized by various funding agencies. Three ANR, one CNRS and one « indo-french » grants were obtained.

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

The team is headed by two senior PIs; they seem to equally share leadership, authority and project management.

- Appreciation on the project

The team aims at continuing to investigate the metabolism and the global responses to oxidative and metal stresses of Synechocystis, focusing on the redox/antioxidant systems and continuing on the characterization of the glutaredoxins, thioredoxins and ferredoxins of this bacterium. In particular, they want to decipher the role of glutaredoxins and glutathione in the regulation of iron and sulfur homeostasis. They also intend to identify glutathionylated proteins under various conditions of growth and under stress and to study the specificity of the various glutaredoxins and thioredoxins by identifying their partners. In parallel to this more fundamental project, they want to start a new one which combines a basic research interest and a potential applied research objective. They should address the problem of hydrogen production by cyanobacteria and study the metabolic adaptation of these microorganisms to high-level production of H2. They mean to use their expertise in cyanobacteria genetics to generate mutants that over-express the enzymes involved in H2 production. The idea is that these mutants could be useful to photo-produce industrial-levels of H2, a fuel containing high energy. Moreover, as oxygen inhibits H2 production, they would use site-directed mutagenesis to engineer the hydrogenase enzyme to make it more tolerant to O2.

This is a very good project, solid, feasible. The team has all the tools and the expertise needed to achieve it. However, regarding the first part of the project, this fails to clearly propose a strategy that will allow to unravel the role of glutathione in iron homeostasis. It also fails to clearly identify the biological question they intend to solve. Thus, a possible pitfall of this strategy is that the team could miss a potentially outstanding discovery by not digging enough. Since thioredoxins and glutaredoxins have already been extensively characterized in other organisms, there is a possibility that the project will only confirm what has been observed in other model organisms. For these reasons, although this project is very good, it is not outstanding. The second project is really attractive. The team wants to address a long-standing problem (the role of hydrogenase) and their results could have a really interesting and useful output. In addition, they are probably among the best experts in the world to try to engineer this strain overproducing hydrogen. This second project could have a potential economical impact.

- Conclusion

– Summary

Overall, it is a well-established team focused on global responses to oxidative and metal stresses with a steady scientific production and worldwide recognition in the study of cyanobacteria. The team has grants, students and postdocs, and the project is attractive.

– Strengths and opportunities

- The team has a strong implementation in the study of the Synechocystis cyanobacteria oxidative stresses responses, and more globally on system level analyses.

- Diversity of approaches: mostly genetics and molecular biology, in particular transcriptomic and metabolomic analyses.

- Development of performant genetic and molecular tools.

– Weaknesses and threats

- Face strong competition from several groups around the world.

- Insufficient international exposure.

– Recommendations

- Define more clearly a few scientific questions;

- Pursue potential outstanding projects, avoiding confirmation of what is already known in other organisms

- Increase its international exposure by attending meetings outside France and Europe and strengthen their international connections and collaborations. This will increase their impact and visibility.

Title of the team : Dynamics of Biological Networks

Team leader : Jean Labarre

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3.3	4
N3: Number of other researchers including post-doctoral fellows (Form 2.2, 2.4 and 2.7 of the application file)	1.7	0
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1.1	1.5
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	0
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

The central interest of the team is the study of metal-mediated stress in yeast cells, particularly in relation to sulfur metabolism, using genome-wide approaches. Important contributions have been generated and the team extended its interests to mathematical modelisation of metabolic processes or computational biology. Based on their expertise in proteomic analyses, the members of the team established internal and external collaborations. This resulted in some dispersion and limited production in what could be considered the core areas of interest for the team.

During the period under evaluation the team members had authorship in a large number of articles (24), generally in journals of medium to very good impact (*JBC*, *EMBO J.*, *Gene & Dev.*, *PNAS*). However, a significant number of them correspond to studies performed by actual team members in other research groups and from collaborations in which the team members have not a central protagonism. After triming these, the number of publications is limited to 7. The team presented a significant number of contributions to national and international meetings, and team members were invited to six scientific conferences.

In addition to the collaborations with other teams of the SBIGeM Unit, which in general are productive, the team has established collaborations with other national and international groups. One of these resulted in one article in 2009, while the others still have to reveal to be productive. The on-going collaboration with a team in Marseille should be important for successful development of the project on protein carbonylation.

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

Several invited participations in international symposia and in diverse committees, involving diverse senior members of the team.

The group is mainly formed by senior scientists. Surprisingly, the number of PhD students has been very limited in the past and is zero at the moment. This may reduce the attractiveness of the team for young graduates intending to carry out PhD research.

Team members do not participate regularly in teaching activities

The team is participating with continuity in funded competitive projects, including EU programmes.

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

This is a small team that seems to function well. Two different subgroups seem to carry out independent research in parallel, with limited common authorship but without apparent disturbance. The presence of experimental researchers and experts in bioinformatics in the same team could be a plus whether the two subgroups were able to find common interests and synergies.

- Appreciation on the project

The proposed project basically continues studying biological problems (protein oxidation, sulfur metabolism, biological networks) in which the team has been interested in the previous period. It therefore does not suppose a turn in the team activities.

The project is divided into three main lines which, in some aspects, reproduce the division of the team based either on employing experimental or on theoretical approaches. The subproject (mathematical models of yeast sulfur metabolism) intends to bridge the above two approaches focusing on a biological problem (sulfur metabolism) in which the team has long experience, having employed proteomic and metabolomic strategies. The project concerning analysis of protein carbonylation and its correlation with subcellular compartmentalization may be somewhat risky. It will require that the team members acquire expertise in cell biology techniques. The project on analysis of biological networks seems rather distant from the other subprojects and closer to the interests of some other teams in SBIGeM.

- Conclusion

  – Summary

The team has two main lines of activities to be continued: studies of oxidative stress by metals and the corresponding cellular responses, and computational biology. Some studies bridge both types of activities, although basically they follow parallel lines, which might lead to the constitution of separate teams in the future.

  – Strengths and opportunities

- Experience in proteomics

- Experience in computational studies.

- Good performance in rising funds in competitive calls.

  – Weaknesses and threats

- Insufficient definition of the research priorities;

- Apparent separation in the research interests between team members;

- Poor performance in publication and thesis production;

- Dispersion through collaborations.

– Recommendations

- The team should concentrate its efforts on a defined project, building on expertise in areas in which it had important contributions in the past.

- Incorporation of new members to the team should be an opportunity to find common interests concerning the research priorities

- Collaborations with external groups should be contemplated only when beneficial for the team priorities.

- The project will be carried out by senior scientists with the assistance of research technicians. Incorporation of post-docs and PhD students would be necessary given the large amount and diversity of the work to be done, and this would fill one of the deficits of the team.

Title of the team : Oxidative stress and cancer

Team leader : Michel Toledano

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1.3	2
N3: Number of other researchers including post-doctoral fellows (Form 2.2, 2.4 and 2.7 of the application file)	2	3
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	1
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	2
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

The team has long experience and international presence in the field of oxidative stress. They mostly use yeast as biological model, although studies using mammalian cells were initiated during the period under evaluation. With the above central interest, six different research lines have been followed during the period, which could signify some dispersion of efforts. Important contibutions have been made recently in proteomic-wide studies of protein oxidation.

The document listed 19 articles during the evaluated period. Considering the 4 articles made by a second senior member of the team during her stay in the USA as a post-doc, one technical article, and 6 articles where only the team leader appears in the list of authors and three reviews (of high impacts), the in-house production within the last 4 years is rather modest considering the history of the group, the number of members and the international presence of the leader. It seems probable that other articles covering studies not yet published will be produced in the near future, although this has to be confirmed. Collaborations have been productive but, most often, the present team is on middle author positions.

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

The team leader frequently participated to international meetings.

During the period under evaluation, the group has incorporated several post-docs and PhD students, some of them from abroad. To be noted, the team leader has successfully supervised three theses in the period, in most cases, leading to a publication.

The group collaborates with partners from six countries. In some cases, this has resulted in good publications with co-authorship.

The team participates regularly in competitive funded projects, although not in EU projects.

One patent

No significant contribution to teaching activities but significant contribution to PhD and grant evaluation.

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

There is a senior researcherin the team and one junior researcher who joined the team one and half year ago. It is expectable that the contribution of the junior researcher (largely based on the expertise acquired in the USA) will be manifested in the near future.

The scientific contribution of the team in the field of oxidative stress responses has been in fact relevant at the international level, and has allowed the initiation of new research lines (redoxin control of gene expression, oxyproteome analysis approaches,…).

In the past, the direction of the several research lines has been under the entire responsibility of the team leader. Surprisingly, no communications in scientific meetings with participation of team members other than the leader are reported. Thus, globally, the scientific visibility of the team is largely centered on the team leader.

- Appreciation on the project

The scientific project will follow two main lines of activities, with several subdivisions each. The first line is focused on redox control and iron metabolism, and continues the historical main interest of the team. It is important for the future project not to reproduce the dispersion of efforts that had occurred in the past.

The second line, described with less detail, will focus on the study of protein quality control and its redox regulation, mainly in mammalian cells. This is a relevant and novel field, which is addressed for the first time by the team. The expertise of the second senior researcher may contribute to the success of these latter studies.

Both the proposed high-throughput proteome approaches and ERQC redox control studies are original and of potential high impact from a strictly scientific point of view.

- Conclusion

  - Summary

This is a competitive team at the international level with large experience and expertise in studies on oxidative stress responses. The group has traditionally employed yeast cells as biological model, although in the past years some studies by the team have begun to be extended to mammalian cells. This is welcome evolution to be pursued.

A large diversity of subprojects has been developed in recent years, although some of them have not yet resulted in publications.

Globally, the articles published in the period under evaluation are of high scientific quality although the number of those describing experimental research made only in the team context is modest. Clearly, this is an aspect to be improved in the future.

– Strengths and opportunities

- Long-term experience in the field of oxidative stress responses, with very relevant contributions ;

- Opportunity for addressing novel biological problems such as redox control of protein quality;

- Potentially high impact results that could be published in the near-future;

- High scientific reputation of the team leader at the international level;

- Stable rising of funds in competitive calls.

– Weaknesses and threats

- Dispersion of efforts among multiple tasks, with modest scientific production in some of them;

- Lack of presence of team members, except the leader, in the international scene;

- Lack of participation in competitive international projects.

– Recommendations

- Set team level priorities ;

- While maintaining the productive collaborations with national and international groups, the team should reinforce the scientific production in which the group members have the major authorship contribution;

- Encourage all team members to give seminars and participates to international meetings.

Title of the team : Genome stability

Team leader : Mr. Carl Mann

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including post-doctoral fellows (Form 2.2, 2.4 and 2.7 of the application file)	2	2
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	2
N7: Number of staff members with a HDR or a similar grade	1	2

- Appreciation on the results

The group has carved a niche in studying the role of chromatin factors following genotoxic stress. In particular, the group focused on the role of the Asf1 chaperone combining genetic, molecular and structural studies performed in close collaboration with the Structural Radiobiology group of the CEA, in Saclay. It successively shed light on the important process of histone deposition in reponse to DNA damage, established the role of the interaction between

the Asf1 chaperone and histone H3, which promotes acetylation of H3-K56 and described the dynamics of the interaction of Asf1 with the Rad53 checkpoint kinase. Binding of Asf1 to Rad53 is competitive with its binding to the histones H3/H4 and and the co-chaperones HIR/CAF-1. This has made seminal contributions linking the activity of DNA damage response factors. This investigation initially conducted in yeast have been extended to mammals using H3-GFP fusion in Hela cells and FRAP analyses. The Asf1-H3 interaction controls the deposition of H3.1 and H3.3 independently and dependently of DNA replication, respectively.

In parallel, a new project concerning oncogene-induced senescence has been initiated and will be continued.

The group reports 8 publications, most of them in high rank peer-reviewed journals (*PNAS*, *MCB*, *Oncogene*) and as last author, thus reflecting the prominent production of the team in these studies.

The group has strong and productive links with research labs outside the Unit, which co-authored a number of excellent publications.

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

The team is known for the extreme technical quality and rigourousity of its research, providing a high capacity for the recruitment of talented scientists. There is no reported awards and, surprisingly, a limited number of seminars in France and NO invitation to international conferences.

In the description of past staff, a good mix of postdocs and students are listed. Team members are mainly from the French area with the sole exception of a PhD student. One member of the team has taken teaching responsabilities.

Funding is mainly national from the ANR and Cancer research associations.

Collaborations are mainly with French groups with the exception of a lab in Cambridge (UK).

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

The scientific achievements of the team are a high quality and well focused to reflect good management.

To be noted, one research member spent time abroad in different labs, including a recent stay in Cambridge (UK) for several months.

Although not abandoning the histone chaperone field, the switch towards a more explicit focus on cellular senescence demonstrates that the group aims at entering the competitive and cutting-edge area of cell progression, signalisation and oncogene expression.

- Appreciation on the project

The team will pursue mechanistic studies of the Asf1-Rad53 interaction and interrogates its role in the response to genotoxic stresses using genetic approaches (mutant analyses based on structural analyses).

Major focus will now concern the oncogene-induced senescence. The team has set up and begun to explore a stable and efficiently inducible cell system to generate, in a few days, large quantities of synchronous oncogene-induced senescent cells. This strongly positions the team to examine the role of individual cyclin-dependent kinases, links to the assembly of repressive heterochromatin in induced senescence and perform powerful proteomics analyses. This is presently a very hot area, following the appreciation that oncogene-induced senescence has a powerful tumor suppressive role. The approaches proposed (exploitation of the RAF-inducible system to study the role of CKIs, Rb family members, sh RNA screens, mass spectrometry on chromatin) and the development of cell systems different from fibroblasts, are original and have the potential to generate exciting new results. All these appealing perspectives of research are highly relevant for cancer research, and indeed complemented by cutting-edge collaborations with a team at Harvard Medical School and the CEA bioactive molecule screening facility in Grenoble to search for small molecules that inhibit or reverse senescence.

- Conclusion

– Summary

This team had major contributions in the field of histone chaperones combining genetics, molecular and structural information. The new focus on oncogene-induced senescence is of major interest and sustained by a recently developed and performant experimental system with already promising preliminary data. The emergence of this new direction of research reflects risk-taking and a clever long-term anticipation of potential cutting-edge researches. This will likely increase the profile and visibility of the group.

– Strengths and opportunities

Long standing interest and expertise in chromatin and genotoxic events, likely to pay off when applied to higher profile subjects.

– Weaknesses and threats

- The cellular senescence field is getting crowded. The group must move fast, maintain sufficient human resources and publish rapidly.

- The gradual focus on one subject (senescence) only and by a group new to the field may be seen as risky. The group should capitalize as much as possible on its core skills.

– Recommendations

- The committee strongly supports the gradual development of the senescence project.

- It encourages the team to apply to international grants such as those from the European Union to allow greater financial revenues and increase the networking benefits.

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

Team 1: Mechanisms of DNA checkpoints

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

Team 2: Mechanistics and Regulation of RNA polymerases

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

Team 3: Nuclear regulation and Stress

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

Team 4: Transcriptional regulation of genomes

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

Team 5: Epigenetic regulation and cancer

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

Team 6: Neurotranscriptomes and Paleogenetics

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

Team 7: Biomolecules study by magnetic resonance

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

Team 8: Plasticity of cellular functions and interactions

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

Team 9: Dynamics of Biological Networks

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

Team 10: Oxidative stress and cancer

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

Team 11: Genome stability

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

energie atomique - energies alternatives

L'Administrateur Général

Monsieur Pierre GLORIEUX
Directeur de la section des Unités de recherche

AERES
20, rue Vivienne
75002 PARIS

Saclay, le 07 mai 2010

N/Réf. : DPg/AN/np/2010-130

Objet : Observations du CEA sur le rapport d'évaluation du « Service de biologie intégrative et génétique moléculaire » (iBiTec-S/SBIGeM)

Monsieur le Directeur,

Je remercie tout d'abord l'AERES pour la qualité du rapport d'évaluation sur l'activité du « Service de biologie intégrative et génétique moléculaire » situé au sein de l'Institut de biologie et de technologies de Saclay et pour la pertinence des recommandations qui ont été faites.

En tant qu'Administrateur Général de l'Etablissement CEA, ce rapport n'appelle pas de commentaires particuliers de ma part. Je puis vous assurer que je prêterai la plus grande attention à la mise en œuvre des actions qui permettront de répondre aux recommandations formulées par l'Agence.

Veuillez agréer, Monsieur le Directeur, l'expression de mes cordiales salutations.

Bernard BIGOT

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Réponses du SBIGeM (iBiTec-S/DSV/CEA) au rapport AERES

We would like to start by thanking the AERES committee and the organizers for all their efforts to enable smooth and effective running of the evaluation of our research unit. The report is very complete and contains a number of highly interesting remarks that will be of great help to the SBIGeM management and to the teams in the near future. The SBIGeM thanks all the members of the committee for this important contribution. We also acknowledge the overall appreciation of the Unit's activities, which provide welcome recognition for all the members of the Unit, whose dynamism and productivity have deservedly achieved international status for scientific excellence.

General comments

For the appreciation team by team, a general problem is related to the "Staff members" tables. More specifically, it is extremely difficult if not possible to correctly fill the "Past" column. The numbers indicated in the document correspond to all the personnel that have been present during a part or the totality the evaluation period (2005-2009) as identified from the SBIGeM document sent to the AERES. The indicated numbers are therefore strongly overestimated, which may lead to a misleading interpretation, for example in terms of efficiency of scientific production.
We suggest the average presence per year for each category members being indicated in the table more than the total number of members during the evaluation period.

In addition to the above general remark, several recommendations or remarks mentioned in the report retained the attention of some teams. The corresponding comments and answers are listed in the following text.

Team 1

Team 1 members agree with most of the committee appreciations, however they would like to comment (i) on the committee feeling that some of our "new" interests are sources of dispersion and (ii) on the issues of scientific animation and contribution to teaching that were considered as "limited".

(i) Confronting theoretical approaches to experimental data has a long-standing tradition in our team, and has been one of our specificities and strengths. This allowed us to tackle the study of DNA replication in a fruitful manner (5 publications over two years). Our success brought us to get engaged in an interdisciplinary consortium (with other groups from ENS Lyon, ENS Paris and University Paris XI) that studies the competitive subject of spatio-temporal program of human genome replication. Therefore, we believe that as we are already successfully engaged in the theoretical and experimental study of DNA replication (which is not "new" to us), it would be a mistake to prevent the further development of this subject in our team.

(ii) Regarding scientific animation and teaching, team 1 members weekly organize inter-team meetings (with colleagues studying structural biology), and monthly organize technical intra-team meetings where subjects and routine problems are discussed. Finally,

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the number of hours devoted to teaching is above the average number for the other teams of the Unit and has allowed to attract many students.

Team 6

Team 6 members appreciate the positive evaluation by the committee of their scientific activity and are happy to note that the original and strong projects carried out in the team have to be continued. The group leader notes that the committee is recommending splitting the team and will discuss this possibility with the Director of the Unit.

Team 9

Team 9 members want to stress out that at the beginning of the period of reference, the team was only composed of 1 researcher and 1 technician. It has deeply changed during that period because of the sequential arrival of 3 researchers and the recent arrival of 1 part-time technician. During the period of reference, the 4 researchers have been the central protagonists of 10 publications (and 4 invited reviews), whether they were yet in the Team 9 or not.
If one considers only the publications where the team is main contributor, the number is 7 (plus 4 invited reviews), which is considered as a "poor performance" but the team members want to stress that the committee did not sufficiently take in account the fact that newly arrived researchers cannot be productive immediately in term of published articles.
The remaining collaborative publications are closely related to the technical expertise and the research areas of the team (studies of oxidative stress and computational biology). Team 9 members do want to emphasize that collaborations are an important aspect of their scientific strategy. These collaborations are not only beneficial for the team (increasing expertise and scientific visibility) and for the collaborators, but also for the advancement of general knowledge.

Team 10

Team 10 members want to comment about three major points that have been missed or disregarded.

1. The in-house scientific production was appreciated as "modest". However 19 articles were published during the evaluated period (plus four book chapters). If one exclude the 4 articles by a second senior member of the team during her stay in the USA, one technical article, and 6 articles where only the team leader appears in the list of authors and 3 (high impact) reviews", it remains five papers corresponding to the in-house scientific production (to which could be added the paper published in January 2010), which should not be qualified as "modest" for a single scientist (the group leader is the only permanent scientist of this team for the most part of the evaluation period).
2. The committee was "surprised that no communications in scientific meetings with participation of team members other than the leader are reported": this is not applicable since the group leader has been the only permanent researcher for most of the time of the evaluation period. Furthermore, the participation of the group leader to international meetings is based on formal invitations to give scientific lectures.

3. The document noted a "Dispersion of efforts among multiple tasks, with modest scientific production in some of them". This critic has not been scientifically substantiated by the evaluation document, and therefore appears very subjective. On the contrary, past projects do not correspond to multiple tasks: the team only followed its field of research initiated by the group leader that incorporates antioxidants, thiol-redox control and protein regulation by oxidation. For instance, the discovery of the yeast sensor was only made possible by simultaneously studying thiol-peroxidases, the thioredoxin and GSH pathways and the Yap1 regulator, and our current project of reconstituting this sensor incorporates in an assay tube Yap1, the GPx3 peroxidase and the thioredoxin pathway. In consequence, we wish to remove the sentences "Dispersion of efforts among multiple tasks, with modest scientific production in some of them" in the paragraph "Weaknesses and threats" and "Avoid tasks dispersion by defining most important strategic research interests" in the "Recommendations" paragraph.

Christophe CARLES
Head of the Integrative Biology and Molecular Genetics Unit