I2BC - Institut de Biologie Intégrative de la Cellule

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Institute for Integrative Biology of the Cell

I2BC

Under the supervision of the following institutions and research bodies:

Université Paris-Sud

Centre national de la recherche scientifique - CNRS

Commissariat à l'énergie atomique et aux énergies alternatives - CEA

January 2014

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

Department for the evaluation of research units

On behalf of AERES, pursuant to the Decree of 3 november 2006[1]*,*

- Mr. Didier HOUSSIN, president
- Mr. Pierre GLAUDES, head of the evaluation of research units department

On behalf of the expert committee,

- Mr. Frédéric BARRAS, chair of the committee

[1] The AERES President "signs [...], the evaluation reports, [...] countersigned for each department by the director concerned" (Article 9, paragraph 3 of the Decree n ° 2006-1334 of 3 November 2006, as amended).

Evaluation report

This report is the result of the evaluation by the experts committee,the composition of which is specified below.

The assessment contained herein are the expression of independent and collegial deliberation of the committee.

Unit name:	Institute for Integrative Biology of the Cell
Unit acronym:	I2BC
Label requested:	UMR
Present no.:	–
Name of Director (2013-2014):	–
Name of Project Leader (2015-2019):	Mr Thierry MEINNEL

Expert committee members

Chair:	Mr Frédéric BARRAS, CNRS
Experts:	
Sub-committee for Departements B3S+Virology	Mr Stephen CUSACK, EMBL, President
	Ms Nathalie ARHEL, Institut Universitaire d'Hématologie. Hôpital Saint Louis – Centre Hayem (representative CoNRS)
	Ms Marie-Thérese GIUDICI-ORTICONI, CNRS (representative CoNRS)
	Mr Eric GOORMAGHTIGH, Université libre de Bruxelles, Belgique
	Mr Urs GREBER, University of Zurich, Switzerland
	Mr Peter HEATHCOTE, Queen Mary University, London, GB
	Mr Franck KOZIELSKI, University College London, GB
	Mr Petr LEIMAN, École Polytechnique Fédérale de Lausanne, Switzerland
	Mr Bernard OFFMAN , Université de Nantes (representative CNU)
	Mr Gabriel WAKSMAN, University College London, GB

Sub-committee for Department Genome Biology	Mr Laurent DURET, President
	Ms Valérie BORDE, CNRS (representative CoNRS)
	Mr Witold FILIPOWICZ, Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland
	Mr Pierre GENEVAUX, CNRS
	Mr Stephen GRUBER, Max Planck Institute of Biochemistry, Martinsried, Germany
	Ms Nouria HERNANDEZ, University of Lausanne, Switzerland
	Mr Alexander MANKIN, University of Illinois at Chicago, USA
	Mr Mathias SPRINGER, CNRS
	Mr Didier TROUCHE, CNRS and Université Paul Sabatier
	Ms Angélique VETILLARD, Centre Universitaire J-F Champollion, Albi, (representative CNU)
	Mr Kenneth WOLFE, University College Dublin, Ireland
Sub-committee for Department Cell Biology	Ms Graça RAPOSO, President
	Ms Renata BASTO, CNRS (representative CoNRS)
	Mr Oliver BLACQUE University College Dublin, Ireland
	Ms Bénédicte DURAND, Université Claude Bernard (representative CNU)
	Mr Nico GELDNER, University of Lausanne, Switzerland
	Ms Rosine HAGUENAUER-TSAPIS, CNRS
	Mr Stefan LINDER, Universitätsklinikum Eppendorf Institut, Hamburg, Germany
	Mr Sébastien MONGRAND, Université Bordeaux Segalen and INRA (representative CoNRS)
	Mr François SCHWEISGUTH, CNRS
Sub-committee for Department Microbiology	Mr Ivan MATIC, President
	Mr Arnold DRIESSEN, University of Groningen, Netherlands
	Mr Marc G.J. FEUILLOLEY, Université de Rouen (representative CNU)
	Mr Christophe GUILHOT, CNRS
	Mr Alexander MANKIN, University of Illinois at Chicago, USA
	Ms Béatrice PY, CNRS
	Mr Ezio RICCA, Università degli Studi di Napoli Federico II, Italy
	Ms Isabelle SCHALK, CNRS (representative CoNRS)

Scientific delegate representing the AERES:

Mr Pierre COUBLE

Mr Jean-Antoine LEPESANT

Representatives of the unit's supervising institutions and bodies:

Mr Jacques BITTOUN, Université Paris-Sud

Mr Gilles BLOCH, CEA

Mr Pierre CAPY (représentant de l'École Doctorale n° 426 "Gènes, génomes, cellules")

Mr Thierry GRANGE, CNRS

Mr Marc PALLARDY (représentant de l'École Doctorale n°425 "Innovation Thérapeutique")

1 • Introduction

History and geographical location of the unit

The I2BC Institute will merge teams from 8 independent units, which are currently located on three different campuses (Gif, Orsay, Saclay). I2BC project includes 77 teams and about 800 personnel on a single site (Campus CNRS Gif-sur-Yvette) and most of the teams will be located within the same building starting 2018. The teams will be organized into 5 disciplinary Departments (Microbiology, Virology, Structural Biology, Genome Biology and Cell Biology) covering numerous facets of Biology together with an impressive series of methodological platforms.

Management team

The I2BC will have a central administration and a single point of entry for financial and human resources. Since September 2012, an "executive committee of I2BC" (EC) has been set up, which includes the General Director, the Scientific Deputy Director, the Managing Director, and the heads of the future departments. For now, it also includes the heads of the current research units. The EC meets on a weekly basis for decisions concerning the organization of the I2BC project. A meeting of a larger committee including the unit directors is planned to be held once per month. The EC is responsible for both Research and Support activities. Research activities are carried out in 5 scientific departments, each under the supervision of a Department Director. The Scientific deputy Director is in charge of transversal scientific activities (programs, education, coordination) and platforms. Support activities are under the supervision of the Managing Director and include Contracts, Innovation, Valorization, Administration, Finances, Human Resources, Stores, Communication, Safety.

AERES nomenclature

SVE1_ LS1, LS2, LS3, LS6

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	85	77
N2: Permanent researchers from Institutions and similar positions	180	155
N3: Other permanent staff (without research duties)	223 (scientific team + support function)	201 (scientific team + support function)
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	3	
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	88	32
N6: Other contractual staff (without research duties, **without 77 M2, M1, L1, L2, BTS student**)	53 (scientific team + support function)	17 + 11 (scientific team + support function)
TOTAL N1 to N6	**632**	**493**

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	127	
Theses defended	202	
Postdoctoral students having spent at least 12 months in the unit*	51	
Number of Research Supervisor Qualifications (HDR) taken	24	
Qualified research supervisors (with an HDR) or similar positions	191	

2 • Overall assessment of the unit

The I2BC project is essential for Life Sciences research in the Paris-Saclay initiative for excellence. It is strongly supported by CNRS, CEA and University Paris Sud (Orsay) and has and will benefit from high levels of funding for building and infrastructures.

Two main motivations lie under this initiative to create this large unit, a vision of what Life Sciences should be in the future and a reorganization of Life Sciences research within the Paris Saclay area. The project is to foster cross-disciplinary collaborations such that biological processes can be studied by a wide array of methods and at different scales, from the atom to the cell, from the nanosecond to the generation time, and throughout multiple organisms and species. It is the objective that an integrative view of biology eventually emerges from such multi-scales/sizes/organisms investigations. To reach this goal, high-quality technological and instrumental platforms will occupy a central part of the project. This is indisputably an important project, which could provide the Paris-Saclay area with a new prestigious, ambitious and attractive Institute dedicated to Life Sciences as well as with a unique multi-disciplinary site for training new generations of students in Biology. A salient feature of the I2BC project was the obtaining of significant financial support to build and rehabilitate laboratories on the Gif campus.

The committee was very impressed by the general scientific level of the teams. About 20% of them can be ranked at the highest international level given their output and international recognition, and conversely very few are weak. The committee was also impressed by the technological level and organization of most platforms, which are bound to be key actors in the success of the I2BC. Importantly, joint intra- or inter-departmental projects were presented to the committee by a significant number of PIs, illustrating the will of many to engage in joint investigations and/or at least knowledge sharing.

The logic beyond the regrouping is also to promote synergy, enhance visibility and avoid inefficient (local) competitions for grant calls. In the very recent past, in the context of the I2BC construction, this proved to be a successful strategy in the case of the Structural Biology platforms, which by gathering expertise split over 3 sites was awarded the status of a node in the FRISBI network. Similarly the BIG project, a Labex funded collaboration, includes both structural biologists from Saclay and molecular geneticists from Orsay, Gif and Saclay.

The I2BC project should start in January 2015 but building delivery and actual moving and regrouping of the teams will not take place before January 2018. A significantly extended transition period is therefore ahead, the good managing of which will be essential to the success of the project. The committee identified among the group leaders a significant level of questioning about the actual scientific added value of the project but overall even cautious attitudes should be convinced to contribute once the project gets going. On the contrary a higher-than-usual level of “anxiety” and “unanswered responses” among the researchers and technicians was evident. As a matter of fact this was already detected and mentioned by the I2BC staff (see SWOT analysis in the written document). The committee is fully aware that this is inherent to any large restructuration process and is not specific to I2BC. However, for the I2BC to become a success story will require full adhesion of most, if not all of its members, and the committee recommends these concerns to be given special and reinforced attention. It is however fair to say that the I2BC staff has somehow anticipated on such difficulties and is actively looking for solutions and procedures which could be acceptable to all agents.

Strengths and opportunities related to the context

- Strong support from University, CEA and CNRS with allocation of large space (36 000 m^2) and secured financial support, via CPER, Idex, PIA or Plan Campus initiatives, for building construction and rehabilitation (47.65 M€).
- Excellent organization and running of platforms, each being controlled and managed by a dedicated researcher or group.
- Creation of a Scientific Delegate Director to set up transversal programs between teams from different disciplines and with different expertise.
- Important implication in Paris Saclay teaching at all levels.

Weaknesses and threats related to the context

- The I2BC will be a very large institute. Such a size will be a source of difficulties for governance and communication at different levels. These difficulties will be enhanced during the transition period.
- A gap still exists between the laudable integrative vision of the management and several group leaders for which research is still very much reductionist. Any lag in getting the project going will reinforce this cautious attitude.
- Integrative biology identity yet to be established.
- Several axes required for integrative biology (systems biology, single molecule analysis, and computational biology) need to be developed or reinforced
- Budget for transversal programs unsecure.
- Limited attractiveness during the transition period.

Recommendations

- The committee recommends that a determined effort be made by the management to increase uptake of European funding and that suitable candidates, particularly young scientists, be identified as potential applicants to the ERC and given appropriate encouragement and mentoring.
- The committee recommends increasing initiatives to keep all categories of staff informed in a clear and “non-managerial” way, by organizing meetings, using counsels and internal committees and group leaders as relays.
- The committee recommends that reallocation of technicians be decided internally within the I2BC and result from concerted discussions between all concerned, i.e. the head of I2BC, the Department head, the group leaders involved and the agent whose location is being discussed.

3 • Detailed assessments

As the evaluation was meant to appreciate the I2BC project, detailed items on achievements during the 2009-2013 period will be dealt with in the analysis of each Department and each team below. Hereafter the reader will find some general information/answer gathered from the written reports but also from meetings, interviews and seminars given during the 4-days visit.

Assessment of scientific quality and outputs

The main goal of the I2BC project is to bring together different scales, different organisms and different methodologies to tackle related scientific questions pertaining to the dynamic and evolution of biological objects, from protein to organisms. Clearly the I2BC forming units all together provide a formidable panel of biodiversity, biological questions and methodological approaches.

The list of model organisms under study is impressive as it includes eubacteria of various interest (models for biology, animal and plant pathogens, biotechnology, environment), archea, yeast, worms, mouse, drosophila, plant, bacteriophages and viruses.

Despite being numerous, sizable number of biological questions/interests shared by more than one Department are easily identifiable among which actin, cytoskeleton, autophagy, endo-exocytosis, organelle biogenesis, metabolism, bioenergy, redox homeostasis, DNA repair, rearrangement, organization, replication and expression, membrane biology, antibiotic developments, RNA structure, function and transcription. These themes are grouped in a series of axes by I2BC staff.

The I2BC founding units include a significant number of top level world-wide leading teams. Present in the different departments, these teams and individuals will be pillars for the new Institute to build on. A certain heterogeneity might appear between departments, but the scientific quality of the ensemble is excellent. On the downside however, the committee noted that only a minority of teams have European funding and the number of ERCs held amongst future I2BC teams is low (5). This is increasingly being considered as a sign of the excellence and competitiveness of an Institute and I2BC should favour any initiative that could help increasing European visibility of its members.

The I2BC founding units will bring an ensemble of remarkable technological platforms in all areas (e.g. imaging, omics, structural biology, bioinformatics and biophysics). The committee was impressed by the management and work already carried out so that these platforms will form the underlying spine of the institute. Maintaining state-of-the-art and sustainable platforms is essential to promote initiation and support of synergies between departments, teams and projects. Specifically the grouping of the NGS and Bioinformatics facilities appear as very positive moves. The Bio Cell facility is part of the France Bio Imaging (FBI) network of IBiSA platforms on state of the art imaging and ranks as one of the most efficient in France. The same goes for the Structural Biology Platform (labelled IBISA and part of the FRSIBI network). A most important feature is that all platforms are led and managed by researchers, who in addition to their own research are involved in these sharing activities. Altogether this will provide the ensemble with great expertise in protein biochemistry, genetics, proteomics, bioinformatic and cell biology as well as top level expertise in ribosome profiling, ChipSeq, single cell analysis, PELDOR technology, Raman spectroscopy, multifrequency EPR spectroscopies and single molecule fluorescence, molecular dynamics, RNA and protein crystallography.

Hence, the trans-departmental themes, the great bio-diversity and the different specific approaches altogether set an ideal ground for the emergence of an Integrative Biology Institute as it is planned. It is important to add that besides generating fundamental knowledge, a significant number of studies have also a great potential for biotechnological and medical applications as well as direct application in agriculture and food safety.

Assessment of the unit's academic reputation and appeal

Several of the PIs present at I2BC are involved in many international consortia and panel expertise (EU consortia, Italian Research Ministry, European Center for Diseases Control, South African Research Foundation, European Bioinformatics Institute, European Cooperation in Science and Technology Action "BM1203 EU-ROS" …).

Several of the PIs present at I2BC have organized or co-organized international meetings such as conferences on "Paramecium Genomics" (Krackow, Poland), Gordon Research Conferences (2012, 2014) on "Thiol based redox regulation and signaling", American-European workshop on site-specific recombination, transposition and DNA dynamics, XXI Phage and Virus Assembly meeting in 2009 or International Congress on Carotenoid molecules in 2011 and 2014.

In the 2009-2013 period, leaders of the teams were actively involved in participation in various evaluating committees and scientific councils both at the national level (CoNRS, French research Ministry, ANR, Ligue Nationale Contre le Cancer, Biophysical Society, Institute for Life Sciences of CNRS, etc.).

In the 2009-2013 period, several members have received prizes and awards such a Bronze Medal, a Microbiology price from the National Academy of Medicine, Chevalier de la Légion d'Honneur, the CNRS Cristal award or a few academic prizes. These will join prizes and awards (Silver Medal CNRS, IUF,…) which were obtained before the last 4 years.

Key members of the teams are actively involved in an impressive number of editorial boards, which is not usual in France and among which one finds PNAS, PLoS Biology, PloS Genetics, Molecular Microbiology, Mol Plant-Microbe Interactions, The Journal of Biological Chemistry, Mol. Cell Proteomics, FEBS Journal Antioxidants and Redox Signaling, BMC Bioinformatics and others.

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

Although transferring knowledge remains low in the priorities of most teams, there are some success stories in this regard. For instance in the Department of Microbiology, a PI has been engaged in technological transfer through the creation of a Start-up in 2011 and was awarded 3 prizes for innovation. A collaborative project with a non-academic partner, the company Oséo (a PhD student with a CIFRE fellowship working on this project) ensued and now the team leader works, as member of a selection committee, in association with HEC school for promoting and coaching innovative companies. Another team created a technological platform that provides R&D, genotyping services and reagents thanks to a license purchased from Luminex®. A startup is under creation. One of the team's theses fellowship was granted by the Merieux foundation.

Other teams have collaborations with non-academic partners (Exiqon, Pherecides Pharma, Adisseo, Merk Millopore, Targanta Therapeutics, biotech start-up CEERAM) that led to patents. In most cases, the group's interaction patents have been filed and a contract that provides additional funding for research was obtained.

Overall, several researches conducted at I2BC could permit a continuum between basic and applied science. The Dept of Microbiology, which has already an excellent record in this context, but also the Dept of Virology, could lead the path towards environmental and translational research. If more efforts towards applications in biotechnology and biomedicine existed, this might provide new ways of getting funds with industrial partners, being more competitive in European calls, and being attractive for a diversified student community.

Contributions to promoting science and research to society is more a matter of each team's motivation but there is no as yet clear strategy to put a great deal of efforts to go into that direction. For instance, in the Genome Biology Dept, a team was very active in promoting its research activities to the public and participated to several events such as Science Festivals and presentations of its research in schools. Another team led a multidisciplinary project in charge of studying the Paleolithic painted caves of Chauvet (and others). Another PI has also been actively involved in teaching and popularizing Science through interviews and events targeting the lay people. In the Dept of Cell Biology, several teams appeared to get very much involved in "La fête de la science", and providing regular lectures for primary/middle and high schools. Also members of a group in the Dept of Microbiology have participated to communication for the general public (publications, radio programs, Wikipedia articles).

Assessment of the unit's organization and life

Each department was well thought of by the I2BC staff. With a very few exceptions, each team is well integrated in a department and for a majority of team leaders interviewed, the creation of the departments was considered as very positive in terms of scientific interactions. Each department has the potential to create synergy within its perimeter as well as embarking on collaborations with other departments as several processes studied are already tackled by different teams in different departments. Indeed, several inter-departmental projects involving teams from the future Genome Biology, Cell Biology and B3S departments are already on-going. In line with the project of promoting inter-departmental, cross-disciplinary researches, a series of initiatives have been conceived and the creation of a dedicated position aiming at creating connections between I2BC teams is a very good step towards concretisation of these plans.

Again, the committee was very impressed by the platforms, for their intrinsic value as well as for the management the I2BC is planning to apply for these platforms to provide up-to-date technology and support to departments and teams. The committee however had some interrogations about the future of the sequencing facility, which is currently led by an emeritus researcher. The I2BC should maintain a group with a strong bioinformatics expertise. The platforms should however not substitute for engineers and technicians within teams. The importance of "team technicians" is equally important as they are pivotal to the daily life and history of the teams. However, there is currently an uneven distribution of technical help amongst the departments and amongst the groups. The job situation in France is not going to help. A fair balance between teams is a requirement and all teams should have at least one technician/engineer.

A large number of groups appear critically small. The recurring question of the "optimal size of a team" might be even more important in the context of such a large institute, wherein teams will be actual building bricks. Availability of funding is an obvious criterion but should not be the only one to be used. Fusing teams might be examined in some case, and this was already decided for 3 or 4 within the I2BC project.

Several of the leading scientists of the I2BC will retire within the next few years. This is true for all Departments. It appeared to the committee that in several cases, the way I2BC will handle these situations was quite unclear. Not all teams should be kept open once their leader retires and a strategy for attracting new group leaders should be set up. Positions (associate professor/professor?) will open at the Paris Sud University and should be a way of reinforcing existing but fragile teams or else bringing in complementary expertise not present in I2BC. This is a crucial opportunity to reinforce disciplines, such as Bioinformatics or Systems Biology, where expertise is lacking or to be reinforced.

The problem however is that the transition period will not be favorable to attract scientists from outside, in particular for Departments that will be moving. Future needs of I2BC should be identified and schemes involving support from Paris Sud, CNRS and CEA be outlined and planned, soft money and students fellowship put in place which might be at reach in the context of the Paris-Saclay initiative. An attractive package, securing at least the first 2-3 years after installation, might be proposed to scientist of interest to I2BC (on the basis of an International call as proposed by the I2BC staff in the written document).

Assessment of the unit's involvement in training through research

The I2BC will be part of the Paris Saclay initiative. The I2BC teams will be affiliated mostly to two Doctoral Schools "Gène Génome Cellules" ED 426 and "Therapeutical Innovation" ED425. In the near future, the Doctoral School "GGC"will merge with another one called "From Genomes to Organisms". This last school is associated to the Universities of Versailles and Evry and the project will be evaluated for the end of this month. So, the new Doctoral School will be called "Structure, Dynamics of Living Systems" and its size will be twice the size of GGC, which will increase the number of fellowships attributed to each doctoral school. In full coherence with the I2BC project this new Doctorate School will have Integrative Biology as a clear objective. Most of the research group of I2BC will be associated to this new School and several of the groups of the five departments have already asked for their association. Researchers at I2BC will be involved and represented in the selection committee (about 1/3 of the committee).

The I2BC project has several plans and initiatives for hosting and training at excellence level PhD students. A PhD programm will be set up. A wide series of opportunities for PhD students to show and talk about their research (seminars, retreat, tutorial) is planned. PhD students, or even Master students, will be given a unique opportunity to evolve and learn in the multidisciplinary context.

Concerning the training of current students, the committee gathered from its meeting with the students that all of them received an excellent training. No students declared being under a lack of supervision, or unfairly treated when it comes to publication, authorship or meeting. However, the 2-3 year transition period will pose a series of problems both for the immediate and for the near future. In particular a (very) small fraction of PhD students that might be forced to move once or twice during their PhD. I2BC might be considering the possibility of setting up a financial system to help those PhD students hit by the move of their laboratory to stay a few months more (3 months) to finish up their thesis.

Over 25% of scientists present at I2BC are faculty members. This allows for a unique and efficient link between students and labs for the profit of both. However, the down side of this is that Professors and Maitres de Conférences teaching at Orsay will now have to commute between labs and amphitheatres. This is good neither for them nor for the efficiency and overall output of I2BC. The committee recommends that Paris Sud University helps these researchers and I2BC to fulfill their dual missions by facilitating grouping of teaching periods and by providing these colleagues with offices and internet connections for them to keep on working when away from I2BC.

The I2BC should allocate a budget to a student/post doc association such that meetings, journal clubs and/or so called 'beer sessions' can be organized and links be established with other Institutions in France but also abroad through organization of inter-Institution retreats for example. Also the I2BC should provide new foreign students and post docs with help and advices in administrative matters.

Assessment of the strategy and the five-year plan

The scientific level of the I2BC undoubtedly ranks among the best and it should find its place within the top institutes of Life Sciences in France. The necessity and the importance of the I2BC project for Life Sciences in the Saclay area is without question. Expertise, models and methods are already present for a major Institute to emerge. Its success will help Paris Saclay, CNRS and CEA to respond to international challenges and competition with great efficiency and breaking through discoveries.

The Departments proposed are somehow heterogeneous in size and quality but overall all will contribute a strong added-value to I2BC and the committee recommends their creation as proposed. Although a majority of the team leaders are still very much into a classic way of conducting research and formulating questions, most of them are positive about the project of a single large institute integrating complementary and multi-scales approaches.

The project however is very much in a preliminary period and the number of projects of "integrative biology" such as systems biology that should be an obvious part of the I2BC once running, is still very low. The result is that, as it stands, I2BC still lacks a real identity in Integrative Biology. However, it is a reality that the ambition and the size of the project demand steps to be taken with caution and thoughtful strategy, were a certain apparent slow motion being the prize to pay. In particular, balance between restructuring/regrouping and scientific vision sharing must be finely tuned. In this regard, disciplinary departments will be of paramount importance as they will have the responsibility to build up excellence in research within an identified discipline, yet to avoid this identity to overshadow the awaited "Integrative" identity.

Indeed, the transition period appears as a quite risky time. Despite the creation of a position specially charged of inter-departmental and cross-disciplinary projects, it will be a very difficult task to promote departmental cohesion and interdisciplinary initiatives among teams spread on different sites before 2018. This will hit in particular the B3S and the Cell Biology Departments. The transition period appears also a source of instability and uncertainty for many people in the teams. The human resources plan proposed appears to have missed some of its objectives. It is crucial that the situation be clarified in particular regarding the future technicians, engineers and members of the administration who wonder whether their future will be in their current team, in I2BC or in another institute in the Paris-Saclay area.

The transition issue will also be detrimental to administrative and common services but the I2BC staff and persons in charge are fully aware of this as illustrated by the installation of a transitive administration entry point to establish as soon as possible an I2BC administration body and a network of computer experts.

4 • Department-by-Department analysis

● Department of Virology

Overall assessment of the department

The future I2BC Virology Department will contain 6 teams mainly from the existing Laboratoire de Virologie Moléculaire et Structurale (VMS) at Gif but also from IGM (1), IBBMC (1) and the Faculty of Pharmacy (1). The members of the Department have published 108 articles in the review period with 56 as lead author, mainly in the top virology journals. The new department will study diverse bacterial (phages T5 and SPP1), archaeal (SSV1) and eukaryotic viruses (rotavirus, flavivirus, rhabdovirus and herpesvirus), including some important human pathogens such as notably rabies and herpes simplex virus-1. Each system will be studied by integrated structural and cell virological approaches with a focus on capsid assembly, cell entry mechanisms, trafficking of viral components, establishment of viral factories, modification of host cell gene expression and molecular warfare against the innate immune system. This integrative approach, with potential bridges to all other departments, justifies the creation of a Virology Department within I2BC.

Strengths and opportunities related to the context

The Department currently has the necessary combined expertise in structural and cellular virology, encompassing crystallography, single particle electron microscopy and electron tomography on the one hand and molecular cell biology and imaging on the other hand. The members of the department have a very positive attitude to joining the I2BC where they see clear benefits from consolidated platforms in structural biology and live cell imaging as well as potential collaborations with other I2BC researchers e.g. in cytoskeleton and cell compartmentalization. The Department should consider becoming more involved in translational research concerning human pathogens. The reinforcement of the Herpes virus team by merging two existing teams, seconding interest from other teams in the Department and recruitment of a medical doctor with a unique mouse model of latency is a very positive move in this direction.

Weaknesses and threats related to the context

Given the reliance of the Department on electron microscopy, it is essential that provision be made for long-term continuity of expertise in this area within the Department and access to advanced electron microscopy within the Institute. There are some small groups in the department that by themselves may not have the critical mass to be effective at the top levels.

Recommendations

- To focus on viruses and topics which will have the highest impact whether on fundamental aspects or medical research.

- To work towards establishing a high level and sustainable EM platform.

- To foster and support young groups that are highly dynamic and use modern methodology that would build bridges to other departments. This would then facilitate the integration of emerging areas of biology, such as systems biology, chemical biology or advanced and quantitative imaging at the light microscopy level into virology.

Team

BACTERIOPHAGES OF GRAM-POSITIVE BACTERIA

Name of team leader:

Mr Paulo TAVARES

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	4	4
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**8**	**8**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

Assessment of scientific quality and outputs

The team uses phage SPP1 as a model system to study the structure and assembly of the particle, including genome packaging and interaction of the phage with its host cell at the initial steps of infection (attachment and genome ejection).

The team employs a combination of molecular biology/genetics with structural biology (X-ray crystallography and EM), super-resolution imaging and systems biology. The team's expertise is molecular biology/genetics. Structural and imaging studies are performed in collaboration with other groups in Europe.

The most remarkable recent achievement of the group is the identification and initial characterization of a host membrane protein complex that is used by SPP1 as the receptor. Furthermore, they have recently characterized gp21, the phage protein that interacts with this receptor during infection.

In 2008-2013, the team published 19 research papers including 9 with team members in key position (first author and/or corresponding author) in PNAS, Mol Micro, JMB, JBC, NAR, etc.

Assessment of the team's academic reputation and appeal

The team is recognized globally for its work on assembly, structure, and function of large macromolecular machines. In 2008-2013, members of the team gave 21 oral presentations on their work at international and national conferences. Of those, 15 were invited talks at such prominent meetings as 2010 EMBO Conference "Viruses of Microbes" (300+ participants, Brussels) and 2010 FASEB Conference on Virus Assembly (130 participants, USA).

The team head co-organized the XXI Phage and Virus Assembly meeting in 2009, which deserves a special recognition, similar to chairing a Gordon Research Conference and a session of the 2010 EMBO conference "Viruses of Microbes".

Contributions from the team have been selected for oral presentation at large international conferences (for example, EMBO conference "Viruses of Microbes" in 2010 and 2012).

The PI is or was a member of committees that evaluate academic and research performance of several European institutions.

Assessment of the team's organization and life

The team currently contains 7 permanent staff members, two PhD students and a post-doc. The team might benefit from additional non-permanent staff. Either a PhD student or a post-doc might bring an infusion of new enthusiasm into the lab.

Assessment of the team's involvement in training through research

In 2008-2013, a number of students were trained in by the team: one M1 student, two M2 students, four PhD students. There were two PhD defenses in that period.

The team participated in 14 PhD defenses as external experts or opponents in France and internationally.

Assessment of the strategy and the five-year plan

The team is recognized worldwide for its work on phages with long tails. The current and future research is in line with what is considered to be state-of-the-art in the field. In 2008-2013 and currently, the team has been supported by 5 ANR grants, one of which runs until 2015 and another until 2016.

Using phages infecting Gram positive bacteria as their model system, the team addresses several important and fundamental biological questions: 1) How is the DNA packaged into the viral capsid? 2) How is the host cell attachment organelle of the phage (the tail) assembled and how does it function? 3) How is the DNA delivered into the host cell? 4) What is the structure of viral factories within the host cells that produce new viruses? In the past few years, the team has been able to make seminal contributions in all of the four areas.

The team collaborates with researches from France, Spain, UK, Germany, Lithuania, and Portugal, making it fully integrated into the network of European science. Nevertheless, it is clear that in all of their collaborative work, the team represents the driving force of these projects.

There is no doubt that the team will continue to be productive in terms of generating important results that are recognized by others in the field. In the next five years, the team plans to continue advancing the existing research directions mentioned above by utilizing their extensive expertise.

Conclusion

- **Strengths and opportunities:**

The team has unparalleled expertise in molecular biology and genetics of phage SPP1. This is a complex bacteriophage and a useful model that is important for understanding how phage tails and the type VI secretion system work.

- **Weaknesses and threats:**

The importance of the contribution of the team is not always properly acknowledged and recognized by their collaborators, which often take key author positions in the author list.

- **Recommendations:**

It would be even better to see a high profile paper from the group that does not involve any collaborator contribution. To this end, the team might benefit from additional non-permanent staff.

Team BACTERIOPHAGE T5

Name of team leader: Ms Pascale BOULANGER

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**3**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	1	1

Assessment of scientific quality and outputs

Thanks to the work of this team over many years, bacteriophage T5 has been one of the archetypical model systems for studying assembly and morphogenesis of complex viruses. The team is currently aiming at understanding how the capsid of T5 assembles and how the T5 tail functions.

The team uses a combination of classical molecular biology and genetics as main methods for addressing scientific questions. The team head collaborates with several laboratories in France and abroad that perform structural studies using mutants and expression vectors created by the group. The team's input in this collaborative work is absolutely essential and the team is a leader in most of its collaborative research. As part of this collaborative work the team has made a significant progress in deciphering the structure and function of phage T5 cell-piercing tail tip and capsid assembly.

In 2008-2012, the team published 11 articles in international journals and 1 book chapter including 5 contributions with a member of the team in key position (first or corresponding author) in such journals as J Virology, J Mol Biol, JBC and Methods of Molecular Biology.

Assessment of the team's academic reputation and appeal

The team has a well-established academic reputation as is demonstrated by their numerous national and international collaborators, most of which are globally recognized leaders in their fields.

In 2006-2009, the team coordinated an ANR grant.

In 2008-2013 the team leader was invited to give three lectures (two in France and one in the USA).

The PI's work was selected for oral presentations at two Phage/Virus Assembly meetings and at the 2012 Viruses of Microbes conference. She and her team presented many posters at various other meetings.

The team leader is a member of review panel for postdoctoral fellowships and grants for the FWO funding agency (Belgium).

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

The PI participates in teaching at the pre-university level. She gives lectures to high school students (Collège Michel Vignaud and lycéens de Terminale, Paris).

Assessment of the team's organization and life

The group currently contains 3 permanent staff and one PhD student. This size is too small to produce high impact results as lead investigator.

Assessment of the team's involvement in training through research

The head of the team participates in thesis evaluation committees.

In 2008-2013, one PhD student defended a thesis and 3 post-docs were trained in the lab. This is a good achievement for such a small team.

Assessment of the strategy and the five-year plan

Over the course of many years of research the team has accumulated a large body of genetic information on phage T5 particle and its various mutants. The team is now aiming to use this information for structural studies of the host cell attachment organelle and the phage capsid. For this purpose, the team has initiated several collaborations with researchers in France, Spain and USA. The five-year research plan represents solid science that involves several cutting edge techniques cryoEM, membrane protein crystallography, SAXS studies of large objects usually in collaboration.

Conclusion

- **Strengths and opportunities:**

The team possesses an unparalleled amount of information about the molecular biology and genetics of phage T5. This is a complex bacteriophage and a useful model that is important for understanding how phage tails and the type VI secretion system work.

- **Weaknesses and threats:**

The team is too small to make quick progress with many of its interesting projects. The team's international recognition can be improved. The team does not appear to have any external funding currently.

- **Recommendations:**

Without significant funding and critical mass in the future in order to make a high impact the group should consider joining forces with another virology group in the Department.

Team

INTEGRATIVE STRUCTURAL VIROLOGY

Name of team leader:

Mr Jean LEPAULT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	4	4
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**8**	**8**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

Assessment of scientific quality and outputs

The group is interested in assembly mechanisms and the structure of the viruses belonging to different viral families, alpha-, flavi-, fusello-, herpes-, rhabdo-, rota- and Nodoviruses. The group is particularly noted for its cryo-EM expertise (both single particle 3D reconstructions and tomography) and has now two X-ray crystallographers, one working on structure and replication of archaeal viruses. In the review period eleven papers have been published but only five as lead or corresponding author. This is indicative that up till now the group has largely worked by collaboration.

Entry of rhabdovirus, VSV G ectodomains induce membrane constraints required for the fusion reaction, involving a structural refolding of pre to post fusion stage, involving a monomeric intermediate state of G protein; published in JCB 2010 (leading role) and PLoS Path 2012 (departmental collaboration).

Structural virology of non-enveloped dsRNA viruses, reovirus/rotavirus, published in JVI 2008 (leading role), and of picobirnavirus in EMBO J 2009 (collaborative role). Cell membrane disrupting peptide of infectious bursal disease virus (IBDV), published in JBC 2010 (collaborative role).

The permanent member studying archaeal systems worked on reverse gyrase, a unique enzyme from hyperthermophilic organisms leading to a paper published in JBC 2008 (collaborative role). Also on an archaeal chromosome resolution protein XerA, publishing in JBC 2010 (collaborative role), PloS One 2013 (leading role) and PLoS Genet 2010 (leading role).

Assessment of the team's academic reputation and appeal

The group has attracted leading European virology collaborators, showing its EM expertise is unique and high in demand in the field of structural virology. Current grant support is mostly from ANR, one grant as a coordinator and one in collaboration. One of the permanent members participated in an FP6 EU network project. Publications are modest in number but some are of high quality. International exposure via invited talks and conferences is very limited, except concerning the archaebacterial work. The PI was co-organizer of an EMBO course on correlative microscopy for three successive years.

Assessment of the team's involvement in training through research

The team is active and involved in training Masters students and apprentices. The PI has had no PhD students during the review period and has only one post-doc at a time. On the other hand, the permanent member working archaebacteria has successfully trained one PhD student and has had several post-docs (but none presently).

Assessment of the strategy and the five-year plan

The group will use X-ray crystallography and cryo-EM of viral structures in vitro and in cells.

1) Structure of HSV inner tegument proteins UL36 and UL37. One fragment of UL36 has already been crystallized. This is a very laudable aim, and will well integrate with the other herpes virus projects in the Department.

2) Structure of SSV1 by cryo-EM and crystallography, one of the first archaeal viruses to be characterized.

-Focus on the capsid proteins VP1, VP3 and C792.

-Plans to study 15.5 kb dsDNA packaging possibly involving VP2.

-Plans to determine the lipid composition of the host Sulfolubus cells.

-Plans to address cell egress of SSV1, in particular if ESCRT is involved.

These projects will combine crystallography, NMR, EM and cell biology. All these are interesting projects and should give new insight into the intriguing archaeal viruses.

3) Structure of rainbow trout sleeping disease virus (RTSDV), an alphavirus. The group wants to image viral membrane fusion complexes, and compare to CHIK, SFV or Sindbis virus. Promising structures are available at 15 A resolution already. Another plan is to determine cell entry of SDV. This makes most sense if done in conjunction with cell biology, and with state of the art methods. Results from the project will cross-fertilize other research in enveloped viruses.

4) Continue the collaborative work with another group on the VSV G-protein structure. This has been successful in the past.

5) Further work in progress on flaviviruses (Yellow fever and Dengue). These are collaborations, and they have been successful in the past. They are feasible.

Given the wealth of projects and the limited amounts of funds and young scientists available, the group should carefully choose which projects to select for in depth follow up studies.

Conclusion

- **Strengths and opportunities:**

Very good outside collaborations have been set up and are actively maintained.

The team has the potential to collaborate more within I2BC, and define topics of interest relating to cell and molecular biology.

- **Weaknesses and threats:**

There are many different projects that the group is working on: HSV (herpes virus), SSV1 (fusellovirus), SDV (alphavirus), VSV rabies (rhabdovirus), Norovirus, yellow fever and dengue (flavivirus). Prioritization is required to obtain in depth, high impact results and to secure grant support.

- **Recommendations:**

Make active efforts to integrate into I2BC. This will provide new opportunities for focused collaborations and in depth projects.

The projects on herpes virus, and membrane interacting proteins are particularly encouraged as there is more critical mass here within the Department

More young scientists should be trained since the EM expertise in the group is unique but not perennial.

Team RHABDOVIRUSES

Name of team leader: Mr Yves GAUDIN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**8**	**7**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

Assessment of scientific quality and outputs

The group has two main focuses, firstly, biochemical and biophysical analysis of Rhabdovirus glycoproteins and their role in the process of membrane fusion and secondly, cellular virology aspects, including interaction with the interferon cascade, intracellular transport of viral components, establishment of viral factories and assembly prior to budding. Most studies are on rabies but also VSV and Chandipura virus are investigated.

The group continues to make major original contributions to the understanding of glycoprotein induced membrane fusion combining several biophysical methods, EM and crystallography to come up with the first convincing evidence for monomeric intermediates and a new model for successive steps in the fusion process. The biophysical work has been published in PLoS Pathogens (2012), but the crystal structures not yet, partly due to their controversial nature.

On the cellular side, it has been shown that Negri bodies are sites of active viral RNA synthesis and also that HSP70 chaperone is an important component. Concerning innate immunity more results have been obtained, in external collaborations, on the role of domains of the rabies phosphoprotein (P) in inhibition of STAT1 signaling and also its interaction with the interferon induced gene product PML. Concerning assembly and budding, the role of the PSAP motif in VSV M protein has been investigated and dynamin I and II have been identified as partners of M and this interaction is important for localization of viral components and thus assembly.

Since 2008 the group has published 6 reviews and 19 papers, of which only nine have group members as lead authors. Most publications are in top virology journals e.g. J Virology (8), PLoS Pathogens (1) and also J Biol Chem (1), J Cell Biol (1).

Assessment of the team's academic reputation and appeal

The team leader has a strong international reputation and regular international lecture invitations (Keystone, Gordon, etc). He has coordinated 2 ANR Blanc grants and an “Equipe FRM” grant, was co-investigator in an EU FP7 grant and is a member of European training network (ITN Virus Entry, FP7). The second PI has on average one invited lecture per year, mainly at the French virology meeting (only one outside Europe) and was a co-investigator in two ANR grants. The group has several productive national and international collaborations (Australia, USA). The team leader is member of many national review and advisory committees. The team has two new young CNRS-CR recruits to strengthen areas of structural virology and innate immunity.

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

The team leader has taken part in public diffusion activities.

Assessment of the team's organization and life

The team is coherent with a well-integrated theme spanning the structural and cellular biology of rhabdoviruses and combining expertise in biochemistry, biophysical methods, crystallography, molecular and cellular virology and innate immunity.

Assessment of the team's involvement in training through research

During the review period 5 PhD students have successfully defended and two are still in progress. Two of these students came through an EU Training Network (ITN).

Assessment of the strategy and the five-year plan

The future research plans are a logical extension of current activities and will exploit a large number of preliminary results. On glycoproteins, the team plans to gain more evidence for their model of viral fusion based on monomeric intermediates and alternative oligomerisation states, try to obtain a structure of rabies G with its receptor (P75NTR) and extend work to BEFV, from a different rhabdovirus genus, which encodes a second, non fusogenic glycoprotein. On innate immunity, more will be done (in an external collaboration) on the role of the viral phosphoprotein (P) modulating STAT1. They will also investigate whether TLRs or RLRs are involved in recognition of viral RNA and the role of sumoylation. On transport and assembly, more will be done on morphogenesis and dynamics of Negri bodies. Several leads on cellular partners of VSV matrix protein (e.g. a-catenin) will be followed up. The project is consistent, credible and feasible, and should illuminate key aspects of virus-host cell interactions.

Conclusion

- **Strengths and opportunities:**

The group has an integrated and competitive project on the structural and cellular biology of rhabdoviruses. Competences are well-balanced within the group and range from structural biology (EM and X-ray) to cellular virology.

- **Weaknesses and threats:**

Apart from the glycoprotein work, the studies lacks major impact, maybe because rhabdoviruses are not high profile human pathogens.

Second PI needs to be more active in funding initiatives and raising the international profile of the cellular virology.

- **Recommendations:**

The group has a number of interesting and promising strings to its bow but should perhaps focus on those that will have the highest impact.

Team

MOLECULAR BIOLOGY OF ROTAVIRUSES

Name of team leader:

Mr Didier PONCET

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**5**	**5**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

Assessment of scientific quality and outputs

The group published 5 primary papers with lead or last authorships in Vir Res, J Mol Biol, FasebJ, J Virol (2x). About 14 collaborative papers in the last 6 years have been published. This is a group with excellent abilities to carry out collaborations. It has a really important glue function for the unit.

Highlights:

NSP2 interacts with tubulin and leads to MT depolymerization: paper in J Virol 2010 (leading role). Whether there is a causal link to the formation of viroplasm is unknown. Also unknown is the mode of action by which NSP2 works on microtubules. Nearly a dozen additional papers in collaboration with international groups. These projects involved:

-A receptor for bovine calicivirus VLPs has been found: paper in 2009.

-study of the self-assembly of norovirus capsid by biophysical means in collaboration: Arch Biochem Biophys in press

-Translation regulation by NSP3 published in J Virol 2010 (leading role): NSP3 interaction with eIF4G and RoXaN.

-NSP5 mainly unstructured with 2 Fe sulfur clusters between monomers: paper in Faseb J 2013 and J Mol Biol 2011 (leading roles). Function of the Fe cluster yet unknown. Speculation that it is involved in replication due to proximity to the domain which binds the NSP2 ATPase.

Reverse genetics system, collaborative paper in J Virol 2010. But system is difficult to introduce point mutations. Alternatively, use TS mutants as helper viruses. 4 TS mutants were fully sequenced and found to be in NSP3: paper in Virus Res 2013 (primary leading role). Additional TS mutants were sequenced and found to contain multiple mutations. This renders mechanistic interpretations difficult.

Assessment of the team's academic reputation and appeal

Very good scientific output, interesting project, focused and tractable. The group is active in national review boards. The group has had very good amount of support by external funds (mostly ANR), very good visibility. Currently, there is no active grant support.

Assessment of the team's involvement in training through research

Active in training and educating 4 PhDs and several Masters students. Group is heavily involved in undergraduate teaching. Teaching also at Pasteur Institute.

Assessment of the strategy and the five-year plan

They deliver a sensible plan with interesting goals involving modern molecular techniques, and promising preliminary results.

The group aims:

(i) to characterize the mechanisms by which rotaviruses hijack the host translation machinery ;

(ii) to elucidate the mechanism responsible for ensuring that each single viral particle contains the complete set of dsRNA segments required for successful rotavirus infection. Likewise, the aims relating to polysome profiling experiments to identify mRNAs that are actively translated are apparently not a priority at present, although the group is still interested in translational regulation in rotavirus infected cells. And this is an interesting aim.

Likewise, the group had plans to further develop a reverse genetics tool for RV biology (done in collaboration with another group). This may turn out to be scientifically difficult, and it would be reasonable to deprioritize the aim.

An additional project that is proposed is how NSP2 and NSP5 are forming a viroplasm. The group wants to investigate the composition and functionality of this protein / RNA cluster. This is also an interesting topic and can lead to novel biological insights, for example, if one considers the particular physical properties of this mesoscopic material.

Another aim concerns the idea to explore ER stress response on RV infection. This is interesting as it is an incomplete UPR induced in RV infected cells. It will be interesting to study which aspects are induced and how others are suppressed or not induced due to missing or suppressed cues.

The group will focus on exon skipping mechanism of NSP3. The PI submitted a grant to ANR on his exciting topic. This project, if granted, will lead the group into innate immunity, and thereby strengthen a common theme of the unit.

Conclusion

- **Strengths and opportunities:**
  - Interesting science on an important human pathogen.
  - Good scientific output, many interesting collaborations.
  - Strong potential and also willingness to integrate with cell biology groups.
  - Strong potential and willingness to integrate with other virology groups, eg, the herpes virus groups.

- **Weaknesses and threats:**
  - No invitations for talks.
  - Increased international exposure, based on good publication record would help the group to recruit national or even international collaborators and new recruits.

- **Recommendations:**
  - Could seek active collaboration with cell biology with regard to translation, and viroplasm formation.
  - More outreach to public and international teams.
  - PI could engage more in direct teaching and public education.
  - Show more leadership in order to hire foreign postdoc / students.

Team

VIRULENCE AND LATENCY OF HERPESVIRUSES

Name of team leader:

Ms Audrey ESCLATINE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions		
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)	4	
TOTAL N1 to N6	**8**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

Assessment of scientific quality and outputs

In the new organization proposed for the department of virology of the Institute for Integrative Biology of the Cell, the group stems from the fusion of two groups (from the Faculty of Pharmacy and from Virologie Moléculaire et Structurale, thus combining expertise on different aspects of the viral cycle of Herpesviridae.

The team leader specializes in processes of autophagy during infection by herpes viruses (HCMV, HSV-1). Since 2008, she has shown that HCMV blocks the induction of autophagy at late stages of infection, in a process involving viral protein TRS1 which interacts with Beclin 1, and has also uncovered the anti-autophagic function of viral protein Us11 in the context of HSV-1 infection. Since 2008, her work has led to 3 original publications as senior author (Autophagy 2008; J Virol 2012; J Virol 2013) and 6 reviews. The PI's work highlights a link to innate immunity against viral infections.

The second PI specializes in latency of herpesviruses and in particular the accumulation of Latency Associated Transcripts (LATs) and more recently in HSV-1 cytoplasmic trafficking with the arrival in 2010 of a post-doctoral researcher. Since 2008, he has shown in collaboration with CellectisTM that meganucleases that recognise specific HSV-1 sequences can inhibit viral infection; he has studied the structural variability of the HSV-1 genome and the role of LATs and characterized HSV-1 intracellular trafficking in collaboration with a group at the University of Glasgow (GB). Since 2008, his work has led to 3 original publications as co-senior author (Mol Therap 2011; J Virol 2012; PloS Pathogens 2012), 3 publications in HSV-1 trafficking (JVI 2013) and many book chapters that underline his considerable expertise in the medical field of herpetic infections.

Assessment of the team's academic reputation and appeal

The PIs are members of very respectable academic boards, including EUCORNEA and CNU. The first PI presented her work as an oral presentation at the Keystone Symposium « Autophagy Immunity and Inflammation » in Montreal in 2013. The second PI is head of the Department of Medical Continuous Education and Department of Ophtalmology. He is the main investigator in a program for the assessment of potential new eye drops against HSV-1 infection, which is the major infectious cause of blindness.

Assessment of the team's involvement in training through research

Both PIs have supervised PhD students over the last AERES period and these have given rise to publications either already published or currently submitted, underlining a good quality of supervision. Both PIs have a very strong participation in teaching at the University level (as PU-PH and MCU), are board members of university authorities and leading actors of training programs. They are also involved in PhD jurys.

Assessment of the strategy and the five-year plan

A real effort has been made to combine the complementary expertise of the two PIs in herpes virology within a single group. An effort is also made to collaborate with the rest of the I2BC, with a collaboration with the Genome Department, and to establish external collaborations (e.g Seattle). However, part of the group's strategy for the next 5 years is uncertain and requires the recruitment of a permanent researcher.

However, no detail is provided to indicate how the team will function with the present group leader nor whether the fusion will give rise to truly collaborative projects. The description of the « modulation of autophagy during HSV-1 latency » project is rather too succinct and the descriptions of obectives suggests the two entities will still be working as individual teams within the same group.

Although the only currently running grants are the ANR Blanc on which the group is co-investigator and a PhD grant from DIM Malinf, grant proposals have been written and the team has several manuscripts in preparation.

Conclusion

- **Strengths and opportunities:**

- The presence of a medical professor in the group is a strength for the I2BC since it provides a tangible connection with human medicine.

- The new group composition is a real effort to combine the complementary expertise of two leading experts in herpes virology.

- Although many lab members left in 2013, new members have arrived and the team is growing.

- **Weaknesses and threats:**

- One of the research themes is dependent on the recruitment of a researcher.

- Concern that the group might function as two separate teams despite the proposed fusion.

- Funding resources are limited at the moment.

- **Recommendations:**

- Study of various aspects of Herpes viruses could become a major focus of the Departments' work.

- Since at least two other group's are involved thus leading to critical mass, this potential strength should be nurtured by appropriate organization and a concerted effort to seek funding.

● Department of Biochemistry, Biophysics and Structural Biology

Overall assessment of the department

The future I2BC Biochemistry, Biophysics and Structural Biology (B3S) Department will contain 16 teams including 9 from the CEA Saclay, 4 from LEBS at Gif, 2 from IBBMC at Orsay and 1 from VMS (Virology, Gif). The new Department will bring together about 150 people who have published around 580 articles in the review period with several in very high impact journals. This attests to the overall high quality and often very original work done by the Department. The teams currently study a broad spectrum of topics which it is proposed will be grouped into the themes of bioenergetics and bioenergy, cytoskeleton, genome integrity, metalloproteins and protein structure, assemblies and interactions. Even if some members of the Department have a cautious attitude to joining the I2BC, many of these research topics find echoes in other I2BC Departments and should become a driving force for integration of scientific activities across the institute.

Strengths and opportunities related to the context

A key strength of B3S is the broad range of technologies available including some chemistry, spectroscopies (IR, Raman, EPR), structure determination methods (X-ray, NMR, EM), biophysical measures of protein interactions, bioinformatics and modelling. Several of these technologies will be consolidated into platforms which will be very beneficial for the both the Department and the rest of I2BC and should allow members access to sustainable, state-of-the-art and properly maintained core facilities. In this respect, a major opportunity, but also a challenge, will be integration of the world-leading spectroscopy instrumentation, now concentrated in expert groups at the CEA, to allow broader exploitation in both the new Department and the new Institute as a whole, as this should be a unique feature of I2BC distinguishing it from other comparable institutes. Given the size of BS3 (the second largest department within I2BC) it has a great opportunity to shape transversal biological themes of the Institute.

Weaknesses and threats related to the context

During the transition period, where the BS3 teams will still be dispersed over three sites, there is a risk that momentum to create a new cohesive department. Careful planning will be required to maintain long-term expertise in the area of spectroscopy given that retirements will occur during the next few years and recruitment in specific areas is difficult in the current system and to maintain state of the art facilities. In general there are several small teams that by themselves may not have the critical mass to be competitive at the international level. There is currently a very uneven distribution of technical help amongst the groups.

Recommendations

The Departmental leadership will need to provide strong incentives and encourage new collaborative initiatives to begin to build a new cohesive departmental (and institutional) mentality during the transition period. The leadership should seek to provide technical help where it enhances impact and not simply follow historical precedent. A careful balance needs to be found between maintaining the unique, but individual, expertise in spectroscopy and trying to broaden its exploitation within BS3 and I2BC. Small teams or new regroupings need to be monitored carefully and mentored if necessary to be able to focus on high impact research.

Team

STRUCTURAL BIOLOGY OF MOLECULAR SWITCHES AND MOTORS

Name of team leader:

Ms Julie MENETREY

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**3**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

Scientific quality and outputs

This is a newly established group working on the structure determination of cytoskeleton cargo proteins (that bind to and are transported by molecular motors) with a focus on proteins related to human pathologies such as neurological diseases and cancer. The projects are well chosen, by providing a disease link and thus making it interesting for society, which is more and more reluctant to invest into purely fundamental projects. The project is nicely complementary to the tubulin-kinesin focus of another group within the Department.

Structural work on kinesin cargo recruitment with a potential to be involved in certain diseases is very interesting but highly competitive. If successful, the implications for the group will be very positive.

Work on Arf GTPases and myosins from the PIs post-doctoral time in the Curie Institute has been published in high impact factor journals such as EMBO J and Molecular Cell. Since being an independent group leader, her group's work has been published in medium (Structure) and higher impact factor journals (EMBO J).

Team's academic reputation

The team's academic reputation is somewhat difficult to judge at this early stage, because it was only recently created. However, first indications are promising: the group leader and group members regularly participated at several scientific meetings in France and abroad.

Nevertheless, the PI is starting to build the group's reputation, first in the myosin and now in the kinesin field. Since both fields are interconnected this is a logical choice of projects.

Interaction with the social, economic and cultural environment

The group leader participated at several events to attract young people to science including Fêtes de la science, Accueil collégien and Science Académie.

Involvement in training through research

Two students finished their PhDs and one PhD student started his PhD recently. The PI participated at two PhD examinations as an external examiner.

Strategy and five-year plan

After concentrating on the understanding of plus-end and minus-end directed motility in molecular detail, an important part of kinesin motor research is now to concentrate on the structural understanding of cargo recruitment. The group project fits into this trend and is suitably ambitious, given the competition, for a junior group leader.

The project is logically built by concentrating first on kinesin-1/tail-cargo interactions and investigating different models of direct (tail-cargo/adaptor) and indirect (tail-KLC-cargo) interactions.

Although the links between kinesins and neurodegenerative diseases are not as clearly elaborated yet as the link between mitotic kinesins and cancer, there is the general expectation in the field that in the future the involvement of these molecular motors in neurodegenerative diseases will become more obvious with potential points of intervention for disease treatment. Medically relevant complexes between kinesins and their associated proteins (cargos/adaptors) may therefore lead to applied projects.

In her five-year plan, the PI concentrates her efforts on the structural basis of cargo recruitment by kinesin-1. Two major complexes have been chosen, which have the potential to lead to publications in higher impact factor journals. Cargos chosen are from proteins involved in diseases (e.g. JIPs and FE21). First diffracting crystals have been obtained and the aims of the project are realistic.

Due to the highly competitive nature of the kinesin-cargo project some adjustments to the direction of the research project may become necessary.

Conclusions

- **Strengths:**

- The PI is a motivated young group leader, who managed to secure funding and permanent positions for her ambitious project. Coming with a background in the myosin-actin field gained at the Institute Curie in Paris, she now extends her projects to the kinesin field with a focus on disease-related kinesin cargo proteins. The next five years will be important to firmly establish her independent reputation in this research area.

- **Weaknesses:**

- The kinesin field, in particular work on kinesin-1 as a prototype motor for plus-end directed motility, is highly competitive with many groups all over the world working on the fundamental aspects of this motor. Several groups work on the structure determination of kinesin-1 tail – adaptor/cargo interactions so it is important for the new group leader to have sufficient support to be competitive particular in follow up work to structural studies and to have backup projects. The current group is of minimal size.

- **Recommendations:**

- Promising young group in the motor field with an interesting mixture of competitive projects, which should be strongly supported.

Team

CYTOSKELETON DYNAMICS AND MOTILITY

Name of team leader:

Mr Christophe LE CLAINCHE and Mr Louis RENAULT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	4	5
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	7	4
N6: Other contractual staff (without research duties)	3	3
TOTAL N1 to N6	**14**	**12**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	7	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	3	3

Scientific quality and outputs

The research group headed by two PIs is the largest of the three I2BC cytoskeleton groups and works in the actin cytoskeleton field, in particular on actin assembly, dynamics, and the function and mechanism of actin related proteins. Together, these three I2BC groups form a powerful unit with complementary interests and projects covering the two important main fields of cytoskeleton research, a strong point for I2BC. Work and ideas carried out by the myosin/actin field will also be investigated in the kinesin/MT field, which often leads to an exchange of ideas and synergistic effects.

The group members published a total of 41 publications in a variety of journals from low to high impact factor journals (Nature Structural Mol. Biol., Nature Communications, J. Biol. Chem., EMBO. J, PNAS, Mol. Cell. In 25 publications they were first or last author, the remainder being collaborative papers with other groups working in the field. The scientific quality and output is outstanding.

Team's academic reputation

The group is an international leader in the actin cytoskeleton field, which is also reflected by the number of important invitations the group members and in particular the former group leader receive to present their work. This includes the participation at several Gordon conferences, as well as EMBO, ESF-EMO, EMBO-FESBS and many other meetings world-wide.

The group maintains a large network of successful collaborations, reflected by the significant amount of manuscripts originating from these collaborations. In summary, the group has an outstanding academic reputation.

Interaction with the social, economic and cultural environment

One group leader participated twice in the Fête de la science.

The team's involvement in training through research

The group supervised 1 PhD student and 10 Master students and were part of three PhD panels.

Strategy and the five-year plan

The team proposes a range of ongoing and future projects that build on the knowledge and expertise of the group and use a multidisciplinary approach. **One focus will be actin assembly and mechanosensitivity in focal adhesions including reconstitution with membrane bound integrins; the latter represents a new departure and could benefit from knowledge of membrane proteins in other group of B3S. Another project will be to further develop novel microfluidics systems to study single actin fibers under mechanical tension and the role of different regulatory proteins. A third project will focus on structure and function of regulators that contain WH2 repeats including such proteins form pathogens. These projects are interesting and feasible.**

Conclusion

- **Strengths and opportunities:**

- A well-established research group with high international reputation and high standing in the field. Formerly headed by another scientist, this group is currently in a transition period and headed by two new group leaders. If this transition goes smoothly, the high standing of the group may be preserved.

- **Weaknesses and threats:**

- The group's reputation is due largely to the outstanding scientific productivity and standing of the former group leader, who has now emeritus status. With her ERC funding, she seems to be still the driving person behind the group: she still provides by far the largest number of publications, by far the largest number of invited talks and secures the largest amount of external funding. It is important that the new group leaders maintain the cohesiveness of the group at the same time as developing their own independent directions. Another issue may be the less defined role of another group member, who seems to be very productive in terms of publications and securing of external research money, but who is not a group leader. This may lead to future tensions in the group. The transition may proceed smoothly, but several other scenarios, that may significantly hamper the group's scientific standing (publications, external funding, teaching) and affect its critical mass, are also likely.

- **Recommendations:**

- This is a historically highly productive and original group now embedded in a larger unit of three I2BC research groups working in the cytoskeleton field. The two new group leaders should be given more opportunities to further develop and strengthen their own profiles and secure their own funding and also develop in house collaborations that build on the I2BC strength and interest in the cytoskeleton field (in BS3, virology and cell biology).

Team

INTERACTIONS AND ASSEMBLY MECHANISMS

Name of team leader: Mr Stéphane BRESSANELLI

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**5**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

Assessment of scientific quality and outputs

This team is composed of 3 Principal Investigators who worked in other teams prior to this evaluation. Their research are in three distinct areas: (i) structural virology, (ii) peptide self-assembly and (iii) molecular modelling and spectroscopic analysis applied to supramolecular and cellular processes. Altogether, they have published 47 papers among which several in high ranking journals in their field like PNAS, Acta Cryst D, JACS, Angewandte Chemie, Arch Biochem Biophys, Langmuir, Biophys J, PLoS Pathol, Biochimie. They have established a very good national and international reputation in structural virology and mechanism of peptide self-assembly.

Major achievements in structural virology:

- Very original results on regulation of viral RNA polymerases of RNA+ viruses were obtained in the framework of well-established national and international collaborations. Amongst these are the detailed analysis of X-ray structures of Hepatitis C Virus polymerase. This topic has led to +10 publications in very good journals.

- Detailed description of interplay in capsid assembly between curvature of the protein shell and specific/non-specific interactions with the RNA genome of a Novovirus (an icosahedral RNA+ virus). This has led to 3 publications in very good journals.

Major achievements in peptide self-assembly that forms long nanotubes:

- The self-assembly mechanism of lanreotide, a dicationic octapeptide which is a therapeutic analogue of somatostatin-14, and the structural determinants at play in nanotube formation was deciphered owing to very elegantly designed set of experiments. Interestingly, it was shown for the first time that nanotube diameter was sequence dependent and the role of peptide-associated counter-ions and electrostatics in the self-assembly mechanism was explained. An original extension of this work was the study of self-assembly properties of the natural peptide hormone somatostatin-14. This lead to +10 publications in high ranking journals.

- A novel pH-induced conformational switch that governs the triptorelin decapeptide nanotube diameter through histidine protonation was very recently characterized. A similar switch seems to be at play in viral fusion proteins.

Major achievements in modelling and resonance spectroscopies applied to supramolecular and cellular processes:

- EPR spectroscopy was used to assess long structural ranges of DNA.

- NMR was used to detail heavy metal chelation and detoxication.

- Bioprobes for magnetic resonance imaging in-vivo were developed.

- Overall, these have led to 16 scientific papers in very good journals.

Assessment of the team's academic reputation and appeal

The team members have coordinated several ANRS or ARC projects and participated in numerous ANR research projects. They are invited to several national and international conferences.

Members were on the board of several research groups or institutional committees like ANR or Research Societies like European Radiation Research Society. One member was director of a national research group (GdR) on supramolecular assemblies.

There is a sustained involvement in scientific management of Institute of Biology and Technology Saclay.

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

- Have been approached by a major pharmaceutical company to create a joint laboratory.
- Joint ANR projects with major pharmaceutical company.
- Two patents with international extension.

Assessment of the team's involvement in training through research

The team members have supervised 4 PhD students and are supervising 2 PhD currently. The number of publications where these 4 PhDs are main authors is 3 which is a rather weak amount.

Seven post-docs have been supervised by the team members and 5 master students have been trained with the team members. No indication about integration of doctors into job market was given.

Team members were involved in setting up and organizing an interdisciplinary school on “Non covalent interactions in supramolecular assemblies” and in a school on “Scientific visualization”. Team members are regularly on the board of PhD and HDR juries as members or reviewers.

Assessment of the strategy and the five-year plan

The proposed project is a continuation of their previous research and mainly focused on assemblies and their interaction with three main areas of focus:

- morphological control of peptide assemblies and new formulations for therapeutic hormones ;
- self-assembly of viral capsids probed by time-resolved and static techniques ;
- dynamics, activation and fidelity of Flaviviridae polymerases.

The project is ambitious, coherent with respect to their respective complementary skills and strength. The partnership with major Pharmas on therapeutic peptide self-assembly opens very good industrial perspectives. The proposed research on RNA+ virus replication and viral capsid self-assembly is well within the frame of their strengths and international reputation. Feasibility of the five-year plan is subjected to appropriate funding, good traction between the team members and additional human resources.

Conclusion

- **Strengths and opportunities:**

- Excellent scientific output.

- Complementary skills in biophysics and spectroscopy.

- Potential very good international outlook.

- Good traction with other virology groups and structural biology and biophysics groups in the I2BC Institute

- **Weaknesses and threats:**

- Small size of the team.

- Productivity of PhD students.

- Thematic dispersion and loss of lead in structural virology.

- International competition.

- Inappropriate funding.

- **Recommendation:**

Considering the small size of the team (3 PIs) and its apparent desire to promote novel, interdisciplinary projects, it should consider carefully where the highest impact will be made and not lose sight of its strengths e.g. in research on RNA+ virus replication and viral capsid self-assembly using spectroscopic and biophysical techniques. Molecular dynamics simulations, though of use, should not be given too high a priority compared to an experimental approach to biological questions.

Team

STRUCTURAL BIOLOGY AND RADIATION BIOLOGY LABORATORY/ NUCLEAR ENVELOPE, TELOMERES AND DNA REPAIR

Name of team leader:

Mr Jean-Baptiste CHARBONNIER, Ms Marie-Hélène LEDU & Ms Sophie ZINN-JUSTIN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	5	5
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	4	2
TOTAL N1 to N6	**10**	**8**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	4	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	5	5

Assessment of scientific quality and outputs

This group contains three PIs with interests in the linked areas of nuclear envelope (lamins and their interactors), yeast and human telomeres and DNA repair (non-homologous end-joining and mismatch repair). They use an integrated structural biology approach, incorporating in cell studies, but have particular expertise in X-ray crystallography and NMR. The group is productive with a total of 31 publications over the review period of which twelve have group members in lead positions. Several papers are in very good journals (Science Signaling, PNAS, NSMB, NAR) indicating originality and a high impact in their areas of research. Highlights include the structure of a mismatch repair complex which allows mapping of human disease mutations, structure of a human double-strand break repair complex which reveals a novel filament structure and structural characterization of a signaling complex at the nuclear membrane.

Assessment of the team's academic reputation and appeal

The PIs each have numerous, mainly national, collaborators which allows them to add value to their structural studies.

Invited talks are mainly national except for one PI who appears to have a more international reputation. The group's work seems to be very well represented by posters at conferences but again mainly national.

The same PI is an editor for FEBS Journal, an organizer of an international NMR conference and is a member of review committees for HFSP. The second PI reviews for several journals and ANR grants. The third one has significant activity in crystallography related committees and meetings. Two PIs are involved in organizing the South Paris node of FRISBI. The group is well funded.

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

Two patents are listed but difficult to assess role of group members.

Participation in the « Fête de la science ».

Assessment of the team's organization and life

Concerning research focus, the team is really three teams without not much subject overlap but who share methodologies and technical support.

Assessment of the team's involvement in training through research

At the moment, the group is training 3 PhD students, 4 others have defended. Many of the higher impact journal publications have PhD students as first authors which is very positive.

The group has several Master students and each of the 3 team leaders teaches in masters courses.

Assessment of the strategy and the five-year plan

The proposed projects are logical continuations in the individual areas of interest of each of the PIs with a trend towards study of larger complexes (e.g. multi-protein complexes in the non-homologous end-joining pathway and shelterin protein-DNA complexes) and the role of post-translational modifications in regulation of nuclear envelope assembly. Given the excellent past record these ambition projects are well within the scope of the group, but not without risk. An interesting initiative is a proposed transversal project involving all PIs on the role of the Ku70/Ku80 heterodimer in both DNA repair and telomere recruitment to the nuclear membrane.

Group members already have a good interaction network with future members of the BS3 and all other I2BS Departments, partly based on scientific common interests but also where the structural biology expertise is made use of (e.g. X-ray or NMR structure determination and modelling).

Conclusion

- **Strengths and opportunities**

A well-funded, active and productive group with ambitious projects linking to human genome biology. Strong technical competence and keen to establish new platforms e.g. insect cell expression of complexes and EM. Well placed to play a central role in cementing the BS3 department and I2BC.

- **Weaknesses and threats**

The team has not the technical help to carry out its ambitious program.

Disconnection between interests of the three PIs is a concern

- **Recommendations**

The development of the transversal project is strongly encouraged.

Team

BIOLOGICAL HIGH-FIELD MAGNETIC RESONANCE

Name of team leader:

Mr Sun UN and Mr Leandro C. TABARES

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**3**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended		
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

Assessment of scientific quality and outputs

This group is mainly interested in the technological developments of high magnetic-field electron paramagnetic resonance and its biological applications in oxidative stress. The models investigated are redox reactive radicals and manganese by EPR. More recently a new subject on Mn *in vivo* by EPR has been developed. The results obtained on the quantification of Mn *in vivo* are interesting, but should be validated by a combination of other approaches.

The team has the only 95 Ghz EPR spectrometer in France and in consequence is leader, and members are internationally recognized experts in this field.

The specificity of this team is also linked to its technological developments in particular PELDOR technology with Mn as model probe.

A rate of 17 publications for 4 years is quite good for the very small size of the team (one until 2010 and 2 after). Very good quality journals have been selected for publications such JACS, BBA, PNAS, Inorg Chem (7 leader positions), most of them are in external collaborations.

Assessment of the team's academic reputation and appeal

The team has a national network of collaborations for biological questions and international collaborators for technology questions. Most of the publications are in collaboration with international or national groups. This is in line with the specificity and the visibility of the team in unique EPR technology.

The group has attracted both international and national external funding to the extent that they are financially autonomous: they are coordinating 2 ANR projects and one CNRS research contract and participating in one other ANR project and one EU project.

The two researchers have a reasonable number of invitations to give invited lectures at important international meetings

Assessment of the team's involvement in training through research

Only two foreign students for short period (3x 2 months), no PhD student, only one post-doc. This constitutes probably one of the major weaknesses of this team.

Assessment of the strategy and the five-year plan

Due to the high competence in HFEPR and in the field of manganese, the project is realistic and in continuity of the work done so far.

In vivo detection of manganese is a real technological challenge but what about the biological question? More interactions with biologists should be developed.

Probably, spin labelling project is the one that will induce more interactions between various teams of I2BC.

The team is scientifically and financially autonomous.

Conclusion

- **Strengths and opportunities:**

International visibility in EPR spectroscopy and development of PELDOR approaches. The team possesses advanced and unique instrumentation.

- **Weaknesses and threats:**

The team is too small and no clear interactions with other groups from I2BC are described.

The project is technology/methods orientated and lacks a strong biological focus.

There is no PhD student in this team. As the team participates/ coordinates various grants, this is not a consequence to a lack of financial support.

- **Recommendations:**

Ideally they need support in terms of reinforcement of the group by technical support.

A challenge will be integration of the world-leading instrumentation and expertise on spectroscopy, now concentrated at the CEA, and the development of new biologically orientated interactions. Spin labelling technology to investigate dynamic of macromolecules is probably the most promising theme and where interactions with other teams of I2BC could be highly profitable.

They also need to recruit PhD students as part of an encouragement of young scientists to take an expert interest in the biological applications of EPR.

Team

BIOENERGETICS, METALLOPROTEINS AND STRESS

Name of team leader:

Mr Bruno ROBERT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	7	7
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)	2	1
TOTAL N1 to N6	**12**	**10**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	4	4

Assessment of scientific quality and outputs

Created in 2010, the BMS team uses multidisciplinary approaches to analyze structure/function relationships of metalloproteins involved in photosynthesis. Major results have been obtained.

A rate of ca 10 publications a year (54 since 2008) is quite good for the size of the team. High quality journals have been selected for publications such as PNAS, J Phys Chem B, J Am Chem Soc, J Biol Chem, etc.

The team is a leader in its field, research is original.

The team is using state-of-the-art methodologies which include Raman spectroscopy, resonance Raman, picosecond Raman spectroscopy, multifrequency EPR spectroscopies and single molecule fluorescence experiments to address conformational and energetic landscapes as well as molecular dynamics e.g. of micellar systems. There is a real benefit from sharing specific expertises within the group as applied to the same biological system.

The quality of the research is clearly apparent from the number and quality of the publications, from the number of invited conferences presented in international meetings, and especially from the ERC grant which underlines the truly exceptional quality of the research.

In particular, the work on light harvesting complex II (LHCII) showing it can adopt two molecular conformations, one for harvesting energy and the other for quenching it has received considerable international attention. The fact that LHCII has a structure very sensitive to the environment and appears to be tuned by the formation of photosystem II supercomplexes is a new important result.

Assessment of the team's academic reputation and appeal

The team's academic reputation is outstanding. The advanced ERC grant obtained by the team leader is by itself recognition of excellence at international level at the highest level. The team leader also became Professor of Physics of Membranes at the Vrije Universiteit Amsterdam (2012-2017) and President of the French Biophysical Society (2009-2013). With about 12 invited lectures every year, the international reputation of the team leader is exceptional.

Most of the publications are in collaboration with international or national groups. This is in line with the specificity and the high visibility of the team in the field of photosynthesis and oxidative stress.

Participation in a EC funded Marie Curie ITN network is also a key feature indicating the integration of the group in the international (here European) environment. It also underlines the high quality of the research as these ITN grants are very competitive. Multiple collaborations with other European and American teams are further indications for high quality and reputation across the academic world.

The team leader contributed to the organization of the International Congress on Carotenoid molecules in 2011 and 2014, of the French Biophysical Society meetings (2008-2012) and an international workshop on light harvesting systems (2010 and 2013).

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

One patent has been filed.

Assessment of the team's organization and life

Meetings are organized every other week in the group. Problems appear to be solved as soon as they appear

Assessment of the team's involvement in training through research

Training through research is well developed in the team. The EU-funded ITN network is precisely oriented to training through research.

PhD students are being trained in the laboratory and in addition a large number of foreign and French students were hosted as external collaborators for typically 1-3 month periods.

Assessment of the strategy and the five-year plan

The team has a coherent view of future research. The plan for the next 5 years includes the continuation of the current research and new developments.

The aim to assess whether supramolecular association of membrane proteins constitutes an additional level of regulation in bioenergetics processes is challenging but is certainly a hot topic worth pursuing. Evaluation of potential structural changes in plant PSII complexes is similarly a challenging but up-to-date research topic.

The first new project is to contribute to the National Infrastructure framework to develop super-resolution microscopy. The nature of the contribution is not described in the report but access to such a technology which is not available today will certainly contribute to the overall competitiveness and quality of the research in the team and could have much wider benefit.

The second new project is dedicated evaluate the low frequency motions of proteins in the excited state and the effect on the quantum yield of the primary charge separation mechanism.

Conclusion

- **Strengths and Opportunities:**

- The scientific output of the group is overall outstanding. Money is not a problem for several years.

- International reputation is at the highest level.

- Development of new project of super resolution microscopy with the aim to perform hyper-spectral super-resolution imaging is a rather risky task but the team has the means and skills to implement.

- International collaborations may increase with the help of the European ITN and ERC grants.

- **Weaknesses and Threats:**

- Considering the size of the team, there is a rather large series of different topics: research on gene regulation in cyanobacteria, LH2 from purple bacteria, structure and reactivity of a series of peroxidases, catalases and bi-functional catalase-peroxidases, molecular structure modelling, etc. These are all interesting but do not all provide the opportunity for an added value and high impact for the group.

- **Recommendations:**

- The group should continue its interactions with first-class scientists around the world and focus on the research, which is expected to have the highest impact considering the techniques mastered by the group and the team.

Team

MOLECULAR ASSEMBLIES AND GENOME INTEGRITY

Name of team leader:

Ms Françoise OCHSENBEIN and Mr Raphaël GUEROIS

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	2	
TOTAL N1 to N6	**5**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

Assessment of scientific quality and outputs

This group works on chaperones which are involved in assembly of large oligomeric structures but which have also emerged as regulators of the cellular interactome. The group developed quite successfully an interdisciplinary approach involving biochemistry, structural biology and bioinformatics to address unsolved questions about the assembly of nucleosomes and proteasomes. Three specific and original topics were developed:

- they analyzed Asf1 interactome in particular its interaction with Rad53 and targeted Asf1 activity using competitive peptidic inhibitors which they rationally designed;
- they contributed significantly towards the understanding of the molecular basis of the interaction network involving Sgt1/Hsp90 co-chaperoning/triggering system and NLR sensors through the first description of Hsp90-Sgt1 complex using both biophysical and modelling approaches;
- they made significant contributions towards the identification of novel proteasome assembly chaperones in human starting from the yeast orthologs uncovered by their collaborators. They are tackling the process of proteasome assembly mainly using X-ray crystallography and have recently released the structure of the complex of the proteasome chaperone Hsm3 bound to a subunit of 19S thus providing insights into their role in chaperoning and scaffolding these regulatory subunits during proteasome assembly.

Their research on assembly chaperones also motivated them to look into protein-protein interfaces in protein complexes using evolutionary information with the aim to improve their understanding of interactomes. One of their major contributions is the development of a novel bioinformatics method to guide coarse-grained docking of proteins which relies on an original database.

The group has a very good track record of publications in very good journals. During the period 2008 to 2013, their members published 27 original papers and reviews in journals such as PNAS, TIBS, EMBO Reports, J Biol Chem, Mol Biol Evol, NAR and are leading authors on 13 of these, while others are related to research they co-develop with collaborators. Their papers are also regularly cited with a total of 72 citations on their 13 lead author 2008/2013 papers. They also have a world patent on peptidic inhibitors of the Asf1-Histone interaction.

Assessment of the team's academic reputation and appeal

The group has a good network of collaborators in France and some collaborations at international level (e.g. with collaborators in Japan).

They are coordinating one ANR project and one CEA research contracts and participating in four other ANR projects.

Members of the group are active in several thematic groups or committees at national level among which the secretariat of the “structural biochemistry” group of the French Society for Biochemistry and Molecular Biology (SFBBM).

They were invited to give several lectures in France and abroad and have been involved in the organization of two national conferences.

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

The group has successfully designed peptides that target Asf1-Histone interaction in a tumor cell proliferation context. A world patent was issued for this invention.

Original databases and methods were developed with the aim to provide further insights into interactomes.

Assessment of the team's involvement in training through research

The group has been very active in training graduate students: a total of 5 PhD students, 6 master students and 3 engineer students were or are being trained in the group.

They also developed a 4 days training program targeting PhD students of two doctoral schools on the topic of protein-protein interactions.

Besides, members are involved in teaching in various Master degrees courses and have regularly served on board of jury of several PhD students.

Assessment of the strategy and the five-year plan

The project of the group is focusing on two different subjects:

- they are planning to perform large scale prediction of protein-protein interactions at play in genome functioning or proteasome biogenesis with specific emphasis on chaperone interactomes. They will rely on the conservation of these interaction networks during evolution and develop methods to better account for evolutionary constraints on a multi-scale level. This work is already supported in the framework of the Investissement d'Avenir BIP-BIP project (2011-2016). How they intend to validate experimentally components of the inferred interactome is not documented.
- they are looking into rationally designing refined peptidic inhibitors for optimized affinity and selectivity towards Asf1 paralogs and to seek POC in animal models. Appropriate funding has been secured through the ANR CHAPINHIB (2012-2016).

The overall plan, though coherent with their previous achievements, looks overall weakly ambitious. Their motivation for pursuing the promising subject of biology of assembly chaperones where they had a strong lead and where they can bring originality is not clear. How the group envision the experimental validation of the inferred interactions is not detailed.

Conclusion

- **Strengths and Opportunities:**

- Complementary skills in structural biology and bioinformatics.

- Excellent scientific output.

- Traction with other teams in I2BC to consolidate research strategy.

- Collaborations with industry on peptide inhibitors of Asf1.

- **Weaknesses and Threats:**

- Team size.

- Ambition of the project.

- The team may lose momentum on the biology of assembly chaperones where they have been quite productive.

- **Recommendations :**

- The team has very good potential and should look into being more ambitious. The peptide inhibitor project might not lead to sufficient research productivity down the road. Continuing research on the biology of assembly chaperones might be more rewarding on the long term owing to their complementary skills and existing collaboration network.

- The leadership of the team must be clarified.

Team PHOTOSYSTEM II

Name of team leader: Mr Alain BOUSSAC

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**3**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

Assessment of scientific quality and outputs

The oxidation of water is probably the most challenging and yet most interesting problem remaining to be solved in studies of photosynthesis, and one that has considerable implications for the design and construction of artificial photosynthetic systems, and optimization of the production of biofuels. This group studies the structure function relationships of PSII to elucidate the chemistry of water oxidation.

The group is arguably amongst the best in the world at preparing samples that can address the mechanism of water splitting, and as a result is collaborating with some of the leading laboratories in the world, including the Institut de Biologie Physcio-Chimique, Paris (optical studies), the Cell Free Science and Technology Centre, Ehime University, Japan (molecular biology and mutants), the Max Planck Institute für Chemisch Energiekonversion, Mülheim, Germany (Advanced EPR) and Umea University Plant Science Centre, Sweden. However, they are much more than just sample makers, they come up with the best samples in terms of trapping intermediate states in water oxidation, and then go these laboratories to answer a series of questions and hypotheses that they have generated. They have with considerable success used Calcium/Strontium and Chloride/Bromide substitutions to probe intermediates in reactions.

More recent developments are the studies of the phenotypes of organisms expressing genes coding for individual protein subunits in PSII, which may lead to functional adaptations, and studies of site-directed mutants.

The 50 publications reflect considerable productivity despite the small size of the group, and include publications in top journals in the fields of chemistry and biochemistry, as well as the multi-disciplinary journal PNAS. This group is now entirely independent of the former group leader, and has an international reputation and plenty of invitations to give invited lectures etc.

Assessment of the team's academic reputation and appeal

The group has a high level of involvement with the top laboratories across the world in studying water oxidation, and are receiving invitations to the most important and significant conferences in this area.

Assessment of the strategy and the five-year plan

The plan for research builds upon the advances made in the last few years, but is still aiming to study a very challenging problem. It is enlarging its studies to include study of adaptation at the cellular level in response to environmental parameters, and to study site-directed mutants that have been generated, which will also insights into the energetics of water oxidation yield. As such the five-year plan is perfectly feasible, although it could be more clearly described. No SWOT analysis was provided.

Conclusion

- **Strengths and opportunities:**

This laboratory is very well placed to continue to contribute to studies of what is a very important process, the mechanism of photosynthetic water oxidation. It has established collaborations with the top laboratories in the field internationally, which means it can draw upon the expertise and resources of these collaborators to ensure that the research is rapidly progressed towards meaningful and significant results, which can be published in the top journals. It is very focused on the problems it studies, but is widening the scope of research to look at regulation and the effect of environmental parameters at a cellular level.

- **Weaknesses and threats:**

This is a very small group that does not seem to recruit or train postdoctoral workers or PhD students. It does not interact to any great extent with the social, economic or cultural environment. It does not lead or set up any significant international networks other than those established during collaborative research. Although there is an impressive list of publications, many of them do not seem to include the team as first or corresponding authors, although there are signs of improvement on this front. It does not collaborate with chemists or spectroscopists or others within I2BC, and does not submit any plans to do so.

There is relatively little external grant income.

- **Recommendations:**

This group should make greater efforts to contribute their expertise within I2BC, and to recruit and train postdoctoral workers and PhD students, which would be aided by more efforts in applying for funding and participation in networks. At the moment, it is a small team that is very well focused on a particular problem with considerable success, but needs to expand and to play a more active role in the new Institute.

Team

REGULATORY MECHANISMS IN PHOTOSYNTHETIC ORGANISMS

Name of team leader:

Ms Diana KIRILOVSKY

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**8**	**6**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	4	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

Assessment of scientific quality and outputs

This group has produced what is some of the most interesting and novel results on the regulation of energy transfer from photosynthetic antenna pigment proteins to the reaction center in the past few years, looking at regulation of the energy flow from the phycobilisome. The discovery and elucidation of the role of the orange carotenoid protein and fluorescence recovery protein has had international impact and recognition. The work has been published in top journals in the field and could have been published in higher impact multi-disciplinary journals. This piece of work is ground-breaking and represents a considerable increase in impact and productivity in recent years.

The work on reaction oxygen species in also near the top of research in the plant physiology and photosynthesis field, and always interesting, and the developing work on the plant alternate oxidase looks very promising and is bound to receive considerable interest as it develops. The work on the redox state of the cell and its influence in regulation is also promising, but has only just commenced.

Overall the group is prolific in publications with 5 book chapters and 51 original papers during the period under review, with some in the top journals in plant physiology, biochemistry and photosynthesis (PNAS, Plant Physiol. J. Biol. Chem. Plant Cell), with the group quite often (32/51) being first or corresponding author.

Assessment of the team's academic reputation and appeal

There is a noteworthy degree of involvement in national and EU networks, and collaboration with some of the top international experts in various fields. Members of the group are members of national and international committees and involved in the organization of meetings and editorial responsibilities. They have had numerous invitations to give invited lectures at the top meetings in their research area, and have recruited high quality postdoctoral research workers and PhD students.

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

The team has had discussions with a biotech industrial company about a possible cyanobacterial product.

Assessment of the team's organization and life

The team has come together relatively recently, and is already working with a coherent and sensible set of scientific objectives, and seems to pool resources to study interdisciplinary problems of international importance. They are also exploring opportunities for collaboration within the I2BC.

Assessment of the team's involvement in training through research

They have considerable experience and success in PhD student supervision and examining, and are involved in postgraduate teaching.

Assessment of the strategy and the five-year plan

The team set out a clear strategy for extending their work on regulation of electron transfer and antioxidative protection to conditions other than simply high light intensity, thus probing a more encompassing and comprehensive treatment of the conditions experienced by these organisms in nature. They will study the role of truncated versions of the orange carotenoid protein and fluorescence recovery protein, and the influence of environmental conditions on secondary metabolite production by cyanobacteria, which is of importance as many of these are bioactive.

Their primary interest is redox regulation in cyanobacteria and describe the development of a number of innovative methods for these studies, some in collaboration. Regulation by control of production of reactive oxygen species is another important topic. The five-year plan for research is achievable and original, and is a logical development from their current success and recognition.

Conclusion

- **Strengths and opportunities:**

A strong group recently formed that has members who have had considerable success, with the work on energy transfer regulation in cyanobacteria being amongst the best in this field in recent years, with characterization of both the regulation and the molecular mechanisms. They work together well and are keen to collaborate within I2BC as well as continuing international collaborations. Their work is recognized in terms of invitation to meetings and they have a good record of external grant funding, and they recruit and train good numbers of post-docs and PhD students.

- **Weaknesses and threats:**

They need to renew external funding in order to continue to reach ambitious targets. Collaboration within the I2BC may be handicapped by the lack of funding for such projects, with it being easier to get funding for international collaborations.

- **Recommendations:**

This group needs support particularly in terms of funding for collaboration within I2BC. They should pursue industrial collaborations as this research should be of interest in that area.

Team

FONCTION ET ARCHITECTURE DES ASSEMBLAGES MACROMOLECULAIRES - FAAM

Name of team leader:

Mr Herman VAN TILBEURGH

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	5	5
N2: Permanent EPST or EPIC researchers and similar positions	1	3
N3: Other permanent staff (without research duties)	2	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**9**	**12**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	5	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	5	5

Assessment of scientific quality and outputs

This is a large group of structural biologists with a crystallography focus with currently eight permanent UPS or CNRS staff and 4 PhD students. The group will be augmented in 2015 by three more permanent staff who focus on small angle X-ray scattering. The team is highly productive in terms of numbers of publications, 49 papers in all, with slightly over half with group members as first or last authors. However the scientific interests of the group are very broad with many different unrelated projects. This reflects the previous involvement of the group in structural genomics for which it acquired and still runs a robotic cloning, protein expression, purification and crystallization platform, which also attracted diverse collaborative projects. The papers are mainly in good (Structure, NAR, Proteins Sci, J Virol, J Mol Biol, RNA, PloS One, etc.) and occasionally in high impact (PNAS, EMBO J, Genes Dev, NSMB) journals. One member who joined the group in 2012 has a more focused research program on bacterial pathogenesis (two component systems and quorum sensing) and has had an acknowledged impact in this field with several publications in Mol Microbiol and also PLoS Biol and recently in PNAS.

Assessment of the team's academic reputation and appeal

The group is responsible for running the Structural Biology Platform (labelled IBISA and part of the French Infrastructure for Integrated Structural Biology (FRSIBI) network) and this involves four permanent staff. Because of this available expertise the group has numerous regional, national or European collaborations (13 are listed) and this, to a large extent, has determined which projects the group works on. The platform is likely to become a central resource for I2BC.

The team leader has been a member of various national and European evaluation committees, but has rather few invited lectures. Another member has quite a few international invites including to a Keystone meeting.

It is to the group's credit that it is expanded by a recent recruitment and in the future of a team which has considerable and well-known expertise in SAXS and good access to Soleil.

Assessment of the team's involvement in training through research

Each of the main PIs has a good record of training PhD students (11 PhDs in total in training in the review period, 6 have successfully defended). Most of the PIs are also heavily involved in university teaching.

Assessment of the strategy and the five-year plan

- Originality of the project and any risk-taking: this is a group with a wide array of interests. Both originality and risk-taking could be improved.
- Overall consistency of the project: the future group will consist of 4 PIs with largely different projects. Those of two PIs on quorum sensing, natural bacterial transformation and bacterial signaling are both linked to bacterial pathogenicity mechanisms and potentially could lead to new antibiotic options. They also have echoes in other I2BC departments e.g. in microbiology. The team leader will continue to study the KEOPS complex, involved in tRNA modification in all kingdoms of life, particularly in multicellular organisms where it may have additional functions, as well as the role of the different fibronectin domains in extracellular matrix. The fourth PI also has a variety of projects, often driven by collaborations on SAXS experiments. These projects are feasible but the overall consistency of the projects within the team as a whole is thus difficult to find.

Conclusion

- **Strengths and opportunities:**

- A productive group which has a lot of collaborations largely by virtue of running a structural biology platform.

- In I2BC the structural biology platform could be of importance in opening up opportunities to in house biologists in all departments who want to include a structural biology component.

- There is also an opportunity for some group members to form an interdepartmental transversal grouping in bacterial pathogenesis.

- The incorporation of SAXS expertise expands further the technical competence of the group in diverse structural biology methods.

- **Weaknesses and threats:**

- Its structural genomics origins have prevented the group from focusing and having an international impact in any particular area of biology.

- **Recommendations:**

- The group needs to rethink its structure and scientific focus if it wants to have a real impact in a given biological area.

- Since it is funded as a service, the structural biology platform should be run in a more transparent and independent way.

Team

STRUCTURAL BIOCHEMISTRY OF MICROTUBULES: MOTORS AND REGULATION

Name of team leader:

Mr Marcel KNOSSOW

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	**5**	**5**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

Scientific quality and outputs

The group works on the elucidation of the mechanisms that govern structural changes induced during the assembly of tubulin into microtubules (MTs) and the disassembly of microtubules into tubulin subunits. Tubulin represents one of the major key cytoskeleton proteins that form the tracks along which a huge variety of microtubule-associated proteins (MAPs) bind to and/or travel. For example one group of proteins, the kinesins, transport cargo uni-directionally along MTs. The tubulin/MT system therefore represents an extremely important and basic system to study the conversion of chemical energy from ATP hydrolysis into mechanical work. Understanding these fundamental processes in molecular detail is very important and of great interest to the general scientific community. The PI and his one of his co-worker rank as the world-leading experts in the elucidation of structural mechanisms influencing the tubulin polymerisation/depolymerisation cycle. In addition, the group started in recent years to also determine the structures of tubulin in complex with MAPs and has made extraordinary progress in this field.

Several of the manuscripts published in recent years are outstanding in their impact. Among these are, for example, the determination of the crystal structures of the tubulin heterodimer in complex with antimitotic inhibitors used in the clinic and their impact in the elucidation of the polymerisation/depolymerisation cycle, to higher and higher resolution over the last years. Equally important was the recent determination of the tubulin – kinesin complex, which however has not been published yet.

Since tubulin and its MAPS play such a fundamental role in the cytoskeleton system, new fundamental revelations have a very high impact not only within academia, but also in the pharmaceutical industry. Although the group mostly concentrates on the fundamental mechanism related to tubulin/MTs, their potential impact in the medical field is also immense.

The group regularly publishes in high impact factor journals thus reaching a large and general audience. In the last 5 years, this involved manuscripts in for example Nat Struc Mol Biol, PNAS, EMBO Rep and medium high impact factor journals such as J Mol Biol and J Biol Chem.

Team's academic reputation

This small team is internationally known for its structural and biochemical work on tubulin alone and in complex with MAPs or drugs used in the clinic. Many groups in Europe and the US have tried over 10 to 15 years to crystallise tubulin and determine its crystal structure, most of them with significant larger resources and man-power, but did not succeed.

The team leader and his coworker have consequently built on their previous success and are driving this field ahead.

They have a small but important set of predominantly international collaborations indicating the high quality of the project. Both are regularly invited to French and International meetings.

Involvement in training through research

The team leader and his coworkers supervised 4 PhDs and 4 Master students.

Strategy and five-year plan

The project will maintain its originality because it continues to answer interesting fundamental questions in cytoskeleton research. This is challenging and therefore risky research but so far the group has succeeded by means of a careful but innovative and focused approach. The project is a continuation of previous research carried out by the group but is feasible and is consistent with generation of new, very interesting results on a reasonable time scale.

Although the PI is predominantly interested in the fundamental aspects of the tubulin/MT system, his work has considerable impact on applied/medical research and the pharmaceutical sector. Several tubulin-targeting inhibitors are in clinical use such as taxanes (taxol, taxotere) and vinca alkaloids (vincristine, vinblastine) and these anti-cancer drugs have been developed in the absence of any structural data. The elucidation of the tubulin crystal structure (together with EM data from a laboratory in Berkeley, USA) had a profound impact on the understanding of these drugs on the molecular level. Last but not least, the high-resolution tubulin structure will allow developing future improved tubulin targeting drugs by applying structure-based drug design.

Due to the dual fundamental and applied aspects of tubulin research, the project is likely to attract partnerships not only within the academic sector, but also with pharmaceutical companies. Within I2BC several groups in structural, cell and genome biology have an interested in cytoskeleton with whom synergies will hopefully develop.

Conclusions

- **Strengths and Opportunities :**

This is a highly interesting and successful project that has been going on for a number of years now and that promises to continue to have high impact in fundamental research on cytoskeleton. Besides its fundamental interest, there is the possibility that this project will open new opportunities for structure-based drug development involving tubulin as a target for drug development in cancer chemotherapy.

- **Weaknesses and Threats :**

The project could continue to have a high impact over the next 5 to 10 years. Depending on the retirement plans of the team leader, a potential successor needs to be identified and gradually take over grant applications and more responsibility for strategy.

- **Recommendations:**

Highly interesting and competitive project with significant current and future potential. If possible, the group should seek more extended support for this project so that it can continue.

Team

MOLECULAR PHOTOPHYSICS AND CATALYSIS

Name of team leader:

Mr Winfried LEIBL

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	4	4
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**10**	**8**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

Assessment of scientific quality and outputs

This was a large and disparate group although departures mean it will be less so.

The work on artificial photosynthesis and hydrogenases is one that the researchers have been in from the start, and is currently a very topical, highly competitive and active area. The research in this area by this group is a real success story. One problem with this area is that there are a number of groups who prioritize the rapid publication of rather phenomenological data simply reporting fast rates of catalysis and turnover. In contrast, the work carried out by this group is thorough and methodical, seeking to obtain a mechanistic understanding of the molecules they develop. As a result they are sometimes scooped or their molecules exploited, because they want to understand their systems and that takes time. The molecules designed and synthesized by these researchers are at least as interesting and promising as those produced by groups ten times the size and with ten times the resources. Their list of publications is impressive and the rate of publication has increased in the last few years with 41 publications during the period under review including 27 where team members are first and/or last authors.

The work on DNA photolyases and cryptochromes is of very high impact and recognition internationally, and has resulted in publications in the very best journals, in what is a highly competitive field.

Assessment of the team's academic reputation and appeal

The team has involvement in a number of national and international networks, and a long list of collaborators. In addition to the long list of post-docs and, to a lesser extent, PhD students recruited and trained, they have also hosted a number of foreign and French PhD students for short periods. Members of the group have a reasonable number of invitations to give invited lectures at important international meetings, including post-docs. They have organised international colloquia.

They have attracted both international and national external funding to the extent that they are financially autonomous.

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

The team has two patents within this period, as well as participation in publicising scientific advances in their field to general audiences at public meetings.

Assessment of the team's organization and life

The project plan shows that this group is organised to pursue coherent and logical scientific objectives, following its formation from a number of different and less related research groups, with the main focus being on artificial photosynthesis/manganese catalysts and oxygen resistant hydrogenases, thus contributing to the bioenergy theme within the I2BC. The research on DNA photolyases and crytochrome will be pursued, but the retirement of the principal investigator in that area means that it will probably reduce over time. The combination of strong synthetic chemistry and detailed physical characterization is strength.

Assessment of the team's involvement in training through research

The group has a good record of supervising a rather small number of research students and Masters students.

Assessment of the strategy and the five-year plan

The project is original. Focusing mainly on the synthesis and characterization of molecules to catalyse artificial photosynthesis and oxygen resistant hydrogen production. The projects outlined are ambitious, but the photoanode/Mn is feasible given the track record and skills of this group, and would be a significant success in this field. The work on oxygen-resistant hydrogenase is perhaps more risky. They have already shown that they can respond to changes in their environment.

Conclusion

- **Strengths and opportunities:**

As indicated above this combination of innovative design and synthesis of molecules and strong and thorough physical characterization means this group has great potential in what is a hot area.

- **Weaknesses and threats:**

- Loss of the work on DNA photolyases and cryptochromes weakens the group overall, although it does improve the coherence of the focus of the group. They are in an extremely competitive and at times ruthless area, but it is directly within one of the major themes of the I2BC.

- They need to attend more meetings.

- **Recommendations:**

- Ideally they need support in terms of reinforcement of the group with someone younger capable of starting up synthesis of molecules within the I2BC. They also need to recruit more PhD students.

Team

OXIDATIVE STRESS AND DETOXIFICATION

Name of team leader:

Mr Pierre DORLET

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	6	6
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**9**	**8**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	8	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	4	4

Assessment of scientific quality and outputs

A rate of ca 12 publications a year is quite good for the size of the team (74 publications in peer-reviewed journals in the last 5 years, among which 28 as lead author). High quality journals have been selected for publications such as PNAS, J Phys Chem B, J Am Chem Soc, J Biol Chem, Angew Chem-Int Edit.

The quality of the research is clearly apparent from the number and quality of the publications and from the number of invited conferences presented in international meetings.

The team members use state-of-the-art techniques to decipher the molecular mechanisms of different enzymes. Methods include stopped-flow and T-mixer coupled to resonance Raman spectroscopy, advanced EPR techniques and recently new *in vitro* tools of cloning and expression, previously missing in the group.

The work on molecular modelling and docking (mostly submitted) has the high quality to consistently refer to experimental data for validation.

Assessment of the team's academic reputation and appeal

Multiple collaborations with European and American teams are further indications for high quality research and very good reputation across the academic world.

Members of the team are regularly invited to present a lecture in international conferences. The team also organized several scientific meetings in France and collaborated to the organization of an international meeting.

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

Two patents have been filed in the last 5 years.

The team organized a conference for the general public on the theme "Which future for research in Biology" and was involved from 2008 to 2013 in helping secondary school students understand jobs in sciences.

Assessment of the team's organization and life

Not applicable.

Assessment of the team's involvement in training through research

Training through research is well developed in the team. Members of the team have been regularly involved in PhD and master thesis student training. Eight PhD theses have been presented since 2008.

Six permanent members of the team are involved in teaching.

Assessment of the strategy and the five-year plan

In January 2015, the team will comprise 4 permanent researchers.

Concerning NOS and NOS-LP, the question of why similar enzymes exhibit different if not opposite biological functions is certainly a valid subject of research for the next 5 years. The team has the tools and the skills to drive a high quality research on this topic.

The part of the project on detoxification processes is interesting but less focused. The targets are the human MGST1 (expressed in L. lactis), microsomal cytochromes P450, deciphering the functionality of the human P-gp and of P-gp isoforms (Hco-Pgp 2 and 9) potentially involved in ivermectin resistant nematodes, plant CYP involved in lignin pathway or in Vinca alkaloids biosynthesis. Not only the number of targets is large, but the difficulty of the task is not fully appreciated in the project.

The nematode Pgp work might not be completed within the next 5 years. The experimental difficulties are immense and not fully recognized. Furthermore, evidences that these 2 Pgp isoforms are really involved in resistance are not strongly established.

Conclusion

- **Strengths and Opportunities:**

- The scientific output of the group is overall very good.

- The group can efficiently compete in the NOS area and in spectroscopy techniques.

- Many of the proteins studied are involved in cellular process of biomedical interest. There is a definite potential to get funding from pharmaceutical companies.

- **Weaknesses and Threats:**

- The project as a whole is oversized considering the manpower available (4 researchers in 2015) and the difficulty of the task.

- Experimental difficulties that will be encountered with membrane proteins such as CYPs and Pgp are not fully considered.

- Funding for the years to come is an issue.

- Relying too much on modelling with too little experimental data could in the future result in invalidated structures with consequences for further use of these structures (docking, drug design,..).

- **Recommendations:**

The group should focus on what it can achieve with the actual team and especially with the team that is expected to be present in 2015. There should be an in-depth thinking about the strengths of the group and a selection of only a few research topics which could have a high impact.

Team

MICROBIOLOGY AND ENZYMOLOGY STRUCTURALES

Name of team leader:

Ms Solange MORERA

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**2**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

Assessment of scientific quality and outputs

This is a small (2PIs, 2PhDs), relatively recent group with expertise in crystallography and biophysical analysis of protein-protein and protein-ligand interactions. There are two unrelated projects driven by the group, one on sensors in plant-bacteria interactions, notably GABA receptors and the second on DNA repair enzymes, e.g. bacterial endonuclease IV and human DNA glycosylase MBD4. Both projects have so far yielded interesting results that have been published in good journals including PNAS (2), JBC (2), Mol Micro. Prior to this focus, a number of other projects have also yielded good publications often in collaboration (e.g. NSMB NAR). Altogether the PI has published 25 papers over the review period of which about 14 are first or corresponding author. Three were driven by a former co-PI who has now left the group. Overall the scientific output is high and of good standard for a small group.

Assessment of the team's academic reputation and appeal

The group collaborates mainly nationally but has recently established a USA collaboration on the agrocin project. Invitations to speak abroad are about 1 per year but apparently at institutes rather than international meetings. The PI is on a number of important national review committees and has notably been president or vice-president of the Soleil Users Committee throughout the review period, including organization of the annual users meeting. The PI supervises the crystallization platform currently at LEBS and could play a useful role in the future structural biology platforms of I2BC.

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

Participation in Fête de la Science activities. Contribution to 1 patent.

Assessment of the involvement in training through research

The group has an excellent training record with 4 PhDs defended (2 in progress) but only 1 post-doc. A large number of graduate and Masters students, including from abroad, have been trained for up to 9 months in the lab.

Assessment of the five-year plan and strategy

The plan is to develop the two focusses of the group. On the sensor project, for which ANR funding has been obtained, structures of bacterial (e.g. A. tumefaciens) periplasmic binding proteins that bind opines will be determined and in collaboration, their role in quorum sensing and virulence will be investigated. The second project (for which an ANR grant has been submitted) is in collaboration with scientists at Villejuif and involves the structural study of full-length human DNA glycosylases and MBD4 with modified bases. This is a project in a more competitive field as it touches on the hot topic of the pathway of active DNA demethylation involving TET proteins. The plan is feasible and appropriate for a relatively small group. Within I2BC the group will have common interests with other groups involved in quorum sensing (BS3 and Microbiology) and with DNA repair (BS3 and Genome biology).

Conclusion

- **Strengths and opportunities:**

A small but productive group that is attractive to students.

- **Weaknesses and threats:**

Split focus on two very different projects detracts from putting major effort into more ambitious goals.

- **Recommendations:**

The group should stay focused on their highest priority projects.

Team

PROTEIN ENGINEERING AND PROTEIN MODELING

Name of team leader:

Mr Philippe MINARD

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**8**	**7**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

Assessment of scientific quality and outputs

The group works on the design of a novel protein scaffold based on a thermostable helicoidal repeat. They achieved their aim by mining Protein Data Bank for a promising fold that turned out to be common in thermophilic microorganisms and thorough analysis of sequence diversity in the corresponding protein family. They successfully identified the signatures in the sequence of the repeat architecture. They used them to design an artificial family of proteins they called alpha-repeat proteins. They were successful in experimentally producing proteins based on this design which showed to be folded as expected and very thermostable. The group thinks the alpha-repeat proteins form an attractive scaffold for molecular recognition because of its large variable, concave surface.

They further developed new methods to yield very diverse repeat libraries through a fine-tuned randomization scheme and improved shuffling process. Optimally a library of more than 109 distinct alpha-repeat proteins was generated and serves as a central resource which can be screened for specific binding activities using phage display.

The group has also developed novel approaches that use Isothermal titration calorimetry to perform direct measurements of kinetic and thermodynamic parameters of enzymatic reactions. They could achieve this using the heat absorbed or released during the reaction progress. Their group has become a regional facility and a reference site for an equipment supplier. Several collaborations were initiated like on the original enzymatic model of glucosamine-6P synthase.

In terms of publications, members of the group have about 40 publications and reviews (source Web of Science) for the period 2008/2013 in good journals such as PNAS, BBRC, Chem Bio Chem, PLoS Biol, J Mol Biol, Phys Chem Chem Phys, Biophys J.

Assessment of the team's academic reputation and appeal

The group has several collaborators in France but few collaborations at the international level. They are participating in three ANR projects.

One of the members is the director of IBBMC. Other members were active in the thematic group Protein directed evolution (2008-2012). A member of the team is one of the initiators of the scientific survey and technology analysis group focused on bio-inspired nano-construction that was supported by OMNT.

Members of the group were invited to give several lectures in France and abroad.

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

The group has a longstanding collaboration with a major biotech company. They have also recently contracted with a biotech start-up company interested in co-development of proprietary scaffold libraries.

Members of the group also have set up a 3-days training programme in microcalorimetry for the industry at national level.

A member is also providing consulting services to pharmaceutical and biotech companies.

Assessment of the team's involvement in training through research

The group has been active in training graduate students: a total of 3 PhD students, 6 Master students and couple other undergraduate students were or are being trained in the group. Besides, members are involved in teaching in various Master degrees courses and have served on board of jury of more than 40 PhD/HDR candidates.

Assessment of the strategy and the five-year plan

Consistently with their research past results, the project of the group mainly focuses on potential applications of alpha-repeat proteins in five different areas:

- finding alpha-repeats proteins for challenging targets like binders for the conformational states of a protein;

- use of alpha-reps to complex proteins that are impossible to crystallize in their free form and henceforth facilitate their crystallization;

- take advantage of the small size and fold ability of alpha-reps binders to conduct inside the cells protein interference experiments that are otherwise difficult to achieve with most antibodies;

- use of alpha-repeat proteins as tools for biomarker imaging namely tumor associated molecular targets;

- on a more prospective ground, to select proteins interacting specifically with different isotropic materials and surfaces to confer them morphosynthetic activity.

The overall plan looks very original and ambitious with good potential outlook both from a basic research perspective as well as from a biotechnological perspective.

Conclusion

- **Strengths and Opportunities:**

- Very original protein scaffold.

- Excellent scientific output.

- Very good outlook in terms of applications.

- Their scaffold should become a resource in the institute for structural biology and cell biology.

- Collaborations with industry.

- **Weaknesses and Threats:**

- Collaborations at international level.

- Inappropriate support and funding.

- **Recommendations:**

- The team needs to assess the feasibility of some aspects of the future plan namely the ideas for protein interference experiments inside cells. In that respect, they are encouraged to look for possible synergy with teams in the Cell Biology Department of I2BC.

- Their scaffold should become a resource in the Institute for structural biology and cell biology.

Team

LABORATORY OF MEMBRANE PROTEINS AND MEMBRANE SYSTEMS

Name of team leader:

Mr Francis HARAUX

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions	8	9
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**14**	**15**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	5	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	8	8

Assessment of scientific quality and outputs

The quality of the research is clearly apparent from the number and quality of the publications (43 publications in peer-reviewed journals). A rate of ca 8 publications a year is good for the size of the team. High quality journals have been selected for publications such as PNAS, J Am Chem Soc, J Biol Chem, PLoS One, Nature Protocols.

The team members use state-of-the-art techniques to decipher the molecular mechanisms of different ATPases.

The team operated a welcome shift from SERCA to other related ATPases such as SERCA-related Ca2+ pump from the malaria pathogen agent Plasmodium falciparum and P4-type ATPases family involved in maintaining transbilayer phospholipid asymmetry in cell membranes. These are new developments for which the team has an excellent expertise, probably among the best in the world.

The team already discovered that a purified P4-ATPase/Cdc50 protein complex relies on direct and specific interactions between transporter and subunit. Interestingly Cdc50 proteins play a direct role in the reaction cycle of P4-ATPases, analogous to the role of ß-subunits in P2-types ATPases. This is an important discovery in the emerging field of lipid transport mechanisms.

The work on insertion of hMRP1 transmembrane segments in micelles is less innovative but could shed some light on the rules governing membrane protein insertion in membranes.

It is very good that the same team simultaneously investigates the structure of proteins and their localization in live cells.

The results obtained on regulation of respiratory complexes and ATP synthase in mitochondria are promising but need more development.

Assessment of the team's academic reputation and appeal

The team is internationally recognized for its work on the Ca2+-ATPase, in particular for the production and characterization of mutants. Yet, even though many high-resolution structures have been obtained of different conformations of the protein, the long-range conformational reorganizations responsible for the coupling between transport and ATP hydrolysis remain to be understood. The laboratory is therefore still improving our structural/functional knowledge of this enzyme.

Multiple collaborations with European and American teams are further indication for high quality and reputation across the academic world.

Members of the team are regularly invited to present lectures in international conferences. The team also contributes to a large body of assessment work within France and outside.

Team members participated in the organization of the French Group of Bioenergetics in 2011 and 2013; of annual meetings and workshops of GDR 3159 “meet Ochondrie”, of GDR 3334 meetings “Assemblages supramoléculaires et membranes biologiques” and of the First Annual Symposium on Molecular Imaging, November 2008, Chiang Mai University, Thailand.

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

Four patents have been filed in the last 5 years.

The team leader gave an interview published in *Sciences et Avenir* 2010.

Assessment of the team's involvement in training through research

The team supervised 11 PhD (7 defended) in the last 5 years, 6 M2, 2 M1, 2L3, 1 L1 and 2 BTS.

Assessment of the strategy and the five-year plan

The project was essentially presented orally. As presented, it contains interesting perspectives. A selection among the most promising topics should be made by the team.

A clear plan for the future of the team should be designed. Priorities should be better defined.

Members of the team have numerous skills and qualities which could be better used for the most promising subjects of research.

Conclusion

- **Strengths and Opportunities:**

The scientific output of the group is overall very good. The group has an outstanding background in membrane proteins and ATPases in particular, with excellent collaborations worldwide. Expertise and tools to carry on an excellent work on membrane proteins are present. Some of the topics are very original, in particular the investigation of an ATPase involved in lipid transport.

The group has excellent international collaborations and could trigger applications at the European level or collaborative applications with US researchers. Every individual researcher should be encouraged to apply for money. Work on the malarial agent ATPase is another obvious possibility to get industry money.

- **Weaknesses and Threats:**

The group gathers researchers interested in quite different topics. Strong management with a focussed view on the future is insufficiently developed.

There is little money for the size of the group for the next two years. A more aggressive strategy to obtain money is encouraged. Too diversified thematic of research could weaken the scientific quality on the long term. Some topics such as “insertion of hMRP1 transmembrane segments in micelles” are with little future and could be dropped. There is a risk of losing essential expertise and relevance of the results if too much emphasis is put on experimental peptide work and on *in silico* modelling.

- **Recommendations:**

A clear plan for the future of the team should be designed and priorities should be clearly defined.

● Department of Genome Biology

Overall assessment of the department

The department of Genome Biology consists of 28 research groups, covering a wide but very coherent range of topics in the field of genome biology (chromosome organization, replication, segregation, programmed genome rearrangements, DNA repair, recombination, meiosis, gene expression and regulation, transcription, coding and non-coding RNAs, translation, post-translational modifications, function, assembly of macromolecular complexes). The department includes a large number of excellent teams, with strong international visibility. The vast majority of the teams are doing extremely solid and interesting work. The creation of the department was an opportunity to fuse some teams that shared similar interests (4 teams were merged into 2 new teams). These reorganizations were perfectly judicious. However there remain a few very small teams that tend to have difficulties in obtaining funding and attracting students. Besides, several teams are facing the problem of aging of their group leaders (5 teams with senior scientists over 60). The involvement of the department of Genome Biology in training through research is very good. The creation of the Institute, bringing together teams from CNRS and CEA with teams of the Paris-Sud university will further facilitate the recruitment of students. The interviews of the different teams clearly demonstrated that the creation of the department was an excellent opportunity to induce new synergies, both in terms of scientific thematics and in terms of sharing of techniques and know-how. Overall, the new department is very strong, and appears as a flagship in the field of genome biology in France.

Strengths and opportunities related to the context

- Many excellent teams.
- Coherence and complementarity of the projects.
- New synergies induced by the creation of the department.
- Complementarities in term of techniques and know-how (ribosome profiling, ChipSeq, single molecule fret, single cell analysis, protein biochemistry, genetics, proteomics, bioinformatics…).
- Coherent set of technical platforms.
- Good critical mass.
- Judicious fusion of 4 teams into 2 teams, and gathering of bioinformaticians who were previously dispersed.
- Arrival of one new team + 3 upcoming professor positions.
- For the vast majority of team leaders interviewed, the creation of the department of Genome Biology is considered very positive in term of scientific interactions.

Weaknesses and threats related to the context

- Several teams are facing the problem of aging of their group leader (retirement of 5 prestigious senior scientists before or at the end of the next term).
- Only 3 bioinformatics research groups, among which one whose PI will retire within 3 years.
- Several very small teams.
- Limited capacity to attract new teams (except with university positions).

Recommendations

- Set up a strategy for attracting new teams (young or confirmed scientists), notably in bioinformatics.
- Anticipate the demographic transition of group leaders and favour the development of the excellent young teams already in the department.

Team

EVOLUTION AND MAINTENANCE OF CIRCULAR CHROMOSOMES

Name of team leader:

Mr François-Xavier BARRE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	3
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**7**	**6**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

Research in this team is centered around the roles of Xer recombinases (1) in the integration of phage DNA into host genomes and (2) in the resolution of chromosome dimers and its coordination with bacterial cell division via the interaction with the DNA motor protein FtsK. DNA recombination by Xer as well as DNA translocation by FtsK are well studied processes and their action is understood in principle. Nevertheless, several important and challenging mechanistic questions remained to be resolved. The work by this team in the last years indicates how FtsK might protect unsegregated chromosomes from scission by the division machinery representing a new cell cycle checkpoint in bacteria. The findings also raise serious doubts on a widely accepted model of how FtsK is operating as a DNA pump with regard to membrane at the division septum. As a second line of investigation, the laboratory is studying the process of exploitation of the host recombination system by integrative mobile elements i.e. phages in Vibrio cholerae. The work has revealed a detailed reaction mechanism for Xer recombination of phage and host DNA and has implicated another host cell factor in this process. These findings are relevant in a wider context since the pathogenicity of many Vibrio strains relies on the integration of phage genomes into the chromosome.

The team has been very productive in the reporting period. It has published in total 12 papers including two invited reviews. Nine papers have both first and senior authors from the group and 5 of these reports are published in high-profile research journals (2 in EMBO J, 2 in PNAS and 1 in PLoS Genetics). In general, the work is executed to a very high standard. The results are significant and well received in the respective field.

Assessment of the unit's academic reputation and appeal

This team is among the leading teams in the respective research field and enjoys highest reputation at the international level. The team leader was frequently (10x) invited to present the team's findings at international meetings and conferences. Two other team members were also invited to give lectures at meetings. The team leader is a member of a scientific committee organizing a joint American-European workshop on site-specific recombination, transposition and DNA dynamics. He will serve as the main organizer of the workshop in 2014. He also participates to several national committees and juries. The team has recently won a prestigious and well-funded starting grant by the European Research Council and several additional national awards. Two foreign postdocs were recruited to the team recently and several members have excellent publication records indicating the high standard of national and international researchers in the team.

Assessment of the unit's involvement in training through research

Two PhD students have defended their thesis in the time of the reporting period. Both of them have one first author publication in a good journal (PLoS Genetics, NAR). Currently, there are two graduate students and four postdocs in the laboratory.

Assessment of the strategy and the five-year plan

The proposed research is built on two independent lines of investigation both performed in Vibrio cholerae: (1) the role of Xer recombination in the integration and excision of several different mobile genetic elements and (2) chromosome segregation and dimer resolution and their connections with cell division. The former is an extension of an existing research theme in the laboratory that will include additional types of phages, which rely on Xer recombination for integration using different molecular mechanisms. The latter approach is aiming to study the organization and segregation of chromosomes in Vibrio cholerae with a special focus on the coordination between chromosome segregation and cell division. This research line is new to the team, however considering the team's prior experience in the study of chromosome segregation and the newly gained expertise in the use of V. cholerae as model system, the risks of failure are very small. The proposed research plans appear credible and feasible. They have high potential to reveal important new insights into fundamental processes.

Conclusion

- **Strengths and opportunities:**

- The team has been very productive in the reporting period.

- Several members have been recruited to the team recently. The team now has very good size and will be able to expand the scope of its research.

- The team is well-funded.

- The planned research is exciting and feasible.

- **Weaknesses and threats:**

The team has recently introduced a new model system in the laboratory (V. cholerae), which will serve as main workhorse in the future. Although unlikely, unforeseeable matters with this model organism could affect future productivity of the team.

- **Recommendations:**

Maintain some successful research lines using E. coli as model system.

Team

ORGANIZATION OF THE BACTERIAL CHROMOSOME

Name of team leader: Mr Frédéric BOCCARD

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**5**	**6**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The research of the team focuses on revealing general principles in the organization of bacterial chromosomes and its molecular mechanisms using *E. coli* and more recently also *Pseudomonas aeruginosa* as model systems. The foundations for this research were laid several years ago by the discovery of chromosomal macrodomains through an elaborate screen based on *in vivo* recombination efficiencies performed in this laboratory. Recent effort is directed towards understanding the molecular basis of macrodomain formation. It has yielded detailed molecular insights into Ter macrodomain structuring by uncovering a MatP protein-mediated DNA bridging mechanism and its interplay with cell cycle events such as cell division (3 separate publications in Cell, Mol Cell and EMBO J). In addition, a new player governing macrodomain organization at the left and right arm of the chromosome was discovered and characterized initially (PLoS Genetics). Furthermore, chromosome organization in *Pseudomonas aeruginosa* throughout the cell cycle was determined establishing new lines of research for future investigation (PLoS Genetics).

The group has been remarkably productive in the reporting period. The group published in total 9 papers, 8 of which have a member of the team as first and/or last author. Six of these papers were published in high-profile research journals (1 in Cell, 1 in Mol Cell, 2 in EMBO J and 2 in PLoS Genetics). The work performed by this group in general is very original and unique. It is executed to a very high standard and well accepted in the field of bacterial chromosome biology and in a wider community addressing diverse questions in bacterial cell biology.

Assessment of the team's academic reputation and appeal

This team is among the leading teams in the respective research field and enjoys highest reputation at the international level. The team leader is frequently invited to present research at leading conferences (9 international meetings including Gordon Research Conference on Chromosome Dynamics) and serves as section editor for an international review journal in microbiology (Current Opinion in Microbiology), both illustrating the highest standing of the team in the wider research community. Other members of the team also have very good scientific track records already when they join the group. They also go to international conferences and present their results.

Assessment of the team's involvement in training through research

The team has an excellent track record in raising PhD students and post-docs that continue to have successful careers in the academic community after finishing their work at this research team. The relatively small size of the team ensures outstanding quality of supervision and education. In the reporting period two students of the team have defended their PhD. Both of them have published first author papers in very good journals (Cell, PLoS Genetics). Currently, two students are pursuing their PhD within the group.

Assessment of the strategy and the five-year plan

The strategy for future research is based on both continuation of already successful projects in the laboratory and on new innovative and challenging projects. Recent work has identified two factors involved in chromosome organization in *E. coli*. The team now addresses the underlying molecular mechanism and has many of the required tools already available. The planned research thus bears relatively little risks of failure. On the other hand the team plans to expand the scope of the studies by establishing for example the chromosome conformation capture assay as a new tool for analyzing chromosome organization in a genome-wide manner (with promising preliminary results). This new technological initiative has great potential and might be instrumental also to other research groups within the Department of Genome Biology. Furthermore, a new model system (*P. aeruginosa*) is being developed to complement the investigation of chromosome organization performed in *E. coli*. Overall, the strategy seems well-balanced, feasible within the five years and likely to yield conceptually new insights into bacterial genome biology. The group also enjoys a stable and good funding situation (ANR 2005-2016).

Conclusion

- **Strength and opportunities:**

- The team has performed ground-breaking research over many years.

- The research plans are well balanced and offer exciting opportunities.

- **Weaknesses and threats:**

A possible threat to the team's continuous success is the increasing administrative duties of the team leader within the I2BC project.

- **Recommendations**

Through its excellent track record the team should qualify for European research funding schemes (e.g. ERC grant). Such funding should be considered to expand the scope of the teams's research.

Team

GENOME STABILITY IN BACTERIA

Name of team leader:

Ms Bénédicte MICHEL

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	**5**	**4**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team has been very productive in the reporting period. In total 7 papers were published by the team, 6 of which have both first and senior authors from the group and are published in general journals with high reputation.

The research is focused on the maintenance of genome stability especially during recurrent arrest of DNA replication forks. In recent years, the laboratory has defined the genetic requirements for maintaining chromosomal stability under conditions of frequent head-on collisions between DNA replication forks and the transcription apparatus at highly expressed genes. These important results show that at least one of several DNA helicases associated with the replisome are required to clear RNA polymerase from DNA likely via the removal of R loops (EMBO J, PLoS Genetics). Furthermore, it was demonstrated that replication fork reversal occurs after head-on collisions and that fork reversal triggers the action of replicative helicases to clear the path of the replication fork (PLoS Genetics). The team also decided to complement their genetic studies by the establishment of single molecule microscopy to be able to trace molecular events at arrested replication forks in living cells. However, due to the alleged fraud by a single member of the team, the corresponding publication will be retracted by the team leader. With the exception of this isolated case, the research studies by the team are performed at a very high scientific standard. The work is well appreciated by the respective research field and in general enjoys high appeal in a broader sense because replication-transcription collisions are likely threatening genome stability in all organisms.

Assessment of the team's academic reputation and appeal

The team gained highest academic reputation both nationally and internationally and is leading in the respective research field internationally. The team leader serves as editor at leading international journals in general biology and microbiology (PLoS Biology, Mol Micro) and is member of several national scientific committees. The team leader is frequently (14) invited to present research at top international meetings and conferences, all of which demonstrates the high level of reputation within the research field and the appeal of the research to a wider research community.

Assessment of the team's involvement in training through research

The team is very active in supervising graduate and undergraduate students in the laboratory. Three students have successfully defended their thesis within the reporting period. All three students have at least one first author publication in a good journal (PLOS Genetics, Mol Micro, J Bact.), which is excellent.

Assessment of the strategy and the five-year plan

The research strategy detailed in the written report was aimed at expanding the use of single-molecule microscopy to study the dynamics of arrested replication forks caused by a variety of different obstructions and lesions on the DNA. These include nicks in double stranded DNA, protein obstacles and loss of helicase activity. Due to the uncertainty regarding the usability of the single-molecule approach (due to experimental limitations) additional lines of research have been developed between the written and oral report. To find new factors required for successful repair of DNA damage linked to DNA replication-transcription conflicts the team will perform a synthetic lethal screen in strains carrying an inverted rRNA locus. Furthermore, the biological effects of the loss of the HolD subunit of DNA polymerase III will be investigated using a comprehensive suppressor screen. Preliminary experiments have revealed several new classes of suppressors that will be identified and characterized in the near future. The research strategy is elaborate despite the challenging situation. The five-year plan has a sufficiently broad scope and high potential to yield significant new insights.

Conclusion

- **Strength and opportunities:**

- The team is very productive, especially when considering its relatively small size.

- The work is appealing and relevant to a larger community and highly visible.

- Several new members have been recruited recently to the team.

- **Weaknesses and threats:**

The upcoming retraction of a paper by the team poses a risk to its academic reputation. Since the problem allegedly resulted from misconduct by a single author - who has since left the group and resigned from his CNRS position - any long-term threat to the reputation of the team will likely be very limited. In addition, the appropriate and swift response to the discovery of the problem by the remaining authors demonstrates their scientific integrity and will likely mitigate potential negative impact brought about by this incident.

- **Recommendation:**

Proceed as quickly as possible to close the case of alleged scientific misconduct so that all focus can be directed towards the new research projects.

Team

DNA REPLICATION DYNAMICS IN HIGHER EUCARYOTES

Name of team leader:

Ms Kathrin MARHEINEKE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**2**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team has been created almost three years ago and aims at understanding the determinants of the spatio temporal replication program during early development using Xenopus laevis as a model system. Indeed, Xenopus provides a unique opportunity to study the replication program during the transition between rapid replication mode without transcription and the slower replication phase during embryogenesis. The PI has a good record in this field, having studied previously the replication program in cycling cell extracts without transcription and showed the existence of large replication domains. In the considered period before the creation of the team, the PI produced five original publications in total, including 4 major contributions in Biotechniques (2008), PLoS ONE (2008), Nucleic Acids Research (2008) and J Cell Science (2009), respectively. Since the team was established, there are no publication but the group has obtained results regarding the quick change of replication program (increase of origin spacing and decrease of fork densities) at the onset of differentiation. The team is currently investigating which factors are responsible for these changes. They are also studying the role of checkpoint proteins in fork speed during normal S phase, similar to what was shown in mammalian cells. They show that this protein is also inhibiting late origins, probably by sensing a limiting amount of replication factors. Finally, they are investigating the link between checkpoint activation and the changes in replication progression they observed during development.

Assessment of the team's academic reputation and appeal

Up to now the team has not displayed a strong attractiveness (no invitation to international conferences, no participation to editorial boards, no post-doc, no on-going international collaboration). However the team is still young (created in Sept. 2010) so it is too early to draw any conclusion The team should become more visible when its first papers will be published

Assessment of the team's involvement in training through research

Since the establishment of her team, the PI has supervised two Master 2 and four Master 1 students.

The team leader has been part of four thesis juries, and has taught in two Master 1 modules.

Assessment of the strategy and the five-year plan

The project is divided into three parts. Two of them rely on preliminary results and aim at (1) identifying the factors that slow down replication during Xenopus development and (2) the mechanism of checkpoint activation upon replication fork stalling during development. The third project aims at establishing genome-wide the replication program and chromatin modification maps in embryonic cells and in a differentiated cell line in order to establish correlations between them. A collaboration with the genome analysis group from the same unit will allow to perform the bioinformatics analyses. The proposed strategy seems feasible but, apart from the third project, it is not clear that it will lead to ground-breaking results compared to what is already known in other systems.

Conclusion

- **Strengths and opportunities:**

- Original subject and good expertise. A PhD student has obtained a fellowship for three years, this is the occasion to really make the project move forward.

- Proximity within the department to group experts in the genome-wide analysis of replication origins.

- **Weaknesses and threats :**

- The committee is worried about the very limited size of the team after three years of existence and the lack of secured funding.

- Competition is high in this field and the team needs to find its niche as compared to other experimental - systems.

- **Recommendations :**

- Quickly finalize a publication taking advantage of the opportunity of having a PhD student. This will be essential to get more competitive funding, and to maintain a functional team.

- The committee felt that the project on the genome-wide identification of replication origins is the most novel and promising and suggests to privilege this direction and get the best out of the collaboration with the genome analysis group who also developed pioneer approaches for the characterization of replication origins in the genome. Given the small size and little funding of the team, a fusion with another group working on similar topics may increase efficiency of research and should be considered.

Team

DNA BIOINFORMATICS AND BIOPHYSICS

Name of team leader:

Ms Marie-Claude MARSOLIER-KERGOAT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**2**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The permanent staff of the team consists of only 2 people. They are theoreticians with interests and expertise in the mathematical modeling of DNA replication processes. There were no other scientists in the team during the 2008-2013 reporting period, but a PhD student was recently recruited (10/2013) to join the team.

A technician left the group in 9/2010 and was not replaced. This technician carried out molecular biology experiments on *Saccharomyces cerevisiae*, and this lab aspect of the team's research has been discontinued since 2010.

During the past 5 years the team studied (1) the biophysics of DNA replication in eukaryotes, modeling the spatio-temporal program of replication origin firing in several species, by collaborations with experimental groups; (2) models of the effects of meiotic recombination and DNA replication on base composition in yeast genomes, with validation of the models by comparison to existing genome sequence data; as well as (3) the discontinued experimental research lines on *S. cerevisiae* DNA repair and ribonucleotide reductase genes.

The team published 18 papers during the 2008-2013 reporting period, of which 12 are primary publications, i.e. members from the DNA Bioinformatics and Biophysics team are first or last author. Most of these articles are in middle-ranking journals such as PLoS One (4 papers). The most impressive primary publications from the team are in Mol Biol Evol, Nucleic Acids Research and Molecular and Cellular Proteomics (one paper in each of these journals).

Several of the collaborative papers are in more prestigious journals (Nature Protocols; PLoS Computational Biology) but the team members are not senior or first authors on any of these papers. In view of the small size of the team and the lack (until recently) of PhD students and postdocs, the approach of collaborating with other groups seems to be a sensible strategy.

Assessment of the team's academic reputation and appeal

The international profile of the team is low. Apart from one 'invited speaker' presentation at an American Physical Society meeting in 2011, all other presentations listed are non-invited and within France.

No editorial board appointments or professional society activities are listed.

The team's external grant funding has come from collaborations (ANR and EDF consortia in which the team is a participant). They have no external grants where a team member is the principal investigator.

Assessment of the team's involvement in training through research

There were no PhD students in the team during the assessment period. A PhD student was recruited on 10/2013.

Three masters students were supervised during the reporting period but none of these students became authors of published papers.

Assessment of the strategy and the five-year plan

The documents do not include an overall vision for the future of this team and its proposed development.

The description of future research plans (section 2.4) consists of two independent personal plans. One team member plans to continue to work through collaborations with experimental groups, incorporating experimental data on chromatin compaction and metabolic changes into his biophysical models of DNA replication. The other team member plans to continue studying base composition in yeast genomes with collaborations with two external laboratories. The bioinformatics projects seem rather short-term and will not require 5 years to execute.

Conclusion

- **Strengths and opportunities:**

- Extensive individual expertise in the field of DNA replication.

- The creation of I2BC brings opportunities to deepen existing collaborations with I2BC colleagues, and to develop new collaborations with other colleagues and expand into new areas.

- Several I2BC molecular biology teams work on DNA replication. They may benefit from their support in aspects of theory or bioinformatics analysis.

- Collaboration with larger teams in I2BC would provide access to students.

- **Weaknesses and threats:**

- Heterogeneity of research topics within the team; lack of critical mass in any one area.

- Low profile, lack of external funding, lack of PhD students, postdocs, technicians.

- Small size of the group.

- **Recommendations:**

- I2BC has several small teams working on aspects of DNA replication, each with its own strengths, but the overall organizational structure needs to be rationalized.

- The justification for retaining the DNA Bioinformatics and Biophysics team as a separate entity within the Department of Genome Biology is not clear to an external reader of the documentation provided. The team consists of a biophysicist and a bioinformatician who seem to work quite independently of each other (only 3 of the 18 papers include both team members as coauthors). The team clearly has difficulty attracting students and raising funds, problems that could potentially be alleviated by merging with larger teams.

Team GENOME ANALYSIS

Name of team leader: Ms Linda SPERLING

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**7**	**5**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The Genome Analysis team (3 permanent researchers, 2 engineers) is highly active and commands an excellent international reputation. The PI is established as a world leader in *Paramecium* genetics and genomics, and her work in this amazing and challenging system has led to insights of great value in the broader fields of epigenetics and genome rearrangement. She will be one of the stars of I2BC. The DNA replication sub-team also has a strong international profile, and it is clear that the entire Genome Analysis team is working well under the PI direction. The team is making substantial progress in their two major research areas – organization, function and evolution of *Paramecium* genomes, and replication of eukaryotic genomes.

Members of the team were authors of 31 peer-reviewed journal articles during the 2008-2013 reporting period, of which 9 articles are primary publications from the team (first or last authorship). These primary publications include 1 in Nature, 2 in Genome Research and 1 in PLoS Genetics. The non-primary publications include 2 more Nature papers (collaborations with groups at Ecole Normale Supérieure-Ulm and Pasteur Institute). This is an excellent scientific production.

Assessment of the team's academic reputation and appeal

The team is very involved in international and French national projects, particularly through its leadership position in *Paramecium* genomics. The PI is member of several steering committees and advisory boards, including Genoscope projects. She is an editor of the leading specialist journal Protist. Other members of the team have won awards including a CNRS Cristal award and a Prize AXA. The PI frequently received invitations to speak at international meetings.

The team has 5 permanent staff and (currently) 1 postdoc, 1 PhD student and 1 CDD (short term contract). They have no apparent difficulty recruiting high-quality research staff. The team has been consistently funded by the ANR (5 grants listed).

Assessment of the team's involvement in training through research

No PhD students graduated from the team during the assessment period. There is 1 current PhD student (recruited 10/2011). The PI is a director of EU COST and national GDRE PhD training projects. Two other team members were organizers/teachers of an AVIESAN bioinformatics training school in 2013.

Assessment of the strategy and the five-year plan

The 5-year plans for future projects are well thought-out and exciting. For Paramecium, they include an international consortium to sequence additional species to test hypotheses about speciation mechanisms; functional studies on IES recognition; and development of the *Paramecium* DB database. For the replication group they include collaboration (with ENS-Ulm) on new technology to map Okazaki fragments, and to study links between replication fork stalling and chromosome rearrangement. These projects appear to have been planned with some care, they are feasible, and they promise to advance the state-of-the-art in their respective fields.

The main threat to the team comes from the age of the PIs. The team leader will probably retire in 3 years and another team member is already emeritus. The team has responsibility for direction of the ImaGif high-throughput sequencing platform, so I2BC needs to plan carefully for the future of this central piece of infrastructure.

Conclusion

- **Strengths and opportunities:**

- World leader in Paramecium community.

- Strong competitive advantage in mammalian DNA replication mapping (Okazaki fragment technology).

- Excellent publications.

- Excellent collaborations.

- **Weaknesses and threats:**

- Age of the team leaders.

- The future of the team after the retirement of its PI is unclear.

- **Recommendations:**

The expertise of this team in genome bioinformatics is very important for the institute. The retirement of its PI may lead to the dissolution of the group. The I2BC should anticipate this reorganization and do its best to maintain a group with this strong bioinformatics expertise. In particular, the I2BC needs to plan for the future of the sequencing facility, which is currently led by an emeritus researcher. This cannot continue indefinitely so a transition of the facility to a younger PI needs to be planned.

Team

PROGRAMMED GENOME REARRANGEMENTS

Name of team leader:

Ms Mireille BETERMIER

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**5**	**4**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team is a recognized leader in the field of programmed genome rearrangements in the ciliate Paramecium tetrauralia. They focus more particularly on the mechanism of precise elimination of the IES (Internal Eliminated Sequences) from the germline micronucleus genome during sexual development.

The team has performed ground-breaking research in the last five years that have moved the field forward. Among these, the two most striking contributions are the first identification of a domesticated transposase, PiggyMac (Pgm), that cleaves at the IES boundaries and induces their elimination of the MIC genome, and the finding that the NHEJ complex mediates the precise rejoining of the IES, providing the new concept that NHEJ can be very precise, the IES often occurring within gene sequences. Another major step for the group's research has been the genome-wide identification of IES from sequencing the macronucleus genome from Pgm mutants, in a fruitful collaboration with the Genome Analysis group of the same unit. The size of IES shows a periodicity that suggests that DNA looping must occur during the cleavage reaction, and opens perspectives on the mechanism of cleavage by the Pgm protein.

The team has been very productive over the considered period. They list a total of twelve publications, with five original research articles as senior author, comprising publications in very high impact journals (one in Genes & Dev, two in PloS Genetics, one in NAR and one in Eukaryotic Cell). They have also contributed an invited review.

Assessment of the team's academic reputation and appeal

The PI is very active in the DNA repair and genome rearrangements communities. She co-organized a national meeting on DNA, and is a member of two European networks. The team has good international and national collaborations, for which it obtained specific grants.

The PI has been able to assemble a very productive team, and in particular to recruit a candidate who got a CNRS position. There is a good balance between permanent and non-permanent scientists, which ensures some stability for the forthcoming years.

The PI was invited regularly to speak in institutes, and to national and international conferences including major meetings (three FASEB conferences), which attests her international visibility.

The team members are also remarkably involved in disseminating the team's research with many oral communications and posters presented at conferences.

Finally, the PI is regularly solicited as a reviewer by several journals and served as an associate editor for PloS Genetics.

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

The team is very active in promoting their research activities to the public and participated to several events such as Science Festivals and presentations of their research in schools.

Assessment of the team's involvement in training through research

During the considered period, 2 PhD and 7 Master students have been supervised. As mentioned above, students from the team have regularly the occasion to present their research orally or as posters at scientific reunions/conferences as part of their research training. The PhD students who defended have first author papers published or submitted.

Several members of the team have teaching duties, and the PI regularly teaches in several master programs and was a member of several thesis juries.

Assessment of the strategy and the five-year plan

In the coming years, the team will be developing several aspects regarding the mechanism of IES elimination following their recent published and unpublished observations. The projects are very well conceived and based on several key preliminary results and all have high potential. The first topic is on the proteins that may assist the PiggyMac protein in performing cleavage. They have already very interesting results regarding the interacting partners of Pgm and have identified another family of genes that are good candidates for participating in the cleavage reaction. The second topic is about chromatin determinants of IES recognition and proposes to combine genome-wide and biochemical approaches, for which the team has already established collaborations with other groups and gathered interesting preliminary observations. Finally, the third topic addresses further the mechanism of DSB repair to excise IES. Unpublished observations open new perspectives on the properties of the programmed DNA cleavage of IES and how this reaction may be coupled with downstream repair events.

As a whole, the team is proposing an original and ambitious research plan and there is a good balance between the size of the team and the number of projects to be completed.

Conclusion

- **Strengths and opportunities:**

The team has been very productive in the last years and has imposed itself as a leader in the programmed genome rearrangement field. They have gathered several key observations that guarantee the success of their future projects. The team plays an active role in the dissemination of their research and is well integrated in the international community.

- **Weaknesses and threats**

None identified

- **Recommendations**

The team should recruit postdocs and PhD students to keep a critical number of people.

Team

SEXUAL DIFFERENTIATION IN FUNGI AND MEIOSIS

Name of team leader:

Mr Robert DEBUCHY

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	1
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	**8**	**5**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The current group is issued from the fusion of two teams who were studying mating-type loci in filamentous fungi and meiosis in *Sordaria macrospora*, respectively. In the project proposed, only the meiosis theme will be continued.

The group working on mating-type showed a reasonably productive research during the last five years [(11 papers including four senior author papers: one in the high profile journal PloS Genetics, two in PloS ONE and one in BMC Research notes] especially considering the small size of the team. In particular, they identified by microarray analyses the targets of the *P. anserina* mating-type transcription factors, and identified a conserved family of HMG-box genes controlling the mating type genes. Finally they elucidated the origin of the alpha-1 domain mating type transcription factor, related to the HMG-box domains. This allows a complete understanding of the mating-type evolution in fungi.

The group studying meiosis was led until now by the PI who developed the model of *Sordaria* for studying meiosis. She is now an emeritus but is still very active in the lab, and the subject will be continued in the proposed project. Thanks to the unique expertise of the team in the genetics and cytological approaches of Sordaria meiosis and the unique advantages of this model, the group has made highly significant contributions to the field of chromosome behavior in meiosis, all published as senior author in major journals (three articles in Genes and Dev, Cell and PNAS). Their major findings relate to the relations between recombination and homologous chromosomes pairing. They made the striking observation that inter-homolog interactions are evenly spaced, suggesting early interference mechanisms between recombination events. They also showed that at the sites of crossing-over, local axis destabilization is observed. Finally, they uncover a new function of meiotic recombination proteins in resolving the entanglements between chromosomes that occur in the process of pairing.

They have recently identified new synaptonemal complex components as well as cytological markers of crossover sites, and have characterized a mutant in which haploid meiosis proceeds, and find that strikingly, crossover interference exists even in the absence of a homolog (unpublished work).

As a whole, the productivity and quality of research of this team is remarkable, especially for the meiosis part.

Assessment of the team's academic reputation and appeal

The PI of the meiosis group has an international reputation in the meiotic chromosome field. She is invited to major international conferences (EMBO, Gordon conference). She has a longstanding collaborative funding from the NIH with a professor at Harvard University who is highly productive in terms of new concepts and publications. They have written together several seminal invited reviews on the field. The meiosis group has also attracted several international postdocs. The PI of the mating type group has a more modest reputation but he and the members of his group present their results regularly at specialized conferences. This group has also collaborated with several international groups and has coordinated an ANR grant from 2006 to 2009.

Assessment of the team's involvement in training through research

During the considered period, both groups have trained several students (8 Master 2 and a professional Master diploma). Only one PhD student was supervised, on the mating type topic, and published a senior author paper. This low number of PhD students is partly explained by the fact that the PI of the meiosis group is an emeritus and thus was not allowed to supervise a student.

Assessment of the strategy and the five-year plan

In the coming years, the team will focus only on meiosis. They will develop various aspects of their main research theme on the process of chromosome pairing and recombination. The fruitful collaboration with the lab at Harvard University will be pursued. The project proposes an ambitious and innovative program that will use new approaches such as live-cell imaging of meiocytes, that they have recently implemented for Sordaria, and tagging of individual chromosomes with fluorescent arrays. They will further characterize Hei10, a new protein marking the sites of crossing-over, and characterize several asynaptic mutants from a previous screen, by whole genome sequencing. A new topic on the potential involvement of non-coding RNAs will also be undertaken.

This five-year plan is highly promising to yield breakthrough results in the field of meiosis. Implementing new technologies such as live-cell imaging and the availability of whole genome sequencing for mutants characterization for studying Sordaria meiosis this team with a unique opportunity to perform original and important research.

Keeping alive the *Sordaria* model for the study of meiosis after the former PI became emeritus was important and it is good that this challenge has been filled. However the committee was concerned by the fact that the PI chosen to lead the team is the one who was previously working on mating type switching and has no expertise in meiosis. The committee feels that a better choice would be the assistant professor who joined the meiosis group three years ago and has already been productive on the subject (one PNAS as first author, one paper as senior author in revision). This would be fully deserved and would allow better visibility of this researcher in the scientific community.

Conclusion

- **Strengths and opportunities:**

- The research on meiosis performed using Sordaria is original and of high quality and continuously yields high impact publications.

- The work is highly visible internationally.

- The long-term collaboration with the Harvard group is definitely a plus.

- **Weaknesses and threats**

- The choice of the PI to lead the team is not in agreement with the reality and may be detrimental to the visibility of the team and the success of grant applications.

- The assistant professor, who should lead the meiosis studies has a heavy load of teaching and may need to rely on experimented team members.

- This researcher does not have yet international visibility.

- **Recommendations**

- Nominate officially the assistant professor as the new PI of the team.

- Get more involved in PhD students training, and for the new PI, expose himself more to the international community by presenting his work more regularly.

Team

RADIORESISTANCE OF BACTERIA AND ARCHAEA

Name of team leader:

Mr Fabrice CONFALONIERI

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	5	5
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**11**	**10**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The proposed team is the fusion of two existing groups: one working mostly on radioresistance mechanisms and mutagenesis in *Deinococcaceae*, and the second on the genomic of *Archaea*.

The first team has been highly productive (17 papers including 12 as first or senior author, including 2 PLoS Genetics) with high impact papers generally published in good journals. In addition, they had excellent collaborations in France and outside France (1 Cell and 1 EMBO J). The international output of the team is very strong.

The second team was less productive, with 6 papers including 4 as first or senior author generally in less good journals, except for 1 Genome Biology paper in 2009. The international output of this team is moderate.

Assessment of the team's academic reputation and appeal

The team has been very good in attracting post-docs (5 post-docs) and PhD students (6), as well as visiting scientists from the US. Their work on *Deinococcaceae* is often presented at conferences. In addition, the team is coordinator in several ANR projects and overall the proposed team has been successful in getting funding for their research. They also have several productive collaborations at the national and international level.

Group members contribute to editorial works and grant reviewing at a good level (editorial board of Frontiers in Microbiology). In addition, two prizes have been given to team members.

The reputation and appeal of the *Deinococcaceae* team is very high.

Assessment of the team's organization and life

The group is composed of 9 permanent staff: 2 researchers at CNRS, 1 AI CNRS, 1 TCE CNRS, 2 PR Paris-SUD and 3 MCF Paris-SUD. The team has a relatively well-balanced organization supported by PhD students (3) and post-docs (2).

The proposed team is the reunion of two teams. The organization is coherent, since they both have interest in radioresistance in different organisms. The scientific objectives are logical and well thought, and the two groups are already working together. The team is well funded and is up to date with new genomic technics. Its integration in a Genome Biology department seems well prepared and logical.

Assessment of the team's involvement in training through research

The team is highly involved in training master students and has a very robust teaching load, with 5 PR or MCF. They are often responsible or co-responsible for teaching modules, setting ups of Master's training programs, members of thesis committees and thesis juries. In addition, they have developed several interesting bioinformatics tools for students.

The team is highly attractive in recruiting PhD students (6) and PhD students from the group generally published well as first authors.

Assessment of the strategy and the five-year plan

This is a basic research-based project without obvious consideration of non-academic partner. The main goal of this project is to better understand the molecular mechanism of radioresistance and the different strategies developed to maintain genome integrity in bacteria and *Archaea*, using *Deinococcus radiodurans* and *Thermococcus gammatolerans* respectively.

As stated above, the fusion is coherent and seems well prepared. The experiments proposed for the next five years are fully in line with previous works by the two teams. They are innovative approaches with a mix of safe and more risky parts. The plan of work seems feasible, both team's expertise will surely be beneficial and similar technologies could be used for both microorganisms.

Conclusion

- **Strengths and opportunities:**

- The proposed team is the fusion of two teams with clear common scientific interests. The overall scientific productivity was very good and the research project is a highly innovative basic research project that fits well in a Genome Biology department.

- The fusion seems valuable to both teams at the scientific and technological level.

- The team is very attractive for students and post-docs and has been well supported financially.

- **Weaknesses and threats:**

- The *Deinococcaceae* group has been highly productive during the last five years, with a highly recognized group leader with strong international reputation. The *Archaea* genomic team was less productive and the future group leader needs to ensure that scientific quality and productivity of both topics will be preserved and further developed.

- The team has a very high teaching load, including the proposed group leader. This may affect for the productivity of the group.

- **Recommendations:**

To ensure continuity and development of the scientific quality of the group, the proposed group leader will have to work in close connection with the previous group leader of the *Deinococcaceae* team.

Team SENESCENCE AND GENOME STABILITY

Name of team leader: Mr Carl MANN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**4**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team is interested in the phenomenon of cellular senescence, a stress response leading to a stable arrest of cell proliferation and accompanying modifications in gene expression. This is a particularly important field of research as it pertains to both malignancy (associated with defects in cellular senescence) and aging. Consequently, there is a large number of laboratories worldwide working on this particular problem. The team has developed, in the past few years, an immortal clonal cell line containing an exogenous, tamoxifen-inducible, activated RAF1 kinase. In these cells, senescence is robustly induced by addition of tamoxifen. The team could show that in this system, about half the cells traversed S phase and experienced replicative stress with synthesis of p21. The other half, however, became senescent without going through DNA replication and replicative stress. Moreover, under conditions where the cells were cultured in 5% oxygen instead of the ambient 21%, induction of activated RAF1 resulted in senescence without the generation of much reactive oxygen species (ROS), indicating that ROS is not required for senescence. The senescent phenotype could be reversed by inactivation of the RAF1 kinase and simultaneous Inhibition of p16 and p21 by RNAi techniques.

Using the cell line described above as well as a proteomics method developed in collaboration with another group at CEA that allows efficient profiling of histone modifications, the team studied the chromatin modification accompanying senescence and found that the histone deacetylase SIRT2 is instrumental in deacetylation of H4K16 and formation of senescence-associated heterochromatic foci (SAHFs) and, importantly, that formation of the SAHFs is not essential for stability of the senescent state. The proteomics method seems very interesting.

Preliminary results include the observation that histone H2A.J, a variant H2A histone, accumulates during senescence caused by DNA damage (but not senescence induced by RAF1 activation). H2A.J is a poorly characterized H2A histone encoded by a gene that, unlike classical histone genes, is not cell-cycle regulated and gives rise to a polyadenylated mRNA. Another intriguing result is the observation that COX2 expression is strongly activated at late times after RASval12 as well as RAF1-induced senescence. COX2 is involved in the conversion of arachidonic acid into prostaglandins, and indeed there is a ten-fold increase in PGE2 secretion by RAS and RAF-induced senescent cells. Inhibition of COX2 abolished PGE2 production but did not prevent senescence. The possibility that COX2 has paracrine functions will be explored.

The research is solid. The team lists nine publications since 2008, five of which have a member of the team as first or last author. Of these five, one is in *Epigenetics and Chromatin* (2012 IF=4.2), one in *Oncogene* (2012 IF=7.4), one in *PNAS* (2012 IF=9.7), one in *Journal of Proteome Research* (2010 IF=5.5) and one in *MCB* (2008 IF 5.4). Thus, the output is very good given the rather small size of the permanent team (2 researchers at CEA", one experienced technician).

All in all, the research program forms a logical project and has opened up several lines of research that will be pursued in the future.

Assessment of the team's academic reputation and appeal

The team has maintained regular external funding. In the report, the last grants listed ended in 2013, but two grants have now been obtained, one from ARC and one from FRM that ensure funding for the next two years. Moreover, several grant applications have been submitted, in particular two ANR applications. This regular external funding and the team's reputation have allowed to attract three post-doctoral fellows in the last five years, as well as two PhD students, two Master students, and one bachelor student.

The PI has presided the Genetics and Oncogenes Commission of the Ligue Nationale Contre le Cancer from 2009 to 2012 and since 2012 he represents the CEA on the Scientific Council of the ITMO of *Biologie cellulaire, développement et évolution* of AVIESAN. The team leader was member of the evaluation committee of the *Programme Blanc et Jeunes Chercheurs* in Biology and Health for the ANR in 2008-2009.

The PI has presented his work in several meetings in France as well as, in 2013, at an international conference at the Karolinska Institute.

In conclusion, the PI is appreciated in his field and recognized as an expert at a national level. The academic reputation and appeal of the group is thus excellent.

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

The team has participated in the program CAMS (*Conduite accompagnée vers les métiers de la science*).

Assessment of the team's involvement in training through research

The team has had two Master students and three graduate students in the last five years. Of the graduate students, two have already defended, one with two first author publications, the other with one first author publication.

Two members of the group are involved in teaching laboratory courses. The training through research is thus deemed excellent.

Assessment of the strategy and the five-year plan

The PI proposes to follow up on solid preliminary results. In one project, he will pursue the observation that the H2A.J histone accumulates at late times in senescent cells. To determine the function of such accumulation, it is proposed to down-regulate H2A.J expression with shRNA vectors and to examine the effect on cell senescence. The plan is to develop an antibody specific to H2A.J so as to be able to study its distribution in the mouse, in different organs and at different ages. In his presentation, the team leader showed that he had been able to develop such an antibody in the last few months, and that H2A.J accumulates at different rates in various mouse organs. Finally, it is proposed to create a knock-out mouse model. Studying the function of a histone variant is an interesting avenue, but the project might be difficult. There is presently no evidence that H2A.J is required for DNA damage-induced senescence, and it is conceivable that a knock-out mouse will show a mild and difficult to characterize phenotype. At this stage of the project, it is difficult to estimate whether important results will come out of this line of research.

In a second project, the role of COX2 will be examined. As mentioned above, it is already clear that COX2 expression is not required for RASVal12 or RAF1-induced senescence (oncogene-induced senescence, OIS). However, the team plans to test the hypothesis that COX activation and PGE2 synthesis in OIS serve to signal the presence of senescent cells to the immune system for elimination. It is planned to test this hypothesis in mouse xenograft models as well as mouse endogenous models. This is a very interesting hypothesis that is worth testing.

A third project is an siRNA screen for genes that, when knocked-down, prevent entry into senescence or DNA compaction, and a fourth project is a screen for small molecules that are specifically toxic for senescent cells. Both projects are worthwhile, the first because it may lead to the identification of new players in the senescence process, and therefore to a deeper understanding of the mechanisms involved, the second because there are indications that elimination of senescent cells may alleviate symptoms associated with aging as well as risks of cancer. In his presentation, the PI showed that the first screen has already identified interesting candidate molecules.

The strategy and five-year plan are considered excellent.

Conclusion

- **Strengths and opportunities:**

- The research subject is highly interesting, and the team has accumulated some preliminary results that form an excellent basis for future research.

- The future plans involve two open-ended, large screen projects, which seemed worrying at first. However, it was encouraging to learn during the presentation that these screens have already been started, in one case with some very promising results. It seems, therefore, highly likely that at least one of these screens will lead to interesting results.

- **Weaknesses and threats:**

The group is a bit small to ensure stable scientific output even when one or the other project is not working.

- **Recommendations:**

It would seem important to seek more abundant external funding to as to be able to have five to six people working in the laboratory at any one time. A large initial effort to produce a “high impact” publication would probably allow obtaining more external funds and enlarging the group slightly, which in turn would help stabilize output.

Team PALEOGENOMICS

Name of team leader: Mr Jean-Marc ELALOUF

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**2**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The activities of the team during the last 5 years reflect an important thematic transition. A first part of its research was devoted to the characterization of the transcriptome and proteome of rodent brain regions. It resulted in three original research articles in journals of good quality (*Mol Cell Proteomics, Neurobiol Aging, Physiol Genomics*). This research topic (which corresponded to the historical field of research of the team) was discontinued two years ago. The team progressively focused all its activities on the analysis of ancient DNA, to study extinct populations and paleoenvironments. It integrated a multidisciplinary project in charge of studying the paleolithic painted caves of Chauvet and Cussac. The team notably sequenced the complete mitochondrial genome of the cave bear. In combination with radiocarbon dating, these sequences allowed a precise timing of speciation and extinction of that species (*PNAS, J Archeol Sci*). Furthermore, the team was pioneer in the analysis of ancient DNA from coprolites. Interestingly, they showed that these samples may contain large amount of DNA, and hence provide information both about the defecator and about its diet. They were notably able to sequence the entire mitochondrial genome of the cave hyena, and to show that the red deer was an abundant component of its diet (*Proc Roy Soc B*). Thus, although the team is relatively new in that field (its first publication on ancient DNA was in 2008) it already succeeded to publish in excellent non-specialized journals (*PNAS*, *Proc Roy Soc B*).

Assessment of the team's academic reputation and appeal

The thematic transition from transcriptomic and proteomic analyses to ancient DNA studies coincides with the departure of two researchers. Up to now, these departures have not been compensated by new arrivals, and hence the group is presently very small (1 researcher, 1 technician, 1 thesis student).

Up to now the attractivness of the group on its new thematic (ancient DNA) appears quite limited (no international post-doc, no collaborative grant). This is probably due to the fact that the publication track record of the team is quite recent. The visibility of the team should increase with its new publications. Noteworthy, the PI was invited to give talks on ancient DNA at two international conferences or summer schools and he was a board member of the French multidisciplinary network (RTP) on paleogenetics.

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

The team is active in promoting its research activities to the public through conferences and articles in science popularization journals. The team is strongly involved in a multidisciplinary project in charge of studying the paleolithic painted caves of Chauvet (and others).

Assessment of the team's involvement in training through research

During the considered period, 2 Master students and 2 thesis students have been supervised (thesis defended with 1 to 3 publications). One thesis is ongoing. This is excellent.

Assessment of the strategy and the five-year plan

In the coming years, the team plans to sequence and analyze the nuclear genome of an ancient wolf specimen from the cave of Chauvet, based on DNA extracted from coprolites. Preliminary analyses already allowed the sequencing of the mitochondrial genome, and suggest that the nuclear genome could be sequenced at a relatively good coverage. These nuclear sequences will be compared to that of extant wolves and dogs. These analyses are expected to shed light on the process of dog domestication. The team also plans to sequence DNA from cave hyena coprolites collected in different regions of France. This should provide a unique data set to study changes of paleobiocenosis through time. Both projects are ambitious and very original. Preliminary data indicate that the project has a good feasibility.

Conclusion

- **Strengths and opportunities:**

- Pioneer in the analysis of ancient DNA from coprolites, which provide information both about the defecator and about its diet.

- Unique access to samples from the Chauvet cave and other caves.

- In very good position to obtain the first complete sequence of the nuclear genome of an ancient wolf.

- **Weaknesses and threats:**

- Very small team with excellent expertise in ancient DNA sampling/sequencing, but relies on collaborations (in Denmark) for large-scale bioinformatics and population genetic analyses.

- The grants that were obtained during the period were relatively limited (but the team was successful at being supported by Genoscope for its sequencing projects).

- The research topic of the team is far from the other groups of the I2BC department and there are limited local interactions, except with the bioinformatics platform.

- **Recommendations:**

This is an excellent project, but the I2BC is not the best environment for it. The team is currently exploring the possibility of joining another research unit that would better corresponds to its scientific project. The committee strongly supports this initiative. The team would strongly benefit of being in a department with research groups having expertise in the field of evolution and population genomics.

Team

NUCLEAR REGULATION AND STRESS

Name of team leader:

Mr Joël ACKER & Mr Olivier LEFEBVRE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**4**	**4**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The team is interested in RNA polymerase (pol) III transcription, more specifically in the identification of the genes transcribed by pol III, of the molecules required for transcription, and of the pathways involved in pol III regulation. The team has contributed major results over the years and is considered one of the important players in this field.

Over the last few years, they have examined the genome organization of a hemiascomycetes yeast (*Yarrowia lipolytica*) and have shown that about half of the 5S gene copies are located 3' of tRNA genes, and these tRNA gene-5S gene tandems are transcribed as dicistronic precursors. Moreover, in these cells, TFIIIA is not essential for survival and may be involved in 5S RNA processing.

The main effort has been dedicated to the identification of further factors involved in pol III transcription. In a very fruitful and long-term collaboration with a laboratory at the Institute of Biochemistry and Biophysics (IBB) in Warsawi (Poland), the group contributed many years ago to the identification of Maf1 as a repressor of pol III transcription. Since then, the group has been involved in the further characterization of Maf1, notably in the identification of Msn5 as a carrier responsible for the relocation of Maf1 to the cytoplasm when cells are transferred from glycerol to glucose, in a structure-function study of Maf1 identifying two conserved domains required for pol III regulation, and in the identification of CK2 as a regulating kinase. They also contributed to showing that in Maf1-depleted cells grown on glycerol, the induction of FBP1, a major gene controlling gluconeogenesis, is reduced, thus linking Maf1 and glucose metabolism.

In addition to Maf1, the group identified Sub1, the yeast ortholog of mammalian PC4, as occupying all pol III genes in a genome-wide location. Sub1 contributes to efficient pol III transcription by increasing the binding of TFIIIB and TFIIIC to DNA. More recent results indicate that during exit from stationary phase, cells lacking Sub1 experience a delay. This delay appears linked to the inability of these cells to establish a proper G1 cell cycle arrest upon entry into the stationary phase; instead, they experience apoptotic DNA degradation and accumulation of reactive oxygen species, in a way dependent on the Ras/PKA and Tor1/Sch9 pathways. Surprisingly, in cells lacking both Sub1 and Maf1, the delay is increased, a very interesting result that the team is now pursuing. Moreover, Maf1 deleted cells appear to be long-lived mutants. These are all highly interesting results, some of which have been submitted for publication.

Another line of research concerns the chromatin structure of pol III genes, in particular the identification of chromatin remodeling and histone modifying factors. These experiments are ongoing and have pointed to a possible role of two histone acetylase or deacetylase.

The research is exciting with a very good publication record. The team lists seventeen publications since 2008. Of these, several are the result of fruitful collaborations, mostly with the Polish group or with another group in UK. On seven of these publications, a member of the team is either first or last author. Of these seven, one is in *Gene* (2013, IF=2.2), one in *Biochimica Biophysica Acta* (2012, IF=3.85), one in *RNA Biology* (2010, IF=5.6), one in *Journal of Biological Chemistry* (2010, IF=5.3), one in FEBS letter (2010, IF=3.6), one in *PNAS* (2009, IF=9.4), and one in *Nucleic Acids Research* (2008, IF=6-9).

Thus, the output including the papers from collaborations is very good, with, in addition, a series of nice results submitted for publication.

Assessment of the team's academic reputation and appeal

The team is well funded with, among others, two ANR grants, one ending in 2014 and one in 2018. The team has presented its work at several international meetings in poster presentations. It has an established reputation within the pol III field, which has allowed the recruitment of four post-docs and two thesis students. In addition, thesis students from the IBB laboratory have worked in the group for periods of several months.

The academic reputation and appeal of the group are thus very good.

Assessment of the team's involvement in training through research

The team has trained several thesis students (3 thesis students, 1 master student) and members of the team supervise laboratory courses for two different masters. The thesis students who already graduated (two of them) have each first author publications. The involvement in training through research is thus outstanding.

Assessment of the strategy and the five-year plan

The team is pursuing several very interesting projects. In one project, they plan to develop methods to identify all of the proteins associated with the 5S RNA genes, using the Déjardin and Kingston method. A first try lead to successful isolation of pol III-occupied 5S genes, but in amounts too small to allow proteomic analysis of the proteins present. They are now attempting the same method on plasmids carrying the 5S gene. In parallel, they are using tandem purifications after in vivo crosslinking, under denaturing conditions, and obtaining the first results. These are highly promising approaches that will certainly lead to the identification of new players in pol III transcription.

In a second broad project, they plan to study Ty LTR retrotransposition, which has been shown by others to occur preferentially upstream of tRNA genes. The influence of pol III transcription on the integration process will be studied in vitro through the development of an in vitro integration-transcription system. In parallel, factors required for integration will be identified, in part through the same type of proteomics approaches described above. This work will be performed in collaboration with a group at the Hematology Institute, Paris and a group at the Pasteur Institute, Paris.

The future plans are exciting and, in the case of the proteomics approach, advanced enough that the first problems have been identified and are being addressed for the first approach. The second approach (tandem purification after crosslinking) has already proven successful and will now be applied to material obtained from yeast grown under different conditions or submitted to various stresses. This will allow the team to focus on proteins that change in different conditions, which is an excellent way of identifying interesting candidates.
The future plans are thus excellent.

Conclusion

The group has an established reputation within the pol III transcription field, and a solid and highly fruitful collaboration with the IBB group. The problems addressed are interesting and likely to bring new insights into the field. The addition of the Ty LTR retrotransposition studies is an excellent opportunity, especially that techniques being developed for the pol III project will be applicable to the Ty LTR project.

The team is presently short on non-permanent members, with only one post-doc. Non-permanent staff are highly important in that they bring new expertise, enthusiasm, and new ideas. With funding secure until 2018, the team will be able to hire a new post-doc. Moreover, the group has hosted Polish PhD students from the IBB group before and they plan to do this again with either thesis students or post-doctoral fellows.

Given the exciting preliminary results and the solid financial situation of the group, it is expected that the next few years will be very productive.

- **Strength and opportunities:**

- Expertise and academic reputation of the team.

- Interest and feasibility of the research plan.

- Funding secured for the next years.

- **Weaknesses and Threats:**

- Too few PhD students and postdocs.

- Recent publications were published in moderate impact journals.

- **Recommendations:**

- To recruit PhD students and post-docs.

- To publish in higher impact journals.

Team

TRANSCRIPTIONAL REGULATION OF GENOMES

Name of team leader:

Mr Michel WERNER

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**6**	**4**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The group is working on the mechanisms underlying the control of RNA pol II- and RNA pol III-dependent transcription, mainly using the yeast *S. cerevisiae* as a model. In the last five years, they investigated three different topics: 1) by studying the genome-wide localization of a pol II transcription factor, TFIIS, they showed that it binds to pol III loci and regulates pol III transcription. This finding, quite unexpected, allowed to further show that the pol II and the pol III machineries share common factors; 2) in collaboration with another team from the Institute, they investigated pol III and TFIIS binding in mouse ES cells. This was one of the first genome-wide characterization of pol III subunits and pol III transcription factors chromatin localization in mammals, and it allowed to demonstrate that the function of TFIIS in pol III transcription is conserved throughout evolution; 3) finally, they studied the function of the yeast mediator. Thanks to thermosensitive mutants, they began to perform an integrative study of its function in transcription, characterizing its target genes at the genomic level and the relative contribution of the various subunits. During the course of this work, they found that the mediator complex recruits TFIIH to promoters, allowing subsequent stimulation of transcription. More recently, they showed that a subunit of the mediator interacts directly with the RPB3 subunit of RNA pol II and that this is important for general transcriptional activation.

Altogether, these studies address very important and pertinent questions, by a whole variety of approaches. The group publishes regularly in excellent journals, indicating that it is very competitive in the field, and is clearly renowned at an international level. In the last five years, 14 publications were generated in total where the group is a major contributor in 12 as first and last authors (Mol Cell 2008, Genes Dev 2008, Mol Cell Biol 2008, Trends Genet 2008, EMBO J 2008, Curr Opin Struct Biol 2009, NAR 2010, FEBS Letter 2011, Curr Genet 2011, Science 2011, NAR 2012, Genes Dev 2013). They have also published 3 book chapters. Thus, the scientific output is of outstanding quality.

Assessment of the team's academic reputation and appeal

The two permanent researchers in the group have been invited to 13 international conferences in the last five years. The group leader has been director of a research unit and is the project leader of the Department of Genome Biology of the I2BC. He is member of a variety of scientific councils and scientific advisory boards. The group attracted many post-docs. Clearly, the group has an outstanding academic reputation and is quite attractive.

Assessment of the team's involvement in training through research

Two PhD students defended their PhD during the last five years, both of them having published in high ranking journals as first authors. Two PhD students are currently in the laboratory, including a fourth year PhD student who also has an excellent first author publication. PhD students are followed by a thesis committee since 2010. Members of the group are involved in a few hours of teaching in various masters.

Assessment of the strategy and the five-year plan

The project focuses on the role of the mediator complex, in yeast as well as in mammals (in collaboration with two other groups within I2BC). As such, it is largely the continuation of the third topic developed during the last five years. It aims at understanding the mechanisms by which the Mediator complex participates in transcriptional activation, and how these mechanisms differ from one promoter to another. The project addresses a very important question, given the major role of the Mediator in transcriptional control, and uses a variety of genetic, biochemical, and molecular biology approaches. It is clearly focused, well defined and highly feasible given the expertise of the group and the tools it developed. Most probably, it will lead to important discoveries and will allow the group to remain at the highest international standard.

Conclusion

- **Strengths and opportunities:**

- The group has reached a critical size.

- Strong expertise of the group in the field.

- Original tools (such as conditional mutations of Mediator) developed by the group.

- Strong international visibility.

- The creation of the I2BC will increase collaboration with teams with complementary expertise within I2BC.

- **Weaknesses and threats:**

Genome-wide data analyses might be a bottleneck of the proposed project at some points.

- **Recommendations:**

To define a workflow for an efficient analysis of genome-wide data, perhaps involving the part-time recruitment of a biostatistician or a day-to-day collaboration with a group with such an expertise.

Team

MAMMALIAN EPIGENOMICS

Name of team leader:

Mr Matthieu GERARD

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**4**	**4**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The group developed three axes in the last five years, all connected with mammalian epigenomics, mainly using genetically modified ES cells and mice derived from it. First, they investigated chromatin modifications associated with facultative and constitutive heterochromatin, uncovering the presence of H3K36me3, a histone mark previously thought to be associated with transcriptional activation. This unexpected finding contributed to show the complex and probably combinatorial role of histone modifications. In a second part, the group has made a tremendous amount of work to tag 10 endogenous ATP-dependent chromatin remodelers in ES cells and has characterized their genomic target sites at the nucleosomal resolution. They extensively characterized their binding to promoters, and correlated it with transcription outputs and with the modifications of gene expression upon depletion of these factors. Manuscripts describing these parts are, or are going to, be submitted. This part will probably give important insights into the function of these remodelers and may provide new concepts of transcriptional regulation. However, the competition in this field may hamper publication in top journals. Finally, in a third very productive part, the group investigated the mechanism of chromatin remodeling during spermatogenesis, in collaboration with a group in Grenoble. The group provided ES cells and mice expressing a tagged version of chromatin binding proteins or histone variants, allowing the study of their function. This original piece of work is highly valuable, but the group was not the main contributor in these studies.

In total, the group has published 5 publications in peer review journals, among which one on its main research topic (Genome Research, 2011). Two originated from the collaboration with the Grenoble group, including a Genes Dev paper signed as last-but-one author in 2013. The other two, including one signed as co-last author in NAR (2012) came from other collaborations.

In summary, the productivity of the group in the last years was very good but needs to be improved. The publication of the papers on its main research topic has clearly to be the priority of the group in the next year and is mandatory to increase visibility and attractiveness of the group.

Assessment of the team's academic reputation and appeal

The group has a moderate academic reputation and appeal, with one invitation to an international scientific meeting and 1 collaborative grant as a coordinator in 2008. This should increase when the main papers will be published. An important and fruitful collaboration with the internationally recognized group in Grenoble has been set up.

Assessment of the team's involvement in training through research

One thesis student has defended in 2010 but does not have yet a first author publication. However, the work is being prepared for publication. Another thesis is ongoing. The PI does a small amount of teaching in the master 2 programs (2 hours). The training through research is good.

Assessment of the strategy and the five-year plan

The project for the next five years is the continuation of the main project of the laboratory on chromatin remodelers. Thanks to the tools they produced, in particular ES cells expressing tagged proteins from the endogenous locus, the applicant is now in a position to pursue three directions:

1) To study the involvement of each remodeler in nucleosome positioning around promoters.

2) To study the dynamics of remodelers recruitment to genomic regions at different stages of differentiation (non differentiated ES cells, neuronal precursor cells and adult neurons).

3) To investigate the role of NURD complexes in the pathogenesis of Alzheimer disease, focusing first on HDAC2 but also on HDAC2-associated remodelers. This last part will be performed in collaboration with an expert in the study of neurodegenerative disease.

In general, the projects are highly feasible given the tools and the expertise raised by the group. They address important but very competitive questions with very appropriate approaches. This project is excellent and should lead to important insights into the function of remodelers in transcriptional control.

Conclusion

- **Strengths and opportunities:**

- The expertise of the group in generating genetically modified ES-cells.

- The existence of fruitful collaborations.

- The development of expertise and methodologies to analyze genome-wide data.

- The interest and feasibility of the research plan.

- **Weaknesses and threats:**

- Moderate publication record, which limits international visibility and attractiveness.

- The competitiveness of the research field.

- The lack of a dedicated bio-statistician.

- **Recommendations:**

- The committee strongly urges the group to publish their results on its main project.

- The committee recommends the recruitment of a biostatistician within the group dedicated to genome-wide data analyses.

- The committee recommends to increase the size of the group in order to reach a critical size. Recruitment of scientists at the post-doctorate level is recommended.

Team

STRUCTURE, FUNCTION, EVOLUTION OF CATALYTIC RNA

Name of team leader:

Mr François MICHEL

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**4**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The team has a world-wide reputation in the field of catalytic RNAs, a field in which the PI made essential discoveries such as the classification of introns and the characterization of their structure and function. In the recent years, the team focused on several important aspects of the biology of group II introns and, in particular, the role of domain VI that contains the bulged A responsible for the first nucleophilic attack of the 5' splice site and lariat formation. Despite the primordial importance of domain VI, the structure of the catalytic core of type II ribozyme determined by the Pyle laboratory lacks that domain. Using comparative sequence analysis, modeling and nucleotide substitutions, the team proposed a specific receptor RNA for the section of domain VI located just distal to the branchpoint. This interaction was shown to be specifically involved in the branching reaction and implied that prior to the exon ligation, the distal part of domain VI must undergo a major translocation (EMBO J, 2011). These are important findings and reinforce the belief that nuclear splicing evolved from intron II splicing.

The team also made the discovery that some mitochondrial ribosomal introns belonging to type IIB1 are able to initiate splicing *in vitro* by hydrolysis at the 5' splice site rather than by branching (RNA, 2011). In addition, the team showed that some specific bacterial group II introns that target rho-independent transcription terminators do not form lariat because of their defective domain VI. The team was able, with a limited number of nucleotide changes to have these introns excised by lariat formation.

A subgroup lead by an associate professor (MdC) studies cell cycle and replication coordination in *E. coli*. They showed that the cycC gene is involved in several activities such as the reactivation of arrested replication forks, the activation of the replication helicase during replication initiation and cytokinesis.

The team published 9 articles. The quality of the publications from the group is very high (1 EMBO J, 1 NAR, 2 RNA, and 1 TIBS). The team also published 2 articles in collaboration. The group also obtained an ANR grant with the PI as coordinator (2011-2013).

Assessment of the team's academic reputation and appeal

As mentioned above, the team has a world-wide reputation in the domain of RNA splicing despite the small size of the group. The general strategy, mainly focused on specific but important problems related to intron II biology, is perfectly adapted to its small size. The team is also engaged in long term collaborations with a team in Canada (student exchange and a publication in RNA) and a team in Strasbourg. The latter collaboration has allowed many important breakthroughs in the past and is still active at the present time (TIBS 2009). Such collaborations are essential considering the small size of the group. The team is not attached to a specific organism. This specificity allows a wide evolutionary approach to biological problems.

The number of oral presentations in national and international meetings is low and does not correspond to the quality of the team.

Assessment of the team's organization and life

The team is small (about 4 members) with 3 permanent staff scientists. In June 2013, the team also included a high level technician but no students. As mentioned above, the team is mainly focused on several aspects of type II intron biology. Considering the small size of the group, it may seem strange that one of its members develops a different subject related to the regulation of replication in *E. coli*. In fact, the PI has always allowed some divergence within his team. This was the case for a senior member, who left the group in 2008 (see departures) to start his own group at the Faculté de Pharmacie in Paris. It is still not obvious that the *E. coli* replication project should be pursued, considering the size of the group. The much larger future environment of I2BC will give the team the opportunity to develop new collaborations, which seems essential for such a small group. The collaboration with structural biologists is essential considering the interests and the size of the team.

Assessment of the team's involvement in training through research

Each of the permanent scientists of the team has worked with a student during the past 5 years. This allowed 2 PhD thesis defenses, one on intron II splicing (1 EMBO J and 1 RNA as first author) and the other on *E. coli* replication (1 PLoS One as first author).

The PI teaches a limited number of courses in several universities and participated in a few thesis committees. The MdC is heavily involved in heavy teaching as a member of the University of Versailles-Saint-Quentin.

Assessment of the strategy and the five-year plan

In the future, the team will quite probably obtain an atomic resolution structure that includes domain VI, study the intron-exon interactions, and try to understand how a specific class of bacterial type II introns integrates close to start and stop codons, possibly with the help of the translation machinery. On a longer time scale, the team will try to solve the structure of complexes between the intron RNA and the intron encoded protein. The project focusing on type II introns is extremely coherent and is a logical consequence of what the group has been doing previously. The originality of the team resides in its multiple approaches: mainly molecular biology, phylogeny, structural model building and, recently, structural biology. Not many persons in the world are able to “understand” intron sequences as well as this team. The project related to introns that interact with the translation machinery could be very promising, leading to new concepts in the field. The structural project is ambitious but an adequate collaboration with a structural biologist within another team of the department makes the project feasible. The PI himself will retire in three years but will certainly ask for an « Eméritat » and will, as a DR1, most probably obtain it. This will allow the team to go on for the next five years either in I2BC or elsewhere.

Conclusion

- **Strengths and opportunities:**

- The strength of the team relies on its rare expertise in the domain of structure and function of self-splicing introns. Despite the effort of several top groups in the field, many aspects of how type II introns are able to splice and transpose remain to be discovered and the team has the knowledge and tools to be very productive in this field.

- The structural project consisting in the determination of an intron II structure that includes domain VI is very ambitious but the preliminary data indicate that the project is feasible. Intron II biology in bacteria with insertions in transcription termination and translation initiation/termination sites offers very interesting perspectives.

- **Weaknesses and threats:**

One of the potential weaknesses of the group is its small size and its involvement in two apparently very different subjects (Intron II biology and E. coli replication regulation). Unfortunately, the small size is not specific to that group in the present and future environments. The creation of I2BC, by concentrating more groups interested in RNA biology, might help.

- **Recommendations:**

A collaboration with good bacterial geneticists should help developing these interesting and potentially important problems. Facilitating such collaborations should be a priority for the group leader and the future institute.

Team

RNA STRUCTURE AND DYNAMICS

Name of team leader:

Mr Dominique FOURMY

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	3
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**5**	**5**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The team works at the intersection of biology and engineering. Three main directions of the research are micro and nanotechnologies related to protein synthesis and microarrays, fundamental mechanisms of translation and cotranslational processing of proteins. The PI created the team at CGM in 2010 after a 3-year stay at the University of Tokyo. The previous research was highly innovative. The 'engineering' aspect of it, which is aimed at generating high-density 'translating' microarrays or single-cell assessing devices, has very good prospects for future industrial and medical applications. Many elegant tools have been developed and implemented in this area by the team members (and four patents have been filed). Because this research has not yet been applied to solving major biological or medical problems, the results of these efforts have been published primarily in engineering or analytical rather than basic or medical research journals.

The studies of the past three years related to mechanisms of translation, frameshift regulation and posttranslational events is equally innovative and fresh. In this area, the team combines well-established, traditional (yet well-performing) techniques of chemical probing, with more innovative approaches, such as molecular tweezers, single molecule FRET and RNA protein crystallography for studying interactions of protein ligands with the ribosome. In the past period, the team has published 22 papers, 7 with the team leaders as the first or corresponding authors. The papers were published in very respectable, highly-cited journals such as Nucleic Acids Research, RNA, J. Mol. Biol., JACS, Biochimie, and others.

Assessment of the team's academic reputation and appeal

The team has considerable international recognition. The team leaders have been invited to give lectures at 9 national and international meetings. There are also many invited lectures presentations at prestigious meetings such as Single Cell Analysis meeting at Cold Spring Harbor Laboratory, USA (2013), Conference Jacques Monod, Roscoff, France (2012), RiboClub RNA meeting, Sherbrook, Canada (2011), RNA meeting, Kyoto, Japan (2011) and others. The leader is an associate editor of the Journal of Biochemistry. Team collaborates with laboratoriess in Denmark, Japan, US. A number of patents have been filed. The team leaders participated in the organization committees of several international scientific meetings, as well as in other scientific committees.

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

Four patents have been filed and a startup company has been spun-off.

Assessment of the team's involvement in training through research

One student has been under the full supervision of a team member at the University of Tokyo. He has published as a first author 4 papers, 1 review article, 2 patents and one paper is submitted for publication. The same team member has helped supervise other students at Tokyo University and Institut d'Optique in Palaiseau who published several papers. One PhD thesis is on-going. Many Master students (between the members of the team). Such a record is good but not stellar.

Assessment of the strategy and the five-year plan

The future research will be focused on two main areas encompassing bacterial and eukaryotic translation. One part of the effort will be dedicated to analyzing structure and function of a newly discovered translation initiation factor in eukaryotic cells, which assists in translation of mRNAs with highly structured 5' UTRs. This direction of the research is interesting and has obvious basic science and medical implications. The second part of their future plans relates to compartmentalization of translation in the bacterial cell. The exact prospects in this direction are currently unclear, especially given high competition in their line of science. However, the group plan to use new research tools which they are so good in developing which may give them a competitive edge.

Conclusion

- **Strengths and opportunities:**

In conclusion, the team comes across as an active, innovative and solid research group. The past research is quite impressive and future plans hold promise for providing exciting scientific data.

- **Weaknesses and threats:**

The average publication rate could be related to reorganizing the team to a new location in 2010.

- **Recommendations:**

The breadth of the research projects is impressive but could become a problem if additional funding is not available, exacerbated by the small size of the team.

Team

GENOMIC, STRUCTURE AND TRANSLATION

Name of team leader:

Mr Olivier NAMY

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	4	3
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	**9**	**7**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The main focus of the team is understanding the mechanisms of recoding and mistranslation in the eukaryotic cell. The previous research organically combines structural analysis and biochemical investigation of the elements and factors involved in programmed frameshifting and stop codon read-through. Their previous cryo-EM studies have indicated a possible function of -1 frameshift inducing pseudoknot. A clever genetic screen helped to identify new eRF1 sites important to the function of the factor in translation termination. An exciting finding that the [PSI+] prion phenotype leads to increased programmed frameshifting at the antizyme gene in yeast showed that a significant fraction of the prion effects come from its influence on polyamine content. The team also provided important insights into the rules that govern aminoglycoside-induced read through of premature stop codons in disease. All these studies are very consistent, insightful and have significantly expanded our understanding of the mechanisms, purposes and consequences of recoding in eukaryotes.

The work is performed at a high level and the results of the recent years have been published in high-profile journals (Nat Cell Biol, PLoS Genet (2), NAR (3), Structure, Mol Micro, 26 papers of the team members total, 19 as the first or the last author).

Assessment of the team's academic reputation and appeal

The team has considerable international reputation. The team leader has been invited to give lectures at 9 national and international meetings, including Gordon Conferences. The other team members presented 5 talks at meetings and a number of posters. Team collaborates with labs in UK (2), Japan, Israel, US and with several French institutions. The team director is an editorial member of FEMS Yeast Research.

Assessment of the team's involvement in training through research

3 PhD thesis defended (2 with publications. For the 3rd one, a paper has been submitted*)*. There are 2 ongoing PhD thesis and many Master students (between the members of the team).

Assessment of the strategy and the five-year plan

The future research plans of the team expand upon their previous work. While the effect of the mRNA secondary structure, specifically the molecular mechanisms of action of a -1 frameshifting pseudoknot has been unraveled, the operation of a pseudoknot in mRNA that stimulates shifting to the +1 frame is more enigmatic. Therefore, the team plans to continue using cryo-EM for understanding the functions of one of the +1-frameshifting RNA structural elements. The recoding studies will be further expanded by the use of single-molecule FRET. This approach has provided important information about functions of the bacterial ribosome. The group has already set up and will now use smFRET in combination with IRES-containing mRNAs for the analysis of the kinetics of translation and recoding. The previous work of the team has led to the conclusion that the termination codon context affects eRF1 activity and that miscoding antibiotics, e.g. aminoglycosides, have unexpected effects upon selection of the aminoacyl-tRNA suppressing premature stop codons. These experiments will be expanded using mass-spec approaches. Furthermore, several HTS screens will be performed to identify compounds that induce premature stop codon read-through either by directly binding to the ribosome or by inhibiting the activity of the release factor. Finally, the group plans to use ribosome profiling to analyze how events leading to miscoding (e.g. the [PSI+] phenotype or the lack of modification in tRNA) affect gene translation at the genome-wide scale. The research plans are well-founded, sufficiently ambitious and are based on the well-established expertise of the team members. There is a very good chance that the proposed studies will generate exciting data to expand our understanding of the basic mechanisms of translation and will have important medical implications.

Conclusion

- **Strengths and opportunities:**

- In conclusion, it is an active and innovative research team, which carries out top-notch studies in an exciting area of modern biology. The future studies may provide important insights into basic biological questions and may have important medical implications.

- Incorporation of the team in the new institute will be highly beneficial for several research groups working in the adjacent areas of molecular biology.

- **Weaknesses and threats:**

The future of the group with critically depend on their ability to have a dedicated, 'in-house' bioinformatician.

- **Recommendations:**

The follow up to the HTS project will require collaboration with experienced medicinal chemists. Identifying such future collaborator at the earlier stages may facilitate optimizing the screening strategies.

Team

SUPRAMOLECULAR ASSEMBLIES AND TRANSLATION

Name of team leader:

Mr Marc MIRANDE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	3	
TOTAL N1 to N6	**5**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The focus of research of the small team composed of two permanent members and three non-permanent personnel is aminoacyl-tRNA synthetases in the eukaryotic cell. Significant effort in the previous period was dedicated to unravelling the structure and biology of the MARS complex composed of 9 amino-acyl tRNA synthestases (RSes) and three auxiliary proteins. Some preliminary basic information about structural organization of the complex has been obtained. Small-angle X-ray scattering experiments yielded information about the overall shape of the complex. These studies have further revealed interesting links between functions of the MARS components in the cellular cytosol and involvement of some of the auxiliary factors in mitochondria. The second main direction of the previous studies was the understanding of the role of mitochondrial Lysyl-tRNA synthetase (LysRS) in packaging of the HIV-1 virion. Demonstration that the mitochondrial, but not the cytosolic, version of LysRS is being packaged in the virion opened new directions for exploring novel classes of HIV inhibitors. Additional investigation of maturation of the mLysRS provided important insights into spatio-temporal regulation of LysRS.

The work is performed at a high level and the results of the recent years have been published in highly reputable journals such as JBC (4), Biochemistry (2), JMB (2) and others (a total of 12 publications) all with the team leader as the corresponding author.

Assessment of the team's academic reputation and appeal

The team has considerable international reputation. The team leader has been invited to give lectures at 10 international meetings. The team actively collaborates with several national and international laboratories, including groups in Taiwan, Russia and Ukraine.

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

The team leader chaired and participated in several important national and international scientific committees.

Assessment of the team's involvement in training through research

3 PhD students, two most recent with several first author publications. Three theses have been defended. 5 Master students.

Assessment of the strategy and the five-year plan

The future research will explore the structure of the MRAS complex, and moonlighting functions of aa-RSes. Crosslinking and assembly of substructures from individually-expressed MARS components outlined in the written project description appeared somewhat traditional, but the attempt to obtain high resolution structures of the subcomplexes discussed in the oral presentation generated more enthusiasm. These approaches may provide interesting insights into organization and possibly function of the complex. The second part of the MARS-centered goal is also appealing. It is focused on the involvement of the GlnRS component of the MARS complex in mitochondrial translation and investigation of the mitochondrial and apoptotic functions of the p43 auxiliary MARS component.

Another main goal of the future research is also very exciting. If successful, the proposed studies will provide a better understanding of the role of mitochondrial LysRS in HIV biology including detailed studies of interactions of mLysRS with tRNA and Pol, visualization of mLysRS packaging in the virion and studying targeting of mLysRS to mitochondria. These studies will be further expanded by HTS for the inhibitors of mLysRS interactions with HIV Pol which may lead to new anti-HIV therapies.

Conclusion

- **Strengths and opportunities:**

This is a small team that nevertheless carries out solid and productive research in an interesting area of life scinces. Compartmentallization of translaiton and asociated cellular factors is a hot topic in the current biology and may provide visibility for the team and venues for high impact publications. The part of the project related to the HIV biology is very innovatvie and the future studies in this area may have important medical implications and serve as source of independent funding.

- **Weaknesses and threats:**

Structural studies of the macromolecular complexes based on traditional biochemistry (e.g. crosslinking) provide only low-resolution information and cannot be viewed as particularly attractive in the age when atomic models of even very complex systems is the state of the art. On the other hand, crystallographic approaches are always ridden with a high probability of failure. Properly balancing the approaches for solving the structure of the MARS complex could be a challenge.

- **Recommendations:**

A better diversification of the journals chosen for publication of the results could be beneficial, especially if a special effort is dedicated to placement of the future papers in the journals with the highest possible impact.

Team

SIGNALISATION ET REÉSEAUX DE REÉGULATIONS BACTEÉRIENS

Name of team leader:

Mr Philippe BOULOC

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**5**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The team studies bacterial transcriptional and post-transcriptional regulatory networks using genetics, bioinformatics and a variety of global "omic" tools. On the transcriptional side, the team recently focused on the way the *E. coli* transcriptome detects and responds to alterations of the bacterial envelope. The work established two important characteristics of stress response in *E. coli*: first, that a given stress solicits the combined responses of several regulatory pathways; second, that each individual pathway controls a discrete set of genes involved in the response, and shows little overlap with other pathways (PLoS Genetics, 2009). The main part of the team's work concerns sRNA (small regulatory RNAs)-mediated post-transcriptional control in several Gram-positive and negative bacteria. The team identified a set of new sRNAs in *Staphylococcus aureus* (3 publications, one in PLoS Pathogens) using molecular genetics in conjunction with bioinformatics (in collaboration with another group in the department) and focused on one of them, which was shown to be responsible for the down-regulation of about 25 genes mainly involved in central metabolism (NAR, 2010).

Recently, the team also started a project on functional genomics of several Vibrio pathogenic species. They identified 28 sRNAs that are conserved in all the studied Vibrios, paving the way to further studies. Interestingly, the results indicate that virulence genes are mostly acquired through horizontal gene transfer, whereas sRNA genes seem to evolve vertically and are mostly species-specific.

During the five last years, the group has published 17 articles in international biology journals. 7 publications are mainly from the laboratory with one in highly rated (PLoS Genetics) and 2 in good international journals (NAR and RNA). Four articles are in a fruitful collaboration with the other team.

The group succeeded very well on the financial side with 4 ANR grants and 4 other grants.

Assessment of the team's academic reputation and appeal

The appeal of the team comes from its way of using a wide range of very different tools (transcriptomics, deep-sequencing, genetics and bioinformatics) to solve basic biological questions related to the regulation of gene expression in bacteria. The team is not attached to a specific organism. This specificity allows a wide evolutionary approach to biological problems. The diversity of the tools used relies on the ability of the team to be involved in many fruitful collaborations with other laboratories. This is especially true for the global "omic studies but also for the Vibrio project, which deals with fish or shellfish pathogens. The long-standing collaboration with the other team is especially fruitful and will fortunately continue since both groups will migrate together in the new institute in the same department. Many sRNAs have multiple targets and one of the most important problems that remains to be to solved is the identification of sRNA targets. The group is deeply involved in the experimental approach and that of the other team in the bioinformatics approach. The long-term collaboration between the two groups allows reciprocal ameliorations of both approaches, the ultimate objective being that the faster bioinformatics approach will be powerful enough to require only simple experimental verifications. This will certainly be useful for the whole community.

The two senior members of the team were invited to talk at a reasonable number of meetings/seminars (12 for the past five years) both in France and abroad. Both are involved in an important number of national committees.

Assessment of the team's organization and life

The team is medium sized (about 7 members) and headed by two senior scientists. Although each of these two researchers has his own projects, both are using the same experimental approaches and many of the concepts are common. These common interests/tools allows both projects to be productive. The team is also comprised of several PhD students, technicians and post-docs. The scientific objectives of the team are perfectly coherent and rely, as mentioned above, on the use of quite a large panel of different biological techniques and logical collaborations.

Assessment of the team's involvement in training through research

During the past five years, the team trained 3 PhD students, one presented his thesis work in 2009 with 1 article as second author (PLoS Genetics in 2009) and 1 as third author (App Environ Micro In 2008). The two senior members of the group are mainly involved in PhD and HDR committees with a little teaching at the master level.

Assessment of the strategy and the five-year plan

The project of the team first consists in improving the detection of sRNA targets using a combination of target capture, bioinformatics and deep sequencing using *E. coli* and *S. aureus* as experimental systems. Second, the team will develop, in collaboration with a group at INRA- Jouy-en-Josas, a method that allows to differentiate between primary and matured/processed RNAs. They have already shown that the vast majority of the bacterial RNAs are processed. Finally, the team will study how horizontal transfer of virulence genes and vertical evolution of sRNA genes can be integrated in a regulatory networks leading to host adaptation and virulence. The project is totally consistent with the interests and the expertise of the group. One of the strength of the team resides in its double technical and conceptual know how.

Until now, the team was headed by two PIs, but the future project will be conducted by only one. This will not make any difference. Both worked together for years and wish to continue. The projects of the two researchers are different but have enough in common to belong to the same team.

Conclusion

- **Strengths and opportunities:**

This is an excellent, very productive, and well-funded medium-sized group. One of the strengths of the team is its capacity to investigate multiple levels of regulation (looking at both transcriptional and post-transcriptional regulation) to study networks. This double specificity is extremely useful because these two levels of regulation are deeply related. A global and valid view of regulatory networks function in bacteria can only be obtained by integrating both levels of regulation. Another strength of the group comes from its modern approach to regulatory networks based on an important number of well thought out collaborations. Some of these collaborations might be facilitated in the new planned institute. The move does not seem to be detrimental to the other collaborations.

- **Weaknesses and threats:**

It appears that the group will, in a near future, need to collaborate with system biologists interested in bacterial regulation. This might be essential to put all the data into a global and theoretical framework.

- **Recommendations:**

The committee recommends that the group, or even better, the new institute, hires a system biologist. The science produced by this team is exactly what should be developed in an institute of “integrated biology”.

Team

GENE REGULATION IN SALMONELLA AND ITS PHAGES

Name of team leader:

Ms Nara FIGUEROA-BOSSI

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**2**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

For the five last years, the team focused mainly on small regulatory RNA (sRNAs)-mediated control of gene expression in bacteria. The interest of that team for this domain started with a genetic identification of a set of genes that are under control of Hfq, a chaperone known to be involved in the interaction of many sRNAs with their mRNA targets. This original approach allowed the development of very elegant genetics of the sRNA-mRNA interactions without perturbing the original stoichiometry. Whereas most of the laboratories in the domain use high copy number plasmid carrying sRNA genes to observe an effect on target mRNAs (without real phenotypes), the team was able to develop purely chromosomal genetics with strong phenotypes. This allowed important progresses in the domain. The first recent and important discovery of the group is a completely new mechanism of sRNA regulation. The expression of many sRNAs is regulated at the level of transcription allowing the induction or repression of their targets under specific physiological conditions. The team had the surprise to identify an sRNA repressor whose expression was not regulated but which was able to regulate its targets under specific physiological conditions. The team resolved this paradox by discovering that under specific conditions, *Salmonella* was able to synthesize an RNA that pairs with the sRNA repressor causing its degradation. This, in turn, allows the normally repressed targets to be induced. This result published in Genes and Development (2009) has been the object of “commentaries” in several journals such as Genes and Development, Molecular Microbiology and Nature.

The team made another interesting discovery showing that the transcription termination protein Rho was able to contribute to sRNA silencing. This finding unraveled the ability of trans-encoded sRNAs to act co-transcriptionally (Genes & Development, 2012).

Very recently, the team discovered a new function of the carbon storage regulator protein CsrA, normally a translational repressor, in rho-dependent transcription termination, a conceptually new and very interesting result that has still to be published.

The team produced 14 articles in total, 9 being mainly from the laboratory and including 4 in high-level journals (2 Genes & development, 2009 and 2012, 2 PLoS Genetics, 2011 and 2014). The team was financially well supported with 2 ANR and 2 other grants.

Assessment of the team's academic reputation and appeal

The main appeal and specificity of the team comes from its extremely clever use of bacterial genetics. Most of the work done in other laboratories on sRNAs relies on classical molecular biology techniques. The team is also involved in fruitful collaborations with several laboratories in France and abroad. One of these collaborations is with another group in the Department on Hfq. The latter group will join the new Institute facilitating the collaboration. Another fruitful collaboration is that on Rho transcription termination factor with a group At the Centre de Biophysique Moléculaire (Orléans) that has a strong expertise with in vitro systems, a know-how complementary to the genetic/in vivo expertise of the team. The important number of collaborations (7 total) was and is essential considering the small size of the team (about 4 persons). The members of the team (mainly the two senior scientists) made 9 oral presentations in diverse meetings mostly abroad. They also gave a number of seminars (14) in France and abroad.

Assessment of the team's organization and life

The team is small (about 4 persons) and headed by two senior scientists working with a limited number of non-permanent staff (PhD students/Post-docs/technicians). The two senior scientists are mostly working together on the same projects. The scientific objectives of the team are totally coherent. Their former work on several biological aspects of Salmonella phage biology is now ended and the team is completely concentrated on sRNA biology.

Assessment of the team's involvement in training through research

The two permanent senior scientists directed the work of 4 PhD students during various internships and welcomed numerous (more than 10) other students for different periods of time during the 5 last years. One student presented his thesis work in 2010 (1 Mol Mic and 1 J Bact as first author) and another just finished his thesis work (1 PLoS genetics as first author). Both senior scientists taught a limited number of courses mostly in France. One gave a conference during the Advanced Bacterial Genetics Course in the Cold Spring Harbor Laboratory. Both senior scientists participated to a number of thesis committees in France and abroad.

Assessment of the strategy and the five-year plan

The project of the team is to have a more general understanding of the role of Rho-dependent transcription termination in sRNA-mediated regulation in bacteria and to study other sRNA-regulated systems that where identified with the original genetic screen. From the information available, it is already possible to guess that the outcome will be interesting and original. For instance, the team is working on the a siderophore receptor specific to *Salmonella* and pathogenic *E. coli*, whose regulation appears to depend on two sRNAs (both homologs of RyhB, a well characterized sRNA involved in iron transport and use) and whose translation activation seems to obey to an unconventional mechanism. Even better, the team is proposing that GcvB, another well-characterized sRNA, regulates the expression of a gene encoding an amino-acid transporter by counteracting a translational enhancer. In addition, the recent (not published) results with the new role of the CsrA protein are very exciting. In conclusion, the next years are very promising and no doubt that the team will obtain conceptually new results in the domain of sRNA biology. The team leader is 61 but will be able to continue for the five next years.

Conclusion

- **Strengths and opportunities:**

- This is an excellent and productive team. As mentioned above the strength of the team in the domain of sRNA biology comes from the originality of its approach based on elegant genetics. This expertise is a unique feature in the domain. This approach has huge advantages and seems more prone than usual strategies to yield unexpected results as those described above. It is already possible to predict that the team will continue to produce original results in the next years.

- Although the team is very focused on bacterial genetic techniques, it is able to collaborate with laboratories with a different expertise.

- The planned institute, because of the large regrouping, should favour new interactions useful to this team but also to other teams of the Genome Biology or other departments. The interactions with a team, which will also join the Genome Biology department, should be easier and very fruitful for both laboratories. This team should benefit from this team's expertise in global (e.g. transcriptomic) techniques and also from another team also joining the same department that has expertise in bioinformatics.

- **Weaknesses and threats:**

It is difficult to find any weaknesses in this group. One could consider that the strong focus on genetical techniques is a threat for the future of the team. However, the recently developed collaboration with biochemists in Orléans shows that the group is able to circumvent this threat. Powerful biophysical single molecule techniques have recently yielded interesting results concerning the mechanism of action of transcription termination factor Rho. A collaboration with a group mastering these techniques has not been developed yet.

- **Recommendations:**

As mentioned for other groups, the team would profit from the presence of a system biology team in the department.

Team

RNA SEQUENCE, STRUCTURE AND FUNCTION

Name of team leader:

Mr Daniel GAUTHERET

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**6**	**4**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	4	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

This team is active and successful in its research program into the structure and functions of RNA molecules. The team consists of 4 permanent staff, 1 postdoc, 1 technician, and currently 4 PhD students.

The team has quite a heterogeneous set of research projects (both current and future) but their scientific quality is uniformly excellent. They range from projects that are fairly straightforward but nonetheless valuable (mapping complete sets of RNA species in RNAseq data to genomic loci to characterize sites of processing and initiation/termination), to 'blue sky' projects that are speculative but potentially very exciting (selex-type laboratory screens for synthetic self-aminoacylating RNAs, relevant to the origin of the genetic code). Most of the team's work is computational.

The group is publishing very well, with 18 senior/first author papers during the reporting period. The most prestigious journals they published in are Genome Research (1), Genome Biology (1), Mol Biol Evol (1), and 7 papers in the journals RNA and RNA Biology (both have IF ~5). The team developed and validated novel methods for predicting new small RNAs from bacterial genome sequences, and discovered a new type of interaction involving the 'elbow' of tRNA molecules. They have taken advantage of the boom in RNAseq studies to search for new RNA molecules in a wide variety of species, both prokaryotic and eukaryotic.

The team has been successful in raising grants (2 ANR Blanc, 1 ANR Bioadapt grants listed).

Assessment of the team's academic reputation and appeal

The team has a very good international profile, with several members both receiving many invitations to give seminars and invited conference talks. The PI is on the scientific advisory board for miRbase at the University of Manchester, an advisor to the European Bioinformatics Institute, and a member of an ERC evaluation panel.

The PI is on the editorial boards of two journals (RNA Biology and BMC Bioinformatics).

The team has no difficulty attracting PhD students to join.

Assessment of the team's organization and life

This team is also very central and important to I2BC because it will be the physical home of the Bioinformatics Pole that will provide bioinformatics support to researchers throughout all of I2BC. Administratively, the Bioinformatics Pole is not part of the Department of Genome Biology, but instead is one of the 'transverse' I2BC coordination platforms directly linked to the Data Distribution Service.

Assessment of the team's involvement in training through research

The team is effective in training PhD students. Three students graduated in 2012. Each of these 3 students published 3 first-author papers, which is very impressive. There are currently 4 PhD students in the team.

Members of the team are highly engaged (co-responsible) in teaching bioinformatics at Master's level. This is a very valuable activity for the I2BC because it provides a stream of bioinformatics-capable students, who can interact with many experimental labs in I2BC.

The team also has been involved in organizing international training workshops.

Assessment of the strategy and the five-year plan

The research plan is ambitious and goes substantially beyond the group's current activities. It is a nicely balanced mixture of 'blue skies' (speculative, exciting) and more conservative (grey skies?) projects that have a higher chance of success and are still very valuable. The blue sky project includes the search for self-aminoacylating ribozymes, and a search for mutations in cancer that act via disrupting small RNAs or epigenetic modifications. The conservative projects include sRNA/mRNA interactions in bacteria (collaboration with another I2BC group); RNA-protein interaction prediction; and mapping of RNAseq transcript processing sites.

The diversity of projects reflects the intellectual curiosity of the team into many different aspects of RNA biology. The plan may be slightly over-ambitious but the team's previous track record gives confidence that the plan is achievable and that it will deliver many successes during the next 5 years.

Conclusion

- **Strengths and opportunities:**

- The team is well-integrated into I2BC due to its strong collaborations with other RNA groups in the institute.

- The bioinformatics Masters program (co-responsibility of this team) is an important strength of I2BC.

- The recent recruitment of a CNRS researcher into the group gives it new strength in computational prediction of RNA-protein interactions.

- **Weaknesses and threats:**

The team needs to be careful that hosting the I2BC Bioinformatics Platform does not 'eat' into the team's research activities. However, the Platform needs to have strong links to an active bioinformatics research group in order not to become stale, so this team is a natural home for the platform.

- **Recommendations:**

Given its excellent track record, the team should apply to European research funding schemes (e.g. ERC grant).

Team

MOLECULAR BIOINFORMATICS

Name of team leader:

Mr Alain DENISE and Mr Olivier LESPINET

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions		
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**4**	**4**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	12	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

This team has been working on two main axes. First, it has been involved in the analysis and functional annotation of fungal genomes. It notably developed a method to identify reliable sets of orthologous genes, which can then be used to infer function by homology. The team has been involved in several collaborative projects of genome annotation, to which it brings its expertise in the analysis of enzymatic activities. Second, the team was involved in the development of new algorithms for the prediction and comparison of RNA structures. It also developed a software tool for the drawing and editing of RNA structures (VARNA), which is very successful (114 citations since 2009). Overall the team published 16 original papers as main authors, most of which in good journals of the field of computational biology (2 in Bioinformatics and RNA, 2 in BMC Genomics and BMC Bioinformatics), or theoretical computing (J Comp Biol, *3* in Theor Comp Sci). Software tools described in these papers are made available via web sites. Members of the team also co-authored 14 other publications, which reflect their contributions to collaborative projects. Given the size of the team (1 professor, 2 assistant professors – who all have a heavy teaching load), this is a good productivity. However, citations of the papers published during the period are somewhat limited (except VARNA). Efforts should be made to make their production more visible and to target journals with higher profile.

Assessment of the team's academic reputation and appeal

The team led two ANR projects, which gathered a large part of the French specialists in RNA bioinformatics. One PI was involved in many important committees (CNRS national committee, expert for the French research Ministry, ANR evaluation committees…). He also co-founded and headed the CNRS GdR Molecular Bioinformatics, which plays a very important role for the scientific animation of the entire French bioinformatics community. However the international visibility of the team is relatively modest (two invitations at international conferences for each PI).

Assessment of the team's organization and life

The two group leaders seem to have worked quite independently of each other (none of the team's 29 papers have them both as coauthors). However they now have a PhD student in co-supervision.

Assessment of the team's involvement in training through research

During the considered period, 3 PhD students have been supervised in the team (+ two ongoing PhD thesis). The 2 PIs are both deeply involved in development of teaching programs (deputy director of the Computer Science department of Paris-Sud University; co-founder and co-director of the Master of Bioinformatics and Biostatistics; head of the bioinformatics course of the bachelor of biology…).

Assessment of the strategy and the five-year plan

In 2015, the team will integrate four new members coming from other groups (2 assistant professors, 1 CEA researcher and 1 CNRS research engineer), with expertise in computational biology, modeling and quantitative genetics. The publication track record of some of the new members is not very strong (1 paper in Bioessays and 2 papers in BMC series published as first or last author during the last 5 years). The gathering into a single team of computational biologists who were dispersed in 3 different wet-biology groups seems to be a good strategy to reach a critical mass.

The new team will focus its activity on the study of biological networks, with two main axes. The first is the study of the dynamics and evolution of metabolic networks, and will build up on the expertise of the team in the study of the evolution of enzymatic activities (BMC Genomics 2010). The second project will be to develop computational approaches to model the biogenesis of protein super-complexes, based on data from protein-protein interaction networks. This axis is an extension of a project already initiated by two of the future team members (BMC Syst Biol 2011). It is a bit surprising that the project does not mention collaborations with wet labs (notably to validate their predictions or to put into practice their methodological developments). It is also surprising that the report does not present any project on RNA bioinformatics, given that during the last 3 years, most of the papers published as main author by the team were on that topic.

Conclusion

- **Strengths and opportunities:**

- Extensive expertise in theoretical computer sciences and computational biology, with strong experience in RNA bioinformatics and genome annotation. The new team will reach a critical mass.

- Good capacity to attract PhD students.

- The team regularly obtained funding.

- Establishment of I2BC brings opportunities to establish collaborations with new colleagues.

- Excellent collaborations in fungal genome projects (Broad Institute; GDR Genolevures).

- Co-directorship of the Masters program in Bioinformatics is an important strength of I2BC.

- **Weaknesses and threats:**

- Lack of publications in high profile journals.

- Up to now, limited interactions among team members.

- Future projects a bit fuzzy.

- **Recommendations:**

- Need to create a real synergy among team members.

- Establish collaborations with strong biology wet labs, to put their methodological developments in practice, and make them more visible through publications in high profile journals.

Team

EPIGENETICS AND CANCER

Name of team leader:

Ms Annick Harel-BELLAN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**6**	**5**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	4	4

• Detailed assessments

Assessment of scientific quality and outputs

The PI is a very accomplished and internationally-recognized senior scientist working in the areas of muscle differentiation, cancer, mechanism of microRNA repression, and - more recently - also importance of RNA interference (RNAi) machinery in epigenetic regulation and mRNA splicing in mammalian cells. Many of the publications of the team in recent years represent true breakthroughs in respective area. Just to list two papers published during the previous evaluation period: the Genes and Development 2007 paper reporting translational regulatory role of lin-28; the Nature Cell Biology 2006 paper on a role of miR-181 in myoblasts differentiation. During the 2008-2013 period the laboratory has published 14 experimental papers, six of them as corresponding senior author, and remaining ones representing a collaborative work. Within the formed group (truly "own" papers), the highlight is the 2012 Nature Str. Mol. Biology paper on a nuclear role of Ago proteins in alternative splicing addressing a very timely and important issue of the role of RNAi pathway in the nucleus of mammalian cells. Importantly, also several of the collaborative papers signed by the team are published in high profile journals like Molecular Cell, Cell Reports or Nature Genetics. They all report very interesting findings. In summary, the output and quality of research is excellent.

Assessment of the team's academic reputation and appeal

The team has been very successful and productive. The group was involved in many European or French consortia. For example, it was part of two recent EU consortia, RIGHT and Sirocco, focused on a role of non-coding RNAs, and grouping key European laboratories in the field. Some important collaborations have resulted from this. Currently, the team collaborates with a half a dozen of other groups both in France and abroad. The team was able to recruit talented collaborators, PhD and Master students, and also host visitors and collaborators from other laboratories, many of them from foreign countries (for example, during 2008-2013, the lab was visited by three senior scientists from USA, China and Italy, and also by four students from four foreign countries). The PI is currently acting as an Associate Editor of Mol Cell Biol, an international journal of high reputation. She frequently chairs sessions at national and international meetings, and actively participates in disseminating scientific knowledge at national level for lay people. The team academic reputation is excellent.

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

The team has established collaborations with non-academic partners (Exiqon). The published work resulted in a genome-wide analysis of miRNAs involved in muscle differentiation and in the identification of some novel miRNA targets.

The group has also developed recently many technologies important for identification of miRNA targets (2010 publication in NAR) and also published theoretical papers addressing mechanisms of miRNA function. One patent on identification of cancer biomarkers, has also been co-signed by the team. The PI also has been actively involved in teaching and popularizing science through interviews and events targeting the lay people. Since 2013 the PI is a scientific coordinator for the evaluation of life sciences research units at the National Agency for Evaluation of Research and Higher Education (AERES).

Assessment of the team's involvement in training through research

Three PhD students were present in the lab in 2008-2014. One obtained the PhD, after co-authoring 3 papers. Two other PhD theses are in progress. Eight Master 2 students were also trained during this time.

Assessment of the strategy and the five-year plan

Most of the future projects represent logical extension of the past work done in the laboratory. Particularly interesting and promising are those regarding further characterization of the miRNA role in muscle differentiation, done at the global level, in mechanistic understanding of the role of RNAi machinery in chromatin regulation and splicing in mammalian cells and also in the regulatory role, at the level of translation, of miRNAs and CREB proteins, and their function in proliferation and cancer. These, and also a new project addressing the role of the RNAi pathway in DNA repair are very timely and important. Indeed, regarding the DNA repair project, so far there are only two

papers published on this topic, and the team with its past experience on chromatin and small non-coding RNAs, is in a good position to get new insight into the problem.

The projects are feasible and realistic. Most importantly, however, they are all exciting and timely.

The PI will be retiring in three years. The team will be disbanded at that time. Current group members are already informed of these plans.

Conclusion

- **Strengths and opportunities:**

Very competitive and successful group. Its very broad expertise in a whole range of topics and methodologies guarantees further success in experimenting. The planned research offers many new opportunities to contribute novel original findings.

- **Weaknesses and threats:**

The PI will be retiring in three years and obviously some of the planned projects might not be completed by that time.

- **Recommendations:**

The closing down of the team will have to be prepared with current team members (as already initiated by the team leader), so as to anticipate their re-orientation while maintaining a fruitful research activity for the next three years.

Team

POST-TRANSCRIPTIONAL REGULATION OF GENE EXPRESSION

Name of team leader:

Ms Anna POLESSKAYA

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**2**	**1**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The group is relatively young. For many years its PI was a member of another group in the same Department, and during that time she was one of the driving forces behind studies related to the role of microRNAs in differentiation and translational control in myoblasts (for example, the first author of the paper in Genes & Development, 2007). Since becoming independent in 2008, the team has published seven experimental papers, three of them as a first or as a corresponding senior author. These three are represented by the Mol Cell Biol 2010 paper, the Oncogene 2013 paper, and a recent PLoS ONE 2012 first author paper, describing the work still done in collaboration with the other group. In the PLoS ONE paper, a genome-wide identification of miRNAs involved in muscle differentiation is described, and several novel mRNAs targeted by miRNAs in muscle cells are also reported. Within the collaborative work, are papers published in J Biol Chem and Nature Communications, two journals of high reputation. In the two above-mentioned publications representing key contributions (Mol Cell Biol 2010 and Oncogene 2013 neither co-authored by the PI of the other group), the team addresses a new topic, on a role of IMP/IGF2BP (Insulin-Like Growth-2 mRNA-binding) proteins 1, 2, and 3 in post-transcriptional regulation of cyclins in cancer cells and also their role in muscle cell mobility. These are very interesting and solid papers. Particularly, the observations published in Oncogene open many interesting questions related to the role of the rather little studied IMP-3 protein in post-transcriptional regulation and also to the role of nuclear regulation in determination of the cytoplasmic fate of mRNA. Interestingly, they have found that IMP-3 in cancer cell lines translocates to the nucleus, and this localization is essential for the post-transcriptional regulation of cyclin mRNAs. The role of RNA-binding proteins in post-transcriptional regulation and their crosstalk with microRNAs represent currently one of the hot areas of research in gene expression. Clearly, the two aforementioned papers together with additional publications position this team very well within international community interested in post-transcriptional regulation and cancer.

Assessment of the team's academic reputation and appeal

As already mentioned above, the team, though relatively small, is productive and also both nationally and internationally active in terms of participating at meetings and presenting their work there in terms of invited oral communications. The group publishes in good quality journals and is involved in a couple of national and international (Brazil, Denmark) collaborations.

Assessment of the team's organization and life

The team still has no independent outside funding and relies on a small budget from CEA and on financial support of the group of with which the PI was previously associated. Hopefully, this situation will change since the team is waiting at the moment for a decision regarding two grant applications.

Assessment of the team's involvement in training through research

As based on the report on teaching/training activities, the team is performing very well. In 2008-2013, the team leader has independently supervised three PhD students. One PhD has already graduated, after publishing – as a first author – a paper in MCB. The thesis work of two other students is in progress, one of them having already published a first author paper. In the past five years, she also supervised 2 BTS, 3 L3 and 4 M2 students. She participated in six PhD examinations and served on one PhD committee as an expert. Overall, this is a very good record.

Assessment of the strategy and the five-year plan

The proposed research is logical and exciting though one would expect more detailed outline of the experimental approaches and also specifying alternative solutions to the strategies the team is planning to use. The preliminary data presented in the report and in plans for the future clearly indicate that IMP-3 is able to determine in the nucleus the translational competence of mRNA in the cytoplasm. In addition, IMP-3 may execute this function while in a complex with several other RNA binding proteins (RBPs). Moreover, IMP-3 appears to determine susceptibility of several mRNAs to microRNA-mediated repression. These are all very interesting lead findings. The team is planning to concentrate on IMP-3 and molecularly explain the aforementioned observations. How is the mRNA translationability determined in the nucleus? What is the role of IMP-3 and other RBPs? How is this complex transported in association with mRNA to the cytoplasm? How does it affect miRNA-mediated regulation? These are all questions of great general importance and it is clear– based on the project description and past experience of the team – that some of these questions will be successfully answered.

Conclusion

Small but very successful group, and its research should be given continued support. It is also very good that the PI research is now almost exclusively focused on her truly own project (IMP proteins), which is both important and exciting. In this way, although the team might also in the future collaborate with the other group, it is gaining its own scientific identity.

- **Strengths and opportunities:**

Broad expertise, strong links with and support from the other group, and interesting preliminary results and working hypothesis.

- **Weaknesses and threats:**

Small size of the group and no specific outside funding.

- **Recommendations:**

It is very essential that the team obtains in a near future its own independent external funding through independent grants.

Team

PROTEASOME: ASSEMBLY, REGULATIONS AND FUNCTIONS (PARF)

Name of team leader:

Ms Anne PEYROCHE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**5**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team has focused on the DNA damage response in yeast, uncovering new factors of the Rad53 kinase pathway. Interestingly, this work has revealed new links between the DNA damage response and the ubiquitin-proteasome system that mediates regulated protein degradation in eukaryotes.

These discoveries are of major importance and general interest since the proteasome is emerging a key target for anticancer chemotherapy.

The work performed by the group is clearly basic research. It is original and groundbreaking. Although the amount of publications produced within this period is relatively low (4 publications), their scientific impact is very high and they generally appear in excellent journals (including Mol Cell, PNAS). The proteasome field is highly competitive but they seem to be well positioned to face this competition and the link with DNA damage is novel and exciting.

Assessment of the team's academic reputation and appeal

The team is very good at attracting post-docs (3), PhD students (3) and non-permanent technician (1), mostly paid on their own contracts. This indicates that the academic reputation and appeal of the team is very good.

The team leader rarely presents the team's research at international meetings. The team has collaborations with French groups and groups in Germany and in the US, and has been very good in getting fundings for their research (the team leader has an ANR JCJC until 2014 and is supported by the ARC).

The group leader contributes to editorial work and grants reviewing at a reasonable level and got two French academic research prizes during this period. There is no apparent editorial responsibility or contribution to the organization of international events. The group leader is part of several committees, including the "CNRS comité national (section 21)", which represents an important administrative responsibility at the national level. The PI should be commanded for this level of implication.

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

The team leader contributed to several scientific events intended for a large public audience.

Assessment of the team's involvement in training through research

Although the group leader is DR CEA, he is significantly involved in teaching. In addition, she actively contributes to the management of the doctoral school, as member of both the scientific committee and the directory. In addition, she contributes to several thesis committees and juries.

The team is highly attractive in recruiting PhD students and the PhD students from the group publish well.

Assessment of the strategy and the five-year plan

The project aims at exploring the assembly and organization of the proteasome, to identify new pathways involving the proteasome and to demonstrate how proteasome functions are modulated or regulated in response to DNA damage. The work will be performed in yeast and extended to mammalian cells when possible. The project for the next five years is in agreement with previous work by the team and may lead to major discoveries in the field. Exciting preliminary results have already been obtained that have groundbreaking potential. The project is very well structured, challenging and feasible.

Conclusion

- **Strengths and opportunities:**

- The overall scientific quality of the research conducted within the group is excellent and of general interest.

- The proposed research project is very interesting, challenging and fits well in the Genome Biology department

- Joining the I2BC will be a great opportunity for the team's visibility and to initiate new collaborations

- The team is very attractive for students and post-docs and has been well supported financially.

- **Weaknesses and threats:**

- Productivity of the team strongly relies on non-permanent staff and thus on the ability of the group leader to get grants

- The group members do not participate in many international conferences.

- **Recommendations:**

As stated above, the scientific productivity of the team relies mainly on non-permanent researchers. To ensure continuity of the scientific quality of the group, the group leader should get support from permanent staff, preferentially researcher or university teacher.

Team

PROTEIN MATURATION, CELL FATE AND THERAPEUTICS

Name of team leader:

Ms Carmela GIGLIONE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	4	4
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	3
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**11**	**10**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The team's main interest concerns the molecular mechanism of N-terminal protein modifications, its cellular role and its impact on protein destiny. The model organism mostly used is *Arabidopsis thaliana*. The work carried out in this group is groundbreaking and is clearly occupying a foremost position within this research field.

This is a highly productive team (24 publications and 2 book chapters) with high impact papers of general interest generally published in excellent journals (PLoS Biology, 4 Plant Cell, plus 1 Science in collaboration). In most cases, members of the team do appear as first and last author, which is remarkable. In addition, the team has very productive collaborations at both national and international levels.

The international visibility and impact of the group is thus excellent.

Assessment of the team's academic reputation and appeal

The team members are regularly invited to present their work at international conferences and the team leaders have been involved in organizing the international Jacques Monod conference on translating ribosome in 2012. In addition, the team was involved in several scientific consortium and programs to facilitate the development of technical platforms and recruitment of new people.

Team members regularly contribute to editorial works and grant reviewing and are editorial board members of several journals, especially journals specialized in proteomics. In addition, they have some administrative responsibilities at the national level, including CNRS selection committees.

The team was very successful in attracting post-docs (7 post-docs), PhD students (4), visiting scientists from abroad (2) and permanent researchers (3). In addition, the team leader is principal investigator in several financially supported projects.

The reputation and appeal of the team is thus excellent.

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

Although not directly involved in drug development, part of the proposed work concerned a better understanding of the interactions between peptide deformylase (PDF) and its inhibitors, thus potentially providing future application of their research in the drug development field. The fact that both senior scientists are involved in consulting for GlaxoSmithKline might bring some interesting perspectives in such direction. To date, there is no patent application or other non-academic partners described in the report.

Contribution of the team to the French scientific community at the organization and administrative level is highly significant. A senior member being prefigured director of the future I2BC significantly contributes to the dissemination and transfer of knowledge and technology and has the ability to regroup different scientific fields to favor the emergence of new research at a very large scale.

Assessment of the team's organization and life

The team is composed of 7 permanents (2 DR CNRS, 2 CR CNRS, 2 ITA CNRS, 1 University teacher) and 5 non-permanents including 2 post-docs, 1 PhD student, 1 DR-Emeritus and 1 visiting Professor form Israel.

The team is well structured with coherent scientific objectives and good financial support. Cooperation between senior members seems to function very well, thus allowing the futur director of I2BC to take up the direction in good conditions. Although not a typical "Genome Biology" type of group, the team is interested in integrating cellular protein modification at a large scale and assimilation in the proposed Genome Biology department seems appropriate.

Assessment of the team's involvement in training through research

The team is very good in recruiting PhD students (4) and all the PhD students from the group published as first author. The team members contribute reasonably well to teaching and training of master students, and regularly participate to PhD juries and thesis committees.

Assessment of the strategy and the five-year plan

The research project proposed is a basic research based project. It aims at characterizing in details the N-terminal modifications of proteins, including the N-terminal methionine excision, N-Myristoylation, N-α-acetylation and S-palmitoylation both *in vitro* and *in vivo* in *A. thaliana* and in human cell lines and in bacteria. Interplay among processing enzymes and other ribosome interacting factors will also be investigated.

The experiments proposed are in full agreement with the team's expertise. The project is well structured, original and based on highly innovative approaches. It is a nice mixture of safe and more risky tasks that seem feasible within the time period, with respect to the team's size and the proposed collaborations outside and inside the I2BC.

Conclusion

- **Strengths and opportunities:**

- The scientific quality and productivity of the research conducted is excellent and of general interest. It is an attractive mixture of explorative basic science and innovative technology

- The team is very attractive for students and post-docs, well supported financially and its international visibility is strong

- Contribution of the team to the scientific community at the organization and administrative level is highly significant.

- **Recommendations:**

- Some of the group's discoveries may lead to important applications and team members might consider creating or consolidating links with non-academic partners

- Revealing interplays among processing enzymes and other ribosome interacting factors will be a major challenge for the team to address.

Team

PHYSIOLOGY AND PATHOGENICITY OF STRESS (PAPS)

Name of team leader:

Mr Stéphane CHÉDIN and Mr Laurent KURAS

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	5	5
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**10**	**8**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The team is a fusion of two previously existing teams, referred to as Team 1 and Team 2. The research direction will change slightly upon the merger, but until the merger occurs, each group plans to finish up ongoing projects.

Team 1 is interested in the cellular impact of various stress conditions including toxic metals, ionizing radiations and exposure to oxidants, using the yeast *Saccharomyces cerevisiae* as model organism. In this case, standard physiological and biochemical methods as well as more global –omics- or mathematical modeling approaches are used. In parallel, the group also developed computational applications for regulatory networks prediction in the cyanobacteria *Synechocystis*, in collaboration with another team team at CEA.

Globally, Team 1 was productive with 19 publications in total, 11 of them being signed by team's members as first and/or last authors. Publications generally appeared in well-respected journals for a broad (Mol. Cell, NAR, J. Biol. Chem., Plos One, PNAS) or a more specialized audience (Proteomics, Bioinformatics, Eukar cell, Mol. Microbiol). In addition, the team has productive collaborations at the national and international level.

The team 2 leader and his colleagues have been interested in two main subjects: i) the role of Met4, a transcription factor that regulates the *MET* gene network, involved in the synthesis of sulfur-containing molecules including methionine, cysteine, S-adenosylmethionine, and glutathione (GSH) and ii) the function of mediator in basal and activated transcription. In the past few years, they have studied the cellular response to the toxic metal cadmium. Cd^{++} induces the *MET* gene network to produce GSH, a well as an isoform of pyruvate decarboxylase (encoded by the *PDC6* gene) containing less sulfur than the regular enzyme. They showed that induction of *PDC6* is under the direct control of Met4 and its cofactors, but requires higher concentrations of Cd^{++} for activation as compared to other Met4 targets. Indeed, the pyruvate decarboxylase *(PDC6)* gene promoter contains only non-canonical Met4 binding sites. Thus, different Met4 targets can be activated at different concentrations of Cd^{++}. It is not clear, however, how this is achieved mechanistically.

The mediator is known to be required for activated transcription, but its role in basal transcription has been less well documented. The team 2 showed that in a setting of activator bypass (by artificial tethering of TBP or TFIIB to an artificial promoter), the mediator was still recruited to the promoter, and inactivation of Med17 led to a decrease in transcription, indicating that the mediator is, in fact, part of the basal transcription machinery. In another project in collaboration with the another group of the Department, the team is generating ts mutants for each of the mediator subunits. They have obtained a series of ts mutants for the Med21, Med6 and Med14 subunits and observed, for each subunit, different transcriptional defects.

Team 2 has published two papers in NAR since 2009 (2010 IF=7.8, 2012 IF=8.3), both with the team leader as senior author, which is a good output. In each case, the publications are of high quality, addressing a well-defined question and providing a clear answer.

Assessment of the team's academic reputation and appeal

Team 1 was relatively successful in attracting post-docs (3) and PhD students (2). The team has been successful in getting grants for their research, both from public and private sources. In addition, they have been very good in getting financial support for interdisciplinary programs of the CEA. Although team members regularly attend international conferences, the two group leaders do not seem to represent their team or be invited outside France.

The team 2 leader presented his work in poster presentations at three international conferences. He was part of an "ANR Programme Blanc", with the PI of the group they collaborate with as the coordinator, from 2009 to 2011. The team also obtained a one year contract with industry to generate a collection of genetically modified yeast strains, with the aim of generating strains overproducing methionine. However, they do not list grants for which they are PIs.Tthey plan to finish the mediator subunit work on money still left from the contract with industry, and they have submitted a new ANR project but it is not yet known whether it will be funded.

The academic reputation and appeal are considered good.

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

The team members contributed to several scientific events intended for schools and large public audience, including “Fête de la Science”.

Although the outcome of their work is mainly basic knowledge, the team leaders have developed connections with industrial partners.

The team had a nice interaction with industry in that it obtained a contract with Adisseo to generate a collection of 150 yeast strains, which was completed.

Assessment of the team's organization and life

Team 2 will fuse with Team 1, which is presently composed of 6 permanents (4 researchers CEA, and 2 technicians CEA, one being at 50%) and one post-doc. In the context of the future I2BC, one of the CEA researchers, the computational biologist will leave the team to join another team of the Department. It is proposed that the present team will merge with Team 2, which is composed of two permanents (1 researcher CR1 CNRS and 1 technician TCS CNRS).

-The departure of the computational biologist from Team 1 is logical since the research topic developed by this researcher was not related to stress response in yeast.

-The fusion with Team 2 is very coherent since both teams have clear common interest in gene regulation in yeast under stress and strong complementary expertise.

-The main challenge will be to establish a viable co-leadership for the group on a long-term basis.

-The plan to fuse and reorganize the team was thus considered excellent.

Assessment of the team's involvement in training through research

Team 1 does not have heavy teaching loads but some members do contribute, especially to practical courses. The team is involved in training master students, participates to PhD juries and thesis committees. The 2 PhD students from Team 1 published well as first authors. The Team 2 leader has trained 1 PhD student, who defended in 2008 and published a co-first author paper in 2010, as well as 5 master students and one Licence student. He has also been part of some thesis juries. The training through research is thus excellent.

Assessment of the strategy and the five-year plan

The Team 2 leader plans a short term project, and then an immediate collaborative project together with Team 1 as well as a long-term collaborative project. The short-term project concerns the role of various mediator subunits in transcription. More specifically, the Team 2 PI will take advantage of the already developed system in which TBP or TFIIB is directly tethered to an artificial promoter (including the inducible, Met4-regulated *MET17* promoter) to determine whether tethering can compensate for mediator mutations that affect transcription activation by specific activators (mostly tail mutations). In addition, the analysis of the already obtained ts mutants (in Med6, Med14, and Med21) will be pursued, with particular emphasis on mutants in Med6, which is at the junction between the Head and Middle modules, and in Med14, at the junction between the Middle and tail modules. RNA Seq will be performed to determine the genome-wide effects of the various mutations.

The short-term project of Team 1 is directly linked to their previous observation showing that a minimal level of GSH is essential for cell viability in response to oxidative stress. More specifically, they wish to understand why activation of Rad53 is reduced upon GSH depletion be investigated and to decipher the antioxidant mechanism of GSH.

The collaborative project focuses on understanding the network of gene expression governing the regulation of the glutathione cycle. Glutathione synthesis from cysteine is regulated by GSH starvation, oxidative stress, exposure to cadmium, and exposure to repressive amounts of methionine, and at least two main transcription factors are involved, Met4 and the activator of the oxidative stress response Yap1. However, the detailed mechanisms of how these factors interact and act on various promoters are unclear. In collaboration with Team 1, Team 2 proposes to elucidate this network, with Team 1 concentrating on defining expression levels (with transcriptomics and

proteomics) and sulfure fluxes, whereas Team 2 will focus on transcription mechanisms (recruitment of transcription factors, role of mediator).

The long term collaborative project will pertain to the study of physiological transitions at the levels of transcription, translation, and enzyme activity levels, in response to stress. The fused teams will first concentrate on sulphur metabolism, but the exact aims will be defined at a later time, as the glutathione work is more advanced.

The short term project is in direct continuation of the work in progress and takes advantage of the strengths of Team 2. It is highly feasible and will undoubtedly bring interesting results. The study of the glutathione cycle is an exciting project, and the division of labor between the Team 1 and 2 seems realistic and highly likely to result in the active involvement of the two groups. The long-term research will be based on the results of this glutathione cycle study and is not well outlined in the report.

As a result of the uncertainty concerning the long-term collaborative project, the strategy and future plans are considered very good.

Conclusion

- **Strengths and opportunities:**

- As stated above, the proposed future team is the fusion of two teams with strong expertise in yeast genetic, molecular biology and physiology. The research topic dealing with the cellular impact of stress is important and concerns a large audience of scientists. There is a clear common scientific interest and the reunion of both teams is an added value for future studies

- Team 1 was well supported financially

- The fusion of Teams 1 and 2 will increase the size of the group, which is good, and will allow a more rounded approach to the problems studied, as a result of the different but complementary competences of the two groups.

- **Weaknesses and threats:**

- The team was involved in many projects, some of them being rather unconnected, thus weakening productivity on their main research topic. This could affect scientific impact and visibility on a long-term basis.

- The uncertainty concerning the long term collaborative project, the strategy and future plans

- Team 2 leader does not seem to be involved in teaching (laboratory courses or ex cathedra courses), which may make it difficult for him to be known among bright students seeking to do a PhD

- The funding of Team 2 will need to be secured.

- **Recommendations:**

- To ensure the scientific quality and productivity of the team on a long-term basis, the group leaders will have to rapidly work together and focus on their joint new research topics involving all lab members. Effort to recruit postdocs and PhD students should be made.

● Department of Cell Biology

Overall assessment of the department

The Department of Cell Biology headed by Mr Renaud LEGOUIS is composed of 13 groups. The teams develop projects aiming at deciphering cellular compartimentation and communication (major aspects by 7 teams) as well as signaling, stress, metabolism and adaptation (major focus of 6 teams). 11 teams were evaluated and 2 were created too recently to be assessed. One of the evaluated groups will be joining another team within the department during the next 1-2 years, therefore 12 groups are thought to compose the Cell Biology Department at I2BC.

The groups have an outstanding (2), excellent (9) to very good (2) scientific output. 3 teams can be considered outstanding as for their reputation, appeal and international recognition. The gathering of the groups together within a single department will certainly be an asset for increasing the general international visibility. Some teams are already collaborating, for example the plant, or mitochondria groups, but there are also transverse collaborations between groups investigating plants, mammalian cells, model organisms. Synergy between projects and sharing of knowledge for studying different organisms could be appreciated by the committee.

Strengths and opportunities related to the context

The projects carried by the groups within the department can be considered outstanding to excellent. Therefore there is a good ground for building a department where excellent science is carried and that can be attractive at the national and international levels. Some groups have already started collaborations and show the need for gathering forces together. The Cell Biology Department will be contributing to the integration of all I2BC departments through the presence of several groups that collaborate across departments and especially through one group that is heavily involved in imaging development and service. This needs to be acknowledged and organized during the transition period.

Weaknesses and threats related to the context

The science carried within the department is excellent and internationally competitive but the committee could appreciate the fragility of some groups because of difficulties in funding or for lack of technical help. Some groups although outstanding or excellent have a real lack of international visibility.

The current geographical distribution is not optimal for promoting more direct interactions and also for starting weekly department seminars in 2015. The department would benefit from the recruitment of dynamic young group leaders with complementary expertises. This will certainly take place when the groups are physically located and the priorities settled. Efforts should be made to attract scientists with appropriate support for starting groups.

Recommendations

Efforts should be made to solve at the best the lack of technical help of some groups. Although meetings are already organized, a scientific council of the department with different representatives (named and elected) could help to improve communication during this period.

Team

FUNCTIONS AND DYSFUNCTIONS OF MITOCHONDRIA

Name of team leader: Ms Agnès DELAHODDE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**8**	**8**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

This research group results from the fusion of two IGM teams.

Team 1:

This team investigates different aspects of mitochondria biology in yeasts and, more recently, in worms. Over the past 5 years, this team has further investigated the regulation of mitochondria morphology and/or activity by the DeUBiquitinase (DUB) Rpn11, a subunit of the proteasome (note: the function of Rpn11 has initially been worked out by T. Rinaldi, 'La Sapienza', Roma). Analysis of specific rpn11 mutant alleles in yeast has provided evidence that Rpn11 regulates the assembly and stability of the 26S proteasome (as well as the formation of proteasome storage granules; PLoS ONE 2013) and also regulates mitochondrial fission (by an as yet unknown molecular mechanism; J Cell Sci 2009). The team has also been involved in a collaborative network aiming at identifying human genes associated with mitochondrial diseases. In this context, the team has focused on the identification of genes involved in mtDNA stability and/or maintenance in yeast and worms. The scientific production of team 1 is good (5 papers signed as first and/or last author including a J. Cell Sci 2009).

Team 2:

This team has mostly used fungi (*Podospora anserina*) to investigate the role of translation (using as an entry point a mutation in the S15 subunit of the cytosolic ribosome) in mtDNA stability with the aim of understanding at the molecular level how defective translation impinges on mtDNA stability. Another aspect of the work of the team concerns the characterization of novel nuclear genes encoding mitochondrial proteins in yeast and fungi. In this context, the function of the mitochondrial protein Lon was investigated. The scientific production of the team 2 is good (4 papers signed as first and/or last author including a PLoS ONE 2012).

Both teams are relatively small and appear to have retained, perharps for historical reasons, a relatively diverse set of questions. As a result, questions of high significance (molecular links between mitochondrial activity/morphology and protein synthesis/degradation) have been difficult to address such as to have a big impact in this field.

Assessment of the team's academic reputation and appeal

Despite their expertise, both teams have a relatively limited international visibility (no meeting/lecture invitation of the PIs since 2011). Nevertheless, the group was contacted by a US team headed by Marion Schmidt to conduct collaborative research and one international post-doc joined team 1 with an international fellowship (Bologneti fellowship from the IP Roma). National visibility of team 1 is very good based on its participation to active research networks that were awarded ANR (2009-12), FRM (2011-13) and AFM (2014-18) grants.

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

A member of team 2 is actively involved in a Vocational Training module on qPCR directed towards research institutions and companies.

Assessment of the team's organization and life

This criterion does not apply to a team of this size. The leadership and organization of the new team born from the merge appear excellent. Otherwise, the IGM website is clear and the pages for these two groups are clear and up-to date.

Assessment of the team's involvement in training through research

The new research group comprises 2 assistant professors (Maitres de conférences: MC) (Paris-Sud and ENS). Additionally, the PI (who holds a non-University position) also actively participates in teaching. This team therefore offers a good balance between teaching and research activities.

Assessment of the strategy and the five-year plan

The new group resulting from the fusion of teams 1 and 2 has three research objectives. A first line of research investigates mtDNA stability and maintenance in yeast, fungi, worms and humans. A chemical screen will be performed in mutant yeasts and active compounds identified in this screen will be futher tested in other model organisms, including human patient cells in the context of a consortium. The issue of mtDNA heteroplasmy will also be investigated, first in fungi, then in worms. The role of Rpn11 in the regulation of proteasome activity will be further investigated, mostly in yeast. Finally, new genes involved in the function and regulation of the respiratory chain will be identified in worms by RNAi screening.

A clear strength of the new group is its expertise in a wide range of model organisms and its integration into a research network addressing questions of direct relevance to human health. To better exploit this strength, the new team might consider focusing its activities on a more limited set of well-defined and outstanding question of fundamental and/or clinical interest.

Conclusion

- **Strengths:**

A clear strength of the new group is its expertise in a wide range of model organisms and its integration into a research network addressing questions of direct relevance to human health. Also, integration of the new teal into the Cell Biology Dept will bring new opportunities for sharing expertise and resources with groups working with yeasts and worms.

- **Weaknesses and threats:**

The proposed research project appears somewhat too diverse (in terms of questions, not in terms of model organisms) for the new group to really benefit from the increase in critical mass. At this stage, it is not clear whether the new group emerging from the fusion will be more competitive and attractive internationally than the sum of its parts.

- **Recommendations:**

While maintaining a diverse set of research lines looks appropriate in a transition period following the merge of the two teams, it is recommended to strengthen the synergy between the two teams. Limiting the number of research topics should help increase the visibility and attractiveness of the new team.

Team

BIOGENESIS AND FUNCTIONING OF MITOCHONDRIAL OXPHOS COMPLEXES IN YEASTS

Name of team leader: Ms Nathalie BONNEFOY

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	1
N2: Permanent EPST or EPIC researchers and similar positions	5	4
N3: Other permanent staff (without research duties)	3	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**11**	**8**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	4	4

Assessment of scientific quality and outputs

This team is one of the examples of a new group resulting from the fusion of two pre-existing teams. This results in a very coherent group focused on the understanding of the genesis and functioning of mitochondrial OXPHOS complexes. The general biological problem of major interest raised by the genesis of these complexes is the dual origin of their components: a few subunits encoded by the mitochondrial DNA and synthesized within mitochondria, and the majority of the other subunits encoded by the nuclear genome, imported into mitochondria, and assembled. Biogenesis of OXPHOS complexes is controlled at multiple levels: expression of mitochondrial-encoded proteins is regulated by specific translational activators, some of which identified by team members (NB) that bind mitochondrial mRNAs. Multiple factors have been identified that are required for assembly of the various subunits of the OXPHOS complexes, including some identified by group members (GD). A tight coupling exists between synthesis of the various subunits, and their subsequent assembly. The different members of the team have already contributed significantly to document some of the relevant questions in this field. The team masters all the approaches used to study S. cerevisiae mitochondria: genetic (nuclear and mitochondrial), genomic, system biology, biochemistry. Notably, they are among the very few labs able to perform biolistic transformation of mitochondria (only 14 publications in PubMed, including 5 signed by group members). They are also among the rare labs that introduced the use of S. pombe as an alternate model organism to study these questions. S. pombe has several particularities making it as an attractive model: it is a “petite”-negative yeast (mutants impairing mitochondrial gene expression do not loose their mitochondrial DNA, unlike S. cerevisiae). In addition, the mitochondrial DNA of S. pombe is closer in several aspects to that of human cells than that of S. cerevisiae. The use in parallel of these two yeast models is one of the strength of the team and already proved fruitful.

One of the recent contributions of the team to the study of mitochondrial gene expression is a genome wide study in S. pombe that led the team to identify nine pentatricopeptide (PPR) proteins (proteins carrying 34 aminoacid tetratricopeptide repeat (TPR), a motif binding RNA), all located in mitochondria, required for efficient respiration, involved in general or specific translation of mitochondrial-encoded proteins. Interestingly, two of these proteins, playing opposite role in the expression of Cox1 mt-RNA are the possible homologs of the LRPPRC involved in a human disease.

There is a longstanding interest in the team for the nuclear-encoded factors involved in assembly of the OXPHOS complexes. They had studied for years Oxa1, a factor embedded into mitochondrial inner membrane required for assembly of three OXPHOS complexes. In the absence of available cristal structure of the protein, a systematic mutational analysis and a search for intragenic compensatory mutations led them to reveal interactions between hydrophobic segments of the protein and hydrophilic loops, and to identify regions having differential effects on the assembly of various OXPHOS complexes. A similar systematic mutational study of the AAA domain of the chaperone Bcs1 (essential for the last step of OXPHOS complex III assembly) allowed modeling the structure of yeast and human Bcs1, the latter mutated in several human diseases. Furthermore, in a brilliant study, they showed that ATP-dependent activity of Bcs1 is a way to couple the rate of complex III biogenesis to the energy-transducing activity of mitochondria.

Other members of the team focused on a structure/function analysis of the assembled OXPHOS complexes, notably OXPHOS III, target of drugs used to impair the proliferation of parasites such as Plasmodium falciparum. They identified the residue in cytochrome bc1 involved in binding to the potent inhibitor HDQ of Plasmodium falciparum growth. They developped an interesting easy colorimetric test allowing screening of chemical libraries for inhibitors of respiratory function, that already allowed identification of new inhibitors.

The overall activity of the team during the 2008-2013 period is very impressive, with a long list of publications (43! among which 22 with PIs as last authors, the other being in collaborations) in good (IF around 5) to very good international journals (IF around 10) such as J. Cell Biology, Plos Genetics, PNAS,. Two of the PIs were invited (together with well-known scientists in this field) to publish reviews in several special issues devoted to various aspects of mitochondria (2009, 2013). Another PI also contributed to important reviews in the field.

Assessment of the team's academic reputation and appeal

Each of the PIs of the team has ongoing collaborations with several French (Paris, Bordeaux) and international labs (Poland/UK/Sweden/Belgium/Germany/USA…), illustrating their excellent international reputation. Some of these collaborations are performed within European networks coordinated by PIs of the team.

Additional proof of the attractivity of the team are the invitations as speakers in international meetings, or the fact that two of the PIs (as well as another group member) received foreign PhD, post-docs and visiting scientists.

Three of the team members organized two French meetings, and one of the PI was one of the organizers of an international conference (2011).

The three PIs are involved in institutes (AERES) and grant evaluations (several private foundations). An additional illustration of the excellent reputation of the team is the fact that four team members are reviewers for multiple high level international journals.

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

Two of the PIs of the team are actively involved in popularisation of science (annual participation to “la fête de la science”, regular lectures for primary/middle and high schools).

Assessment of the team's involvement in training through research

The team is very active in training through research. Seven international students, 1 L2, 3 L3, 3 M1, 3 M2 and 8 PhD students (among which 6 already attended) were received for training. These students were trained mainly by 4 team members, a 5th one also participated by receiving an ERASMUS student. Importantly, 12 publications of the team were signed as first authors by PhD students.

Last but not least, four team members are frequently requested to participate to PhD jurys (16 as reporters) and HDR jurys (4).

The team participated for three years within the doctoral school GGC to the organization of one week course on “Mitochondria”.

In addition to this participation in training within the French system, that includes the work of one member of the team as a teacher (heavy teaching plus responsibility in recruitment committee), or that of another member in M1 jury, it must be underlined that the group leader participated to a high level international practical course (EMBO course, 2012).

Assessment of the strategy and the five-year plan

The project presented by the team will be a continuation of prior studies, made using all the methodological tools mastered in the team, that already proved to be fruitful in the identification of factors involved at various steps of the biogenesis and functioning of OXPHOS complexes.

If the global function of the mitochondrial PPR proteins of S. pombe have already been identified, the precise mechanisms underlying the function of these proteins remains to be documented, and their partners identified. The team will also investigate the basis of the unexpected link between proteasome function and mitochondrial energy production. They propose to determine the “PPR-RNA binding code”, and the committee thinks they have the know-how, knowledge of the field and ongoing methodological and conceptual progresses to achieve their project.

One interesting feature of the assembly of OXPHOS complexes, is the formation of supercomplexes, a point yet poorly documented, that will be addressed, notably in connection with the translation of mitochondrially-encoded subunits. The interesting role of Bcs1 in mediating a link between the intra-mitochodrial pool of ATP and the regulation of complex III biogenesis will be further documented by the whole panoply of genetic approaches mastered by the team.

Finally the structure function of complexes II and IV will be further documented in two main direction: studying, using yeast as model system, the differences between yeast/human P. falciparum enzymes, with the aim to characterize antimalarial drugs, and to find new drugs. A second study developed within an international collaboration will be devoted to characterization of the non-catalytic subunits of cytochrome oxidase that display multiple isoforms. No doubt that the team has the know-how to humanize yeast cytochrome oxidase for a structure/function analysis of these isoforms.

This five-year plan is devoted to interesting questions, including one with potential medical applications. There is no doubt that these projects can be studied using the vast panoply of approaches mastered by the team.

Conclusion

- **Strengths and opportunities:**

The past work and the project of the team constitutes a brilliant continuation of the fruitful research on mitochondria biogenesis and functioning using yeast as a model organism, historically developed in Gif by well-known scientists. In addition to the traditional use of *S. cerevisiae*, the team is among the few labs also using as a model organism *S. pombe* for the study of specific questions, and the parallel use of these two model systems appears very fruitful. In addition to fundamental research, the team included some potentially applied projects. The team was very productive during the last five years, and recognized by the French and international communities (collaboration with scientists from several countries (European and American), involvement in several French and European networks, several PI reviewers in many good international journals. The team was able to perform excellent research, together with a strong investment in training by research, and to obtain financing.

- **Weaknesses and threats:**

No obvious weaknesses were detected.

- **Recommendations:**

The recommendation to the team is to go on their way…

Team

BIOGENESIS AND FUNCTION OF CENTRIOLAR AND CILIARY STRUCTURE

Name of team leader:

Ms Anne-Marie TASSIN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	4	4
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)	2	2
TOTAL N1 to N6	**9**	**9**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	4	4

• Detailed assessments

Assessment of scientific quality and outputs

The team is a fusion of two groups, one originally from the Institute Curie Orsay (Team 1) and one from the CGM in Gif-Sur-Yvette (Team 2).

Team 1 has been employing mammalian cell culture models to investigate centrosome and centriole biology. They published a senior author cryoEM paper uncovering new insights into the initial structural events governing procentriole assembly (EMBO J, 2010; 29 citations), and contributed to a collaborative study with a group at the Centre de Recherche en Cancérologie de Marseille on the role of the FOP-FGFR1 kinase in recruiting PI3 kinase and phospholipase C-gamma to the centrosome (Mol Cancer, 2008). The group also has exciting submitted work (now in revision in Nature Communications) on a novel ciliogenesis role for the tumour suppressor CYLD deubiquitinase at the centrosome.

Team 2 has been using the single celled multi-ciliated protist, *Paramecium*, to investigate various aspects of ciliary composition, growth, and basal body/centriole duplication. A major achievement of the group has been the development of CILDB, which is the world's most comprehensive searchable database for interrogating published 'omic'-based studies for evolutionarily conserved centrosomal and ciliary related proteins (Database 2009). This has allowed the group to uncover new candidate ciliary proteins such as Bug22, which they showed is required for ciliary motility in *Paramecium* (Eukaryotic Cell, 2010). A similar finding in *Chlamydomonas* has since been made by a team at Tsinghua University). Team 2 has also focused on identifying and characterising proteins involved in basal body/centriole duplication and anchoring. They describe a role for BLD10 in the assembly and stability of the centriole cartwheel in *Paramecium* (Cytoskeleton, 2010), similar to what was previously found in *Chlamydomonas* by the Hirono group. In collaboration with a group at Curie Institute, they also describe a nucleating role for *Paramecium* SAS-4 in basal body duplication (Mol Biol Cell, 2011). Recently, the group described a novel role for transition zone-localised FOR20 in basal body docking (J Cell Science, 2012), and this finding has formed the basis for one of their key research objectives, namely the role of the transition zone in basal body anchoring. Also, a very recent paper from the group describes a Centrin3-dependent transient appendage that regulates daughter basal body positioning (Protist 2013). Overall, the group has published 5 senior author papers (Database, 2009; Cytoskeleton, 2010, Eukaryotic cell, 2010; J Cell Sci, 2012 and Protist, 2013), and collaborated in 6 others (Nature, 2008; Genome research, 2008; BMC genomics, 2010; Eukaryotic cell, 2011; Eukaryotic cell, 2012; Cilia, 2013).

Basal body assembly and docking mechanisms, and the biology of the transition zone, are major topics in the field of cilia and ciliary disease research, and have been the subject of many recent high impact publications and conference proceedings. For example, the transition zone was the sole focus of a special subgroup meeting at the 2012 ASCB meeting in San Francisco. Thus, the team's published works to date on these topics will have gained significant attention, especially since the quality is good. However, one concern is that with the exception of the EMBO J and J Cell Sci papers, all other senior author papers were published in journals possessing relatively low impact factors (<5.0). Although the journal impact factor is far from the perfect metric to appraise good science, a low level of publications in journals with high impact factors will make the team less competitive for external grant funding, and will result in lower international exposure for the team's findings.

Assessment of the team's academic reputation and appeal

Team 2 leader has excellent international visibility in cilia and flagella research, mostly on account of the exceptional CILDB database that he has established. He has also delivered short talks at the last two FASEB summer meetings on the Biology of cilia and flagella (2010; 2013), where the world's cilia community meets every 3 years. He also chaired a session at one of these meetings. He has given talks at the French Cilia/Centriole meeting (2010, 2011). His European/national visibility is good based on relatively frequent talks, editor of Eukaryotic cell (2002-2013; impact factor 3.6) and minor participation in two small ANR grants. This PI is a long standing world expert in *Paramecium* genetics. He coordinated the *Paramecium* genome sequencing project, and was an organiser of '*Paramecium* Genomics' conferences in 2008 (Potzberg, Germany) and 2009 (Krackow, Poland).

The team 1 leader has limited international visibility, citing just one oral communication in the last 5 years. However, she did present at this year's FASEB cilia/flagella meeting, and her published senior author paper in EMBO J will have been noticed by many cilia researchers on account of its very high quality EM. Also, she has acted as a grant reviewer for the Wellcome Trust (2010-12) and the Austrian Science Fund (2010-12).

A senior member of the team has limited international visibility outside Europe (no talks, invited lectures) and moderate visibility in Europe based on talks in Spain and France.

Neither group has published a review on cilia/flagella in the last 5 years, and no international postdocs have been recruited.

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

A member of the team has initiated collaboration with Merck Millipore to commercialise a monoclonal antibody against tubulin post-translational modifications.

Assessment of the team's organization and life

The two groups complement each other, using two established cilia/centriole models, *Paramecium* and mammalian cell culture. This organization brings strength to the project because it allows cross validation of findings in evolutionarily divergent systems and allows a greater range of questions to be experimentally addressed. Importantly, both groups are interested in (and have track records in) centriole/basal body biology, and should therefore work well as a unit towards a common research goal (although the two groups have yet to co-author a research paper). There is a concern that the team organization is not optimally balanced. Most of the recent output has come from one group (the other group has not published since 2010, although there is a paper now submitted). Also, the team has no postdocs and only 1 PhD student. Websites, although up to date in terms of publications, could contain more detail about the scientific programs. The Dept of Cell Biology (I2BC) is an appropriate site for the team's research activities due to research synergies with other groups and the availability of advanced imaging platforms.

Assessment of the team's involvement in training through research

Three PhD students and 2 Masters students have graduated from the group in the last 5 years. The PhD students have all produced one first author publication (for one student a manuscript is submitted). The current team has 1 PhD student, 5 masters students and one MCF (Paris-Sud).

Assessment of the strategy and the five-year plan

The team proposes three research strands.

(1) Molecular dissection of basal body (BB) anchoring in *Paramecium*. Using RNAi, protein localisation (GFP tags), fluorescence and electron microscopy, the group will investigate 6-7 putative anchoring/docking regulators published in the literature (e.g., OFD1, Cep78, Cep164, Meckelin, POC5), with the hope of shedding new light on where exactly these proteins function in the sequence of events leading to BB anchoring. They hope to test new findings in mammalian cells. The sequence of events in BB anchoring/docking is a very important question to the cilia field and the team has a real advantage because they have demonstrated through publication the ability to dissect these steps using high quality EM in the *Paramecium* model. The model itself is ideal for ultrastructural studies because of its multiciliated nature. There is one technical concern about the RNAi experiment in that differences in gene knockdown levels may confound the placement of components to a specific functional step in the docking process. However, it seems that the team can achieve very high level knockdown levels in *Paramecium*, thus this concern is only minor.

(2) Ultrastructural dissection of the *Paramecium* transition zone using cryoelectron tomography on isolated basal bodies from WT cells and various RNAi knockdown lines. This work is connected to the above BB anchoring studies. The team has high levels of expertise in EM and cryoEM and will also be helped by collaboration with a team at Gif and thus are well positioned to do this work.

(3) Ubiquitination and ciliogenesis. Submitted work (Nature Communciatons) on the deubiquitinase CYLD will be taken further by uncovering its substrates using candidate gene (CAP350, Cep192, Dvl, Plk1) and proteomics approaches (collaboration with another the team within I2BC) . Identified binding partners/substrates will be tested for ciliogenesis functions and localisations in mammalian cells, *Xenopus* (collaboration with a team at Orsay) and *Paramecium*. In parallel, a more general assessment of ubiquitination and ciliogenesis/BB anchoring will be taken in *Paramecium* by investigating K63 ubiquitination pathway enzymes (e.g., UBC13, USP21). Preliminary data suggests a role for UBC13 in ciliary function. There are a number of published studies since 2009 on ubiquitination and ciliogenesis/deciliation and it seems likely this theme will be a fruitful research avenue going forward.

Conclusion

- **Strengths and opportunities:**

Complementary model systems to cross validate research findings, and open up new experimental possibilities. High level EM for ultrastructural studies.

Mutual long standing interest in centrioles/basal body biology.

Research questions, whilst ambitious, are achievable. Project is generally well integrated.

- **Weaknesses and threats:**

The team is not yet operating as a cohesive single unit (merged groups have not yet co-authored a paper or grant application).

- **Recommendations:**

Publication level needs to improve, although the submitted Nature communications paper (in revision) helps to alleviate this concern.

Lack of external funding poses a threat to the project, and it will be important for the team, and especially the Team 1 group, to secure significant funding in the short to medium term.

Team CYTOSKELETON IN CELL MORPHOGENESIS

Name of team leader: Mr Alexis GAUTREAU

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	**6**	**6**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The group was established in 2008 and has since then been focused on the subcellular regulation of actin networks generated by the activity of Arp2/3 complex and its positive and negative regulators. The team has worked on the impact of two positive regulators of Arp2/3, the nucleation promoting factors WASH and WAVE, and more recently also on a negative regulator, Arpin.

The impact of this work to the field of actin cytoskeleton regulation has been very substantial and wide-ranging. 1) The team showed that the endocytic coat protein clathrin is an activator of the WAVE complex, and thus involved in the generation of lamellipodia (J Cell Sci, 2011). 2) The group purified the WASH complex and demonstrated that WASH regulates the generation of actin networks at the surface of endosomes, which constitutes an essential step in the formation of transport intermediates from endosomes. Moreover, WASH-generated actin networks at the endosomal surface are probably also important for the establishment and upkeep of protein/lipid domains at the endosome surface. This body of work has been published in a number of highly respected and well cited publications (Dev Cell, 2009; PLoS ONE, 2012; Biol Cell, 2013). In collaboration with other groups, the role of WASH-dependent actin regulation has also been demonstrated for infectious and genetic diseases (Cellular Microbiol, 2010; Hum Mol Genet, 2011). 3) The work part with the perhaps most wide-raging impact is the recent identification and characterization of Arpin, the so far only known negative regulator of the Arp2/3 complex. This highly original and important work has now been published in Nature (2013).

As original research papers, the group has published 6 combined first and last authorship papers with impact factors ranging from 4 to 6, but also including 2 stand-out publications in Dev Cell (IF: 13) and Nature (IF: 37). Published work also includes 4 multiple co-authorships in well-respected journals, including a publication in Science (IF: 31).

Assessment of the team's academic reputation and appeal

The work of the group has gained widespread attention in the cell biological and larger scientific community, as evidenced by numerous editorial articles, highlighting in post-publication reviews such as Faculty of 1000 and also by a long list of invited lectures of the group members at national and international meetings, as well as selection of abstracts for oral presentations.

Furthermore, the group published 8 review and secondary articles or book chapters, mostly with both first and last authorships, in good journals, including two reviews in the prestigious Trends in Cell Biol (IF: 12).

The team leader has also received both the Bronze Medal of CNRS and the *Prime d´Excellence Scientifique* of CNRS. He is the Adjunct Director of the Laboratoire d´Enzymologie et Biochimie Structurales and also a member of the Conseil National des Universités and of the Société de Biologie Cellulaire de France.

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

The group´s work on Arpin resulted in a pending patent.

The team organized a course for European PhD students in Institut Curie, and contributed to teaching in the course in following years. They also organize a day on Actin and Cell Migration of the Master 2 GCDE in Paris-Sud since 2010.

The team leader is also a member of the GDRI, From Molecular Events to Cellular Events in Human Pathology between France, Russia, Ukraine, Latvia and Armenia.

Assessment of the team's organization and life

The group consists of 7 members, 4 of which are permanent staff (group leader, 1 technician, 2 staff researchers) and 3 are non-permanent (post docs and graduate students). Two further graduate students and 1 post-doc have left the lab during the evaluated period.

Assessment of the team's involvement in training through research

The team has trained a large number of students, including 3 graduate students, 1 Master 1 student, 7 Master 2 students, and 1 Bachelor, 1 Licence 2 and 1 Licence 3 student. Three of them stayed in the lab for the next level of their education. One has been very successful as a first author of 3 original and 5 secondary publications, including a first authorship in Dev Cell, and also several co-authorships. He also received the "Prix de la Chancellerie des Universités". The second one is the first author of a J Cell Sci article, and the third is the first author of a paper in BioEssays and also of the recent work on Arpin published in Nature. She received the Prix L´Oreal/UNESCO pour les femmes et la Science. The team leader has also been a member of several thesis committees.

Assessment of the strategy and the five-year plan

Work for the next years will focus on the WASH complex and its role in actin-dependent force generation, and also on Arpin and its regulation in migration and invading cells.

To understand the role of WASH in organizing microdomains on the endosomal surface, the group will follow a reconstitution approach using purified WASH and giant unilamellar vesicles of specific composition. Application of force by optical tweezers will mimic the budding of endosomal membranes. The group has obtained ANR funding for this project, and will collaborate with vesicle specialists from Institut Curie.

Activation of Arpin appears to depend on Rac, as shown previously by the group, and also on reversible posttranslational modifications. The group will study these modifications by using mass spectrometry and comparison of modified and unmodified Arpin in actin polymerization assays. Additional input will also come from a structural biology project funded by ANR, which studies the conformational dynamics of Arpin using NMR. Affinity chromatography and yeast two hybrid screens will be further used to detect binding partners that mediate activation of Arpin by Rac. A further focus will be the role of Arpin in cell invasion, especially in the formation of invasion-mediating invadopodia. In collaboration with experts at Institut Curie, the group will study 3D invasion of invadopodia-forming cells and also use a set of 450 characterized breast tumor samples to detect changes in expression of nucleation promoting factors in these cells that parallel downregulation of Arpin.

Conclusion

- **Strengths and opportunities:**

The proposal for the 5-year plan develops stringently from the successful previous work period. The expertise of the group for further in-depth studies of WASH and Arpin is evident and well-matched to the plan. Additional expertise such as in giant vesicle or invadopodia formation has been solicited, and funding has already been obtained.

- **Weaknesses and threats:**

The proposal presents no major weaknesses or bottlenecks

- **Recommendations:**

The proposal promises further important insights into the spatiotemporal regulation of Arp2/3-generated actin networks and their impact on cell migration and invasion.

Team

IMAGING, ENDOCYTOSIS AND THE ACTIN CYTOSKELETON

Name of team leader:

Mr Christien J. MERRIFIELD

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	**2**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions		

• Detailed assessments

Assessment of scientific quality and outputs

The PI has a long-standing expertise as a leader in the field of clathrin-mediated endocytosis. The lab has particularly pushed the live microscopy analysis of endocytic events to an unprecedented level. The group is now able to visualize single clathrin-mediated endocytotic (CEM) events using Total Internal Reflection Fluorescence (TIRF) microscopy and pH-sensitive reporter tags. Based on this expertise, the team has developed a "dynamics map" of clathrin-mediated endocytosis and characterized the recruitment profile of 34 associated proteins, allowing their grouping into functional modules (PLoS Biol, 2011). The group also showed that actin polymerization is not absolutely essential for CME, but is facilitating it. Moreover, the existence of a positive feedback loop between actin dynamics and the dynamin activity was demonstrated for CME (PLoS Biol, 2012). A recent project concerns the study of ligand-triggered endocytosis. Data from studies of internatilization of GPCR and TfR suggest that clathrin coated pits are not specialized for the uptake of specific cargo, addressing an long-unresolved question in the field.

Recent work has been published in several prominent publications. The PI has 2 senior authorships in PLoS Biol (IF: 14) and a coauthorship in J Cell Biol (IF: 11). It has also to be mentioned that prior to the evaluated period, he published a string of high-class papers as first or senior author in journals such as Nature, Cell Biol, Curr Biol, Cell or Dev Cell.

Assessment of the team's academic reputation and appeal

The PI is an internationally recognized expert in the field of endocytosis. This is evident by numerous invited lectures at international conferences. Recently, he also published a comment in Nature Cell Biol (IF: 15). He is also the author of a submitted book chapter on clathrin-mediated endocytosis.

The group has recently attracted 2 grants: "Amorçage de Jeune équipe" and "Fondation ARC".

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

The PI has been a co-organizer of and lecturer at the UK Advanced Microscopy Course in Plymouth (2004-2012). He also taught at the École de Neuroscience, Paris (2012).

Assessment of the team's organization and life

The team has been established only recently at Gif in 2012. It consisted of the PI, 1 postdoc and 1 engineer. The postdoc has left in December 2013. The team needs to attract good students and postdocs. The PI is an internationally recognized researcher with high appeal and should be strongly supported in hís efforts to build up the group. Permanent positions for the group members are recommended.

Assessment of the team's involvement in training through research

Not applicable.

Assessment of the strategy and the five-year plan

The proposed 5-year plan is focused on the potential link between EGFR ubiquitination, actin polymerization and clathrin coated pit invagination, as suggested by several lines of evidence, including formation of a complex between active EGFR and curvature sensing/inducing endophilin II. The group will apply their expertise in visualization of single internalization events to this project. They will measure the kinetics of EGFR clustering at clathrin coated pits and the trafficking of EGFR through the CME pathway. Fluorescent labelling of ubiquitinating enzymes will be used to elucidate the spatiotemporal dynamics of this machinery relative to single scission events. The dependency of these events on actin polymerization, as well as on endophilin II and other regulators of membrane curvature will also be studied.

The project is internally consistent, and the group has the necessary expertise to perform the proposed experiments. Funding has been obtained, and collaborations with other groups have been established. The expected results should have wide-ranging impact on the field of clathrin-mediated endocytosis in general. Depending on the results, several side branches of the project could also be investigated.

Conclusion

- **Strengths and opportunities:**

The proposal of the team capitalizes on the experimental strength of the group in the visualization and spatiotemporal analysis of clathrin-mediated endocytosis. It is risky in the sense that it follows an unproven hypothesis, namely the potential link between clathrin-mediated endocytosis and ubiquitination of EGFR. At the same time, it is flexible enough to present no real bottlenecks. In any case, further studies on the highly time resolved trafficking of EGFR from clathrin coated pits and the dependency of this system on actin polymerization should provide novel and important insights.

- **Weaknesses and threats:**

The weaknesses stands on the fragility of a very small group within which the group leader is basically for the moment alone in designing and performing the experiments.

- **Recommendation:**

It is strongly recommended that the PI finds support in establishing his group at Gif. He should also receive mentoring in adjusting to the French academia system. This will be of mutual benefit to both the group and to I2BC, its general scientific expertise and its continuing attractiveness for other international groups.

Team

CELLULAR SIGNALING AND UBIQUITINATION

Name of team leader:

Mr Grégory VERT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**3**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions		

• Detailed assessments

Assessment of scientific quality and outputs

This is a young team, recently created in 2012 at ISV by the team leader after he moved from a Montpellier lab of world renown for iron nutrition in plants.

In his previous work, the PI demonstrated that the root iron transporter IRT1 could be used as a model to decipher the signaling pathways and regulatory mechanisms allowing plants to respond to low iron conditions in soils. This work showed the role of ubiquitination in the regulation of IRT1. Consequently, the team is using Arabidopsis thaliana as a model to reoriente its work on polyubiquitin chain formation and its biological and cellular roles in plants, focusing on the mechanisms driving K63 polyubiquitin chain formation and its functions in the endocytosis of plasma membrane proteins. K63-type polyUb is of particular interest because it involves a proteasome-independent functions including endocytosis.

The team plans to deconstruct K63 polyubiquitination, with a focus on the characterization of Ub-mediated endocytic processes (in particular, metal-dependent and ubiquitin-mediated endocytosis of IRT1, and search for factors driving Ub cargo targeting to the vacuole) It will also investigate new roles for K63 polyubiquitination using plants as model for a genome-wide mapping of K63 polyUb-dependent processes and a search for E3 Ub ligases involved in K63 polyUb. These last aspects will constitute important breakthrough in the field.

The team is composed of 2 CR-CNRS, 1 AI CNRS and several PhD and Master students.

In the last 5 years, the team published in high-ranked journals, mostly as first or last authors (PNAS, Plant Cell, Plant J…). The team leader published also reviews in the field of iron or brassinosteroids in the best revues of biology (Curr op, Cell, Nat Cell Biol…).

Assessment of the team's academic reputation and appeal

In the last 5 years, the team leader was invited to four international conferences (Gordon conference in 2012). He obtained a Career Development Award from Human Frontier Science Program (2008-2010, 300k$) and obtained an ANR Programme (JCJC 2009-2011, 180 k€) as coordinator and unique participant in both cases. He is referee for the Austrian Science Fund and Belgium National Fund for Scientific Research. He supervised the EMBO Long-Term Fellowship of Alicia Sivitz 2009-2010. He was a member of the organization committee of the 2009 European Network for Plant Endomembrane Research in Montpellier (150 attendees).

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

Iron nutrition is of primary importance for plant industry and agronomy, the knowledge acquired by this team will be helpful not only at the basic scientific level, but also in term of applied agronomy.

Assessment of the team's organization and life

The team is led with a very coherent and logical scientific objective in mind. The team collaborates with a number of groups of high science quality in the world at ENS Lyon, France, VIB Ghent, Belgium, Salk Institute, USA, and University of Lausanne, Switzerland.

Assessment of the team's involvement in training through research

The team trained several students (3 PhD, 2 Master, 2 Licence). The PI participated in teaching of Master lessons in France (16h/year).

Assessment of the strategy and the five-year plan

Using different approaches the team will generate the first map of K63 polyUb networks at the level of a multicellular organism, and will identify cellular processes relying on this K63 linkage type of polyUb. Because of the large-scale and the comprehensive analyses, the results will be valuable not only for plants, but also certainly on conserved functions of K63 polyUb in a living organism (animals and fungi).

Conclusion

- **Strengths and opportunities:**

The young age of the group leader and the presence of dynamic young scientists, providing new methods and approaches, is a great asset to this team. The recent recruitment of a CR2-CNRS is very positive.

The integration within I2BC of this team together with two other teams from the Labex Saclay Plant Sciences, will provide a strong template for the development of bioinformatic approaches in the Cell Biology Department by promoting a transition from descriptive to more integrative and predictive cell biology.

- **Weaknesses and threats:**

Ubiquitination is a very competitive field, but the team seems to have found an interesting niche in the study K63 related processes.

- **Recommendations:**

It is an ambitious project for which the team acquired all the required expertises.

Team

AUTOPHAGY AND DEVELOPMENT

Name of team leader:

Mr Renaud LEGOUIS

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	6	5

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The group has made excellent progress over the past five years in the field of autophagy, using the *C. elegans* genetic model. They have published 6 senior author primary research papers, all in journals of good or exceptional standing (Biol Cell 2009, FEBS J 2009, Autophagy 2010, Science 2011, J Cell Sci 2012, Developmental Cell 2014). The group has also published 4 review articles and 2 book chapters, and contributed to work in 6 collaborative publications.

One part of the work has addressed the functional links between endosomal maturation and autophagy, and more specifically why autophagy is affected in ESCRT mutants, an observation made by multiple labs in multiple systems. The group has shown that *C. elegans* autophagy induction is an adaptive response promoting cell survival; however, unlike flies and mammals, increase in autophagosome number is not due to a blockage of fusion (J Cell Sci 2012), which has led to their conclusion that ESCRT proteins have complex roles in autophagy. The group was also the first to detect amphisomes in worms. A second part of their work has investigated the function of Atg8 ubiquitin-like proteins (LGG-1, LGG-2) in *C. elegans* autophagosome formation and found synergistic roles in starvation survival (dauer stage) and longevity (Autophagy 2010). Following up on this work is an exciting study just published in Dev Cell showing that autophagosome formation is fully dependent on LGG-1, which functions upstream of a lysosomal fusion role for LGG-2. A third part of their work, in equal collaboration with another group at university Paris 6, uncovered a role for autophagy in nematode fertilization, required for degrading paternal mitochondria (Science 2011; 62 citations).

Autophagy is a very fast moving and topical research theme in cell and molecular biology, and medicine (>2000 reviews in the past 5 years!). Despite the many labs working in this field, the group has carved out a solid niche for their autophagy/development work, as evidenced by their published primary research papers and reviews. A principle reason for this success is their use of the *C. elegans* model, which affords the group with many experimental advantages, not least the availability of mutant alleles and a stereotypical development pattern that is relatively well understood compared with other metazoans. Also, the group appears to have successfully implemented an impressive range of imaging (confocal, EM) and biochemical techniques necessary for this field.

Assessment of the team's academic reputation and appeal

The team appears to have moderate to good international visibility. For what is still a relatively young group, they have an excellent level of publications in the autophagy field, including a 2011 Science paper, a 2014 Developmental Cell paper and some very recent review articles and book chapters. The group has also presented their work as posters at multiple international meetings such as the International Autophagy Meeting (Japan 2012), the International Worm Meetings (UCLA, USA 2009 & 2013) and the Harden Autophagy conference (UK 2011). The team leader has coordinated a number of small national grants from the ARC and IFR, and is a participant in a recently awarded ANR grant. He has also been an organizer of a regional colloquium, and is a representative on the national user committee of Bioimaging. Also, the team leader has acted as reviewer for various journals (JCS, Autophagy and FEBS J) and national and international funding agencies (e.g., NSF USA, Cancer Research UK). One of the postdocs is an international researcher. One concern to the international reputation is that only one international oral presentation has been delivered since 2008 (European Worm meeting, Seville 2008) but this should be relatively easy to address, especially given the just-published Dev Cell paper.

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

The team participated in the Fête de la Science. It hosted and trained a 3-month student project in collaboration with BioQuanta.

Assessment of the team's organization and life

The team comprised of 4 permanent staff members, together with 2 postdocs and a PhD student seems well balanced. One postdoc and the PhD student are funded to the end of 2015, thus the team has a solid platform to build from. The Dept of Cell Biology (I2BC) is an appropriate site for the team's research activities due to the clear research synergies they have with other groups and the availability of advanced imaging platforms. The Website is up to date.

Assessment of the team's involvement in training through research

Two PhD students have graduated from the group, and one post-doc has been trained. All three individuals have published at least one first author paper and all have presented (poster or oral) at conferences. In the current team, the post-doc is first author on a submitted paper and has presented posters at international meetings.

Assessment of the strategy and the five-year plan

The team proposes four research strands.

(1) Analyze the mechanisms of autophagosome formation and maturation in vivo (C. elegans embryo). The team will investigate LGG-1 and LGG-2 (Atg8/LC3 homologues) positive autophagosomes, in terms of their formation, interaction and roles in the canonical autophagic pathway.

(2) Investigate the selectivity of autophagy around specific substrates/interactors. The group will focus on the ATG8/LC3 proteins, which form an autophagic hub. Specifically, the team will identify the C. elegans LGG-1/2 interactomes using yeast-2-hybrid screening and affinity proteomics (co-IP and mass spec). Also, the group will assess candidate proteins from a 2010 Nature study that described a mammalian autophagic network derived from 32 autophagy/vesicle trafficking protein interactomes (including interactomes from 6 human ATG8 proteins). One small concern is how exactly the team will select candidates from the 2010 paper.

(3) Building on their recent work, the group will analyse the role of autophagy during organogenesis and epithelial differentiation by focusing on the relatively simple epithelial cell organization of the nematode intestine. They will characterize autophagosome populations, dynamics of autophagic flux, and selectivity (taking into account findings from research strand 2).

(4) Role of autophagy during phagocytosis (LC3-associated phagocytosis; LAP) of apoptotic corpses. Based on preliminary data showing accumulation of apoptotic corpses following LGG-1/2 inactivation, the group will ask if LGG-1 and LGG-2 are required for phagosome degradation and interaction with the lysosome. They will also ask if ced-1/6/7 and ced-2/5/12 regulate these putative LGG-1/2 functions.

The presented plans are well justified and thought out, with clear rationales for each research strand. The different strands appear to be well connected and complement each other. Also, the plan does not rely on any one strand being successful, which would bring significant risk to the project. Instead, the work looks mostly feasible and should bring exciting data. There are a couple of small issues that were not perfectly addressed, namely (1) what candidates will be selected from the published 2010 Nature paper, and (2) can the team (in collaboration with…) optimally perform the required proteomics. It also needs to be kept in mind that other groups have been doing similar experiments for the mammalian Atg protein interactomes.

Conclusion

- **Strengths and opportunities:**

The group has clear ambition and is aiming high as evidenced by published work in Science, Developmental Cell and Autophagy (IF 12.2). The team appears to be using a very suitable *in vivo* model for their research questions; plus, they have a long standing expertise working with *C. elegans*.

- **Weaknesses and Threats:**

Very few. International visibility is not as high as it should be (lack of oral presentations), based on the high level science being conducted by the group. Minor concern about the group's proteomics experience, but as this work will be conducted by a collaborator with extensive expertise (although not using worm samples), this concern is somewhat alleviated.

- **Recommendations:**

Work on increasing international visibility further. Ensure an optimal balance between departmental head duties and research team.

Team

MEMBRANE TRAFFIC AND CELL COORDINATION

Name of team leader:

Ms Marie-Hélène CUIF

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions		
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**2**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team studies Tre2-Bub2-Cdc16 (TBC) domain-containing RAB-specific GTPase-activating proteins (TBC/RABGAPs) using *S. cerevisiae* as a model organism. TBC/RABGAPs are interesting proteins: they are not only negative regulators of Rab GTPases, they also act as key regulatory nodes, integrating signaling between RABs and other small GTPases. The subclass of RabGAP including GAPCENA, are not only involved in trafficking, but also in cell cycle checkpoint. The team focused on the nearest homologs of GAPCENA in yeast, RAbGAP Gyp5 and Gyl1. In a first study (prior the present report period), the group demonstrated that Gyp5 and Gyl1 are partly colocalized at the bud emergence site, the bud tip and the bud neck, *i. e.* sites of polarized exocytosis, and that their absence leads to a cold sensitive slow growth phenotype and reduced secretion (J Cell Sci, 2004). A follow up of these studies allowed to demonstrate that Gyp5 and Gyl1, that interact directly, are mutually required for recruitment to the sites of polarized growth, and that their localization is also dependent on actin, and on the formins Bni1 and Bnr1. These two rabGAPs appear to be transported on secretory vesicles to the sites of polarized growth (Traffic 2008). In a more recent work, the team established that interestingly, Gyp5 and Gyl1 interact with the N-BAR-domain and SH3-domain containing protein Rvs167 (the yeast analog of amphiphysin), that was described for its role in endocytosis. They established that Gyp5 and Gyl1 are involved to the localization of Rvs167 at the tips of small buds during polarized growth, and that this depends on the proline-rich region of Gyp5 and Gyl1, and on conserved residue in the SH3 domain of Rvs167. They also showed, notably by a genetic approach, that Rvs167 is involved in exocytosis at the small bud stage, an observation quite unexpected (Traffic 2011).

This work, in a difficult area, allowed better understanding of the properties and function of an interesting class of proteins, at the crossroad between trafficking and cell cycle. The main work described above published during the last years by the team (presently administratively integrated in a group within IGM at Orsay) relies on multiple approaches: molecular biology, genetics, biochemistry, electron microscopy, and beautiful imaging (both life cell imaging and immunofluorescence), showing that the team masters all these approaches (and in the case of electron microscopy could establish the appropriate collaboration). It is published in good international journals (J Cell Sci, Traffic, both very solid publications, recognized in their field with IF in the range 5-6).

In addition to this main work, the involvement of both the PI and a permanent staff member of the team, as scientific and technical supervisors respectively of the imaging platform of the CNRS-UMR 8621 led them to be also involved in multiple outside projects leading to 6 publications in good journals (IF in the range 4-6).

Given the small size of the group (2 permanent positions), the difficulty of the subject (study of proteins belonging to a family of redundant proteins, with multiple functions, at the crossroad between trafficking and signalling), the main responsibilities of the group leader as a teacher, the production of the group can be considered as very good.

Assessment of the team's academic reputation and appeal

The group leader is regularly sollicitated for participation in PhD jurys in well known labs. She has ongoing collaborations with internationally recognized scientists in France at Institut Jacques Monod, Curie Institute, and Sophia Antipolis). In addition to her recognition in France (oral presentations at national meetings), she is also recognized internationally (oral presentation at the selective “Yeast Cell Biology Meeting”, Cold Spring Harbor, 2011).

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

One of the two permanent staff of the group participated actively in the “Fête de la Science” for several years by showing microscopy experiments to the public.

Assessment of the team's involvement in training through research

It is necessary to emphasize that the work was performed in a very small group (two permanent positions including the group leader). With this small size, the group successfully trained several students (1 L2, 1 L3, 3 M1, 2 M2, and 1 PhD (the engineer of the group). Moreover, the engineer trained 33 persons for imaging.

The PhD students trained in the group in the last years have both excellent reputation. One was selected as post-doc in a very competitive group at Curie, then Pasteur Institute. The engineer was involved in multiple collaborative projects. A post-doc in the team was recruited as a teacher (MC, Orsay university).

The team leader is also often solicited in PhD jurys and committees.

The group is directed by a teacher having heavy responsibilities with not only over two hundred annual hours of teaching but also multiple responsibilities in the organization of teaching (licence/M1/M2), and in the setting of new formations.

Assessment of the strategy and the five-year plan

In the next years, the group plans to follow up on studies of RabGAP Gyp5 focusing on potential new functions of this protein. Gyp5, as three other rabGAPs (Gyp1, Gyp3, Gyp7), was shown to have *in vitro* GAP activity towards Ypt1, which was recently implicated in the formation of preautophagosomal structures. They will test whether these four rabGAPs are involved in autophagy, and more specifically in the balance exocytosis/autophagy. They have the tools to address this question.

A second question of interest is based on the unexpected interactions between Gyp5, Gyl1 and Rvs167, as well as three proteins involved in actin polymerisation (Lsb2,3 and 4) with proteins involved in DNA replication. The team will explore the possibility of a role of their proteins of interest in coordinating the initiation of DNA replication with bud formation. They have preliminary genetic observations that support this hypothesis.

In addition, if they obtain financial support, they will study the involvement of human paralogs of Gyp5 and Gyl1 RabGAP proteins in the trafficking of CXCR4 in hematopoetic cells.

Conclusion

- **Strengths and opportunities:**

In spite of the heavy work of the team leader as a teacher with multiple responsibilities, and the very small size of her group, they succeeded in publishing their work in good international journals, and presenting regularly the data in French and international meetings. It must also be underlined that the team leader and the permanent staff engineer developed a very good imaging platform for the benefit of the collectivity. The team leader has the background in both yeast and mammalian cells. The research project is nice and exciting.

- **Weaknesses and threats:**

The team leader is conscious that the size of the team is too small for the future, she plans to join one of two groups in the department, depending on the evolution of the work, and on the evolution of the interactions with these two teams.

- **Recommendation**

The only possible recommendation is to encourage the group both for developing their present project, and for their potential new affiliation.

Team

DYNAMICS OF CELL COMPARTMENTATION & CELL IMAGING

Name of team leader: Mrs Béatrice SATIAT-JEUNEMAITRE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	3	1
TOTAL N1 to N6	9	7

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The team members and the team leader have a good visibility, nationally and internationally in the field of plant biology but also optical and electron microscopy. The scientific output presented in the report covers interesting and timely topics of plant cell biology such as the role of sphingolipids in cell cycle, cell plate growth and polar axis development (The Plant Journal, The Plant Cell, J. Cell Science) but also on endomembrane dynamics in plant cells by exploiting new interesting photoconvertible tools (The Plant Cell). The reputation of the scientific journals in which the team's results are published are good, but not excellent, especially when considering the number of publications on which the team members are the leading authors. There is a strong part of collaborative papers on which the team members are not senior or first authors. The papers in which the team members appear as co-authors are often published in very good (Plos Genetics, Plos Biology, PNAS and high profile journals (Science, Plant Cell) and it is recognized that the expertise of the team members involved in of extreme value for these publications to be published in these journals. The scientific contribution of this team is not easily assessed by its sole contribution as authors to publication as there is important aspect of providing competences and expertise in microscopy to many other groups through the Imagif platform. The team's activities certainly have been instrumental in developing and maintaining excellency in microscopy and imaging in France, especially in the challenging field of plant cell biology. The team could therefore become a cornerstone of the integration of groups within the department and among departments of the I2BC. A more detailed description of the impact of this contribution would have been warranted. Also, it is important to assess the part of the team efforts that go into providing services to other groups and those that are invested into their own genuine research efforts.

Assessment of the team's academic reputation and appeal

The team appears well-integrated at the national and international level and has visibility beyond national borders. There is a strong implication in national networks and committees. The team is especially active in the promotion of technological expertise in imaging, having organized a number of workshops and colloquia, especially at a national level. The team has a very high reputation within the national landscape, especially for their efforts in technology development, training and service in imaging and cell sorting techniques. The participation of the team members in scientific meetings is good, although there is a strong bias toward national meetings. The team members have contributed to a number of reviews and book chapters in specialized books.

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

The team members have a track record of participation in events aimed at outreach to the public as well as communication and organisation within the scientific community. The quality, type and success of these activities cannot be judged from the short mentions in the report, but there is no reason to assume that they are not attractive and successful.

Assessment of the team's organization and life

The topics as presented in the results section are rather diverse and do not amount to an entirely coherent research direction. This is neither surprising - nor necessarily bad - for a newly founded team. Yet it raises the need for a strong vision of how the different research directions can be followed up, finished or re-oriented and of how the resources in terms of personnel and finances can be allocated. The description of the project is rather short which makes it difficult to judge how the team will be structured and oriented in the next five years. It is especially important to obtain a clear vision of how much efforts will be allocated to technology development and services to the Institute and the Department, and how much will be invested in the specific research topics of the group and how these two research axes will be delineated and how they might interact in a synergistic fashion.

Assessment of the team's involvement in training through research

The information provided in the report is sufficient to judge that the team actively participates in the training of master and PhD students, both within their group, as well as external supervisors/experts throughout France.

Again, there is a clear focus of activities in training of microscopy and imaging techniques, especially at the master programs of the different Universities in the region.

Assessment of the strategy and the five-year plan

There is certainly a high potential and interest in the new authophagosome project but also in the cytoskeleton related project.The strategy for the future is very short and lacks the delineation between the group's own research efforts and their contribution to technology development and service.

Conclusion

- **Strengths and opportunities:**

The team is extremely active in developing imaging methods. They have complementary expertises in different electron microscopy approaches from conventional, immunocytochemistry and cryo microscopy. They are also developing correlative light electron microscopy and they are part of the French network Infrastructure Biologie Santé France BioImaging. Members of the group are also developing research projects wich focus on autophagy and intracellular trafficking /cytoskeleton in plants. Plant Biology is the field of expertise and collaborations are settled with the other plant groups, but the expertise is also extending to imaging applied to eukaryotic cells. The team is extremely active in training future experts in imaging which is viewed as a real strength because many institutions are trying to settle imaging facilities.

- **Weaknesses and threats:**

Although the team is highly active in national teaching and national networks the international visibility is relatively low.

- **Recommendations:**

In light of the large effort of the majority of the team members in activities related to the imaging platform, it is very important that a promising, lean and focused research project is put into place that will allow the team to be leader in an increasing number of publications and gain international visibility and attractiveness.

Team

CELL SIGNALING AND MORPHOGENESIS

Name of team leader:

Ms Anne-Marie PRET

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	6	6
N2: Permanent EPST or EPIC researchers and similar positions		
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**6**	**6**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

This team addresses fundamental questions of general scientific interest in Developmental Biology (genetic control of morphogenesis) using the fruit fly as a model organism.

Two distinct and well-characterized settings are being studied in the context of Drosophila oogenesis. First, the team investigates the role of adhesion and apoptosis in the control of the number of polar cells within the follicular epithelium (topic 1). In this context, one major focus is on the regulation and output of JAK/STAT signalling. Second, the team addresses how morphogenesis is regulated in the developing ovary with a specific focus on the number of terminal filaments (topic 2). Here, a major aspect is on the regulation of cell proliferation, cell death and cell-cell intercalation by a family of BTB/POZ proteins. Studying the genetic control of this morphogenetic event is particularly relevant due to its interesting evo-devo implications (this morphogenetic event controls the number of ovarioles, hence a possible link to fecundity). Importantly, genetic tools, reagents and expertise can be shared between these two topics.

The work performed during the 2009-13 period is of high quality (with some really nice high-resolution phenotypic analysis). This work, however, has led so far to only a limited number (3) of very good publications (Development 2013, Cell Death and Differentiation 2011 – topic 1; PLoS ONE 2012 – topic 2).

Assessment of the team's academic reputation and appeal

This is both a weak point and a concern: the team has a limited international visibility (3 Oral presentations at international meetings (Gordon 2013, European Drosophila Conference 2011 and Drosophila Research Conference 2008; 1 international seminar given by the PI; no meeting invitation); no formal participation in international/national network/project is reported; a post-doc has been recruited for 2 years; no prize/awards has been awarded. Of particular concern, no research grant has been awarded to this team since 2008: an ARC subvention has been obtained for a 4th year of PhD and ANR proposal in 2013 has been classified in the complementary list but not financed.

Assessment of the team's organization and life

This criterion does not apply to a team of this size. However, it appears that the CGM web site (http://www.cnrs-gif.fr/cgm/pret/index_gb.html) is not up-to-date (in terms of research topics, people and publications).

Assessment of the team's involvement in training through research

This is a strong point of this team. Indeed, this research groups comprises 6 University teaching staff (Prof/MC) from 2 universities (Paris-Sud & Versailles). Of note, one professor has recently been appointed as the director of the Master program 'Biologie Santé' at the Paris-Sud University. Additionally, each of the four PhD students have signed a publication as first-author including very good publications (PLoSONE 2012 and Development 2013), indicative of effective guidance of doctoral students.

The fact that this team is composed of only university teaching staff can be viewed as a strength because of strong teaching/research links but also as a major weakness since French universities system leave little time free for research to its professors.

Assessment of the strategy and the five-year plan

The proposed project directly stems from the past two projects. It is focused and straightforward. On one hand, this project may appear as moderately ambitious. On the other hand, considering the lack of 'full-time' scientists in the lab and the current lack of external funding, it may be seen as realistic. As an aside, topic 2 addresses a very important question that could be formulated and addressed experimentally in a broader manner (with bab simply providing an entry point into a more general problem with important evo-devo implications which could be more directly addressed).

Conclusion

- **Strengths and opportunities**

Major strengths include the scientific relevance of the questions addressed here, the high quality of the work that is being performed and, therefore, the excellent training of doctoral students.

- **Weaknesses and threats:**

A major concern is the lack of external funding (research grants) in the past years despite the quality of the research. To a lesser extent, another concern is the lack of visibility, hence attractiveness, of the team. It is likely that the strong involvement of this team in teaching is detrimental to its scientific output and visibility.

- **Recommendation:**

The proposed scientific project merely appears as a continuation of the past research, making unclear whether it will be easier to fund. Considering the high quality of the work, it is recommended that a more ambitious project be submitted to funding bodies.

Team GROW & METABOLISM IN DROSOPHILA

Name of team leader: Mr Jacques MONTAGNE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**3**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

Detailed assessments

Assessment of scientific quality and outputs

This team studies growth and metabolism using Drosophila melanogaster as a model organism.

One of the major research interests relates to the control of S6K proteins, which are kinases that regulate cellular growth in response to nutrients. This group has identified a role for a nuclear receptor DHR3 in controlling growth in a S6K dependent manner. Another axis of research concerns the control of development induced by ecdysone, a steroid hormone. In particular this teams addresses the regulation of the ecdysone cycle. A third and final axis studies fatty acid (FA) metabolism to understand the differential contribution of FA metabolism in different fly tissues. Recently, they have shown a role for ooenocytes from the fat body in the generation of long chains of FAs, which plays a role in the respiratory system.

The work developed by this team led to the publication of two articles in one good journal. PLoS genetics (2X)- with the team leader as first (2010) and last (2012) author.

Assessment of the team's academic reputation and appeal

This team does not have much international recognition. In the past 5 years the seminars by the team leader and all group members took place in France. In addition, most of these seminars did not take place in international meetings but rather in French meetings or clubs, like Drosophila French society. There are no international collaborations established but there are two with French groups in Gif-sur-Yvette and University of Marseille. This team has recruited two post-docs in the past but has not recruited new post-docs since 2009. In terms of funding a single ANR was obtained that finished in 2009. In 2013 this team ANR's was classified in supplementary list.

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

Metabolism is a very trendy area of research with several associations with human disease. It is therefore a potential area of interest to collaborations with other academic groups or with industry.

Assessment of the team's organization and life

Currently this team is very small with only four members. One CR1 (The team leader), one MC (less time left to do research as his teaching commitments are quite important), one ITA and one PhD student. The small size is quite problematic when most of the work proposed depends on genetic screens as a initial starting point. The team's webpage does not seem to be up to date on the CGM's website.

Assessment of the team's involvement in training through research

This team has trained 22 students in the past 5 years. This is an impressive number suggesting that the team leader and the team makes the effort of training many students. However, this might be quite problematic since 8 of these students were at the Licence level and so required a lot of training for the amount of time spent in the lab. One positive point is the fact that one team member is an assistant professor (MC), who can recruit good students.

Assessment of the strategy and the five-year plan

In terms of projects the team want to continue the work of FA metabolism. This appears as a good choice since it allows some focusing on a single subject. In silico work performed by this team has identified about 200 genes that might work as effectors of FA metabolism. The team plans to use in vivo RNAi to identify lethal phenotypes initially. The identification of tissue specific FA effectors and possible contribution to tumourigenesis by combination with appropriate fly tumour models will follow…

The project proposed here is focused on FA metabolism. It is an ambitious project. Its starting point is very broad with the identification of lethal phenotypes before studying the role of each gene in a particular tissue. This might be too demanding for such a small team. Also the importance of FA metabolism in tumour growth is a really interesting and important aspect of this project, but it also an extremely competitive one. It might be important to define well which tissue to study instead of doing a larges cale screen and then characterise the identified effector in this particular tissue. Then a more global analysis extended to other tissues might be justifiable.

Conclusion

- **Strengths and opportunities:**

Ambitious project and important to several areas of research such as growth, metabolism, development and tumourigenesis. This team has experience in fly genetics and metabolism and so the team has the expertise required to develop such a project. The team leader has taken the advantage of having several short-period students to develop his RNAi screens by modules and most of this work has already been done.

- **Weaknesses and threats:**

The committee encourages the team leader to maintain a certain degree of focusing so that the project can rapidly generate the data that will allow its publication.

- **Recommendations:**

The project described here is ambitious and can deliver important results. It is important to secure funding. At this point, funding will not only allow this team to continue to work in the best conditions, it will also contribute to the possibility of recruitment of other team members such as post-docs.

Team OXIDATIVE STRESS AND CANCER

Name of team leader: Mr Michel TOLEDANO

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**6**	**4**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The group focuses on oxidative stress pathways and redox homeostasis in eukaryotic cells. The team followed several parallel and independent research tracks in the last 5 years. They made several significant contributions to the field. An important contribution came from their analysis of yeast cells either depleted of glutathione or overloaded with glutathione which led to the conclusion that glutathione does not play a major role in thiol-redox homeostasis of the cell but is essential for iron sulfur complex assembly, which challenges the accepted view of the function of gluthatione. This was published in EMBO J in 2011.

Another major significant contribution was done in collaboration with a group in Sweden and was published in Molecular Cell in 2011. They show that increased life span in response to Caloric Restriction depends on the peroxideroxins Tsa1 and Srx1 in budding yeast.

The group also brought novel understandings of the functions of sulfiredoxin in mice, and how oxidizing agents control KEAP1 capacity to stabilize the downstream effector of the oxidative stress response, the transcription factor NRF2.

Last, a novel research direction was also initiated, by a junior member in continuation of her postdoctoral project. She addressed the function of Ring finger protein (RNF) in ER associated degradation (ERAD) pathways in muscle disorders. She showed that RNF185 is a novel E3 ligase that targets Cystic Fibrosis Conductance Regulator to the ERAD pathway. This opens new research perspectives for the team.

Overall the team contributed to 5 senior author research articles and 2 method articles. The research articles are in good impact journals (5<IF<10), with broad (JBC, EMBO J) or more specialized (Antioxidants and Redox Signaling) audiences. The team also produced 6 collaborative publications, one of which is of high standards. In addition the junior member contributed to 3 publications in good journals from her postdoctoral experience. The team also produced several reviews and previews illustrating its influence in the field.

Assessment of the team's academic reputation and appeal

The team leader has an excellent national and international visibility. He was invited for lectures in more than 20 international meetings in the last 5 years. He is a member of the editorial board of “The Journal of Biological Chemistry“ and of “Antioxidants and Redox Signaling”. The team belongs to the national GDR network “redoxines” and is involved in the European Cooperation in Science and Technology Action “BM1203 EU-ROS”. The team leader was/is involved in the organization of two Gordon Research Conferences (2012, 2014) on “Thiol based redox regulation and signaling” and one international symposium organized in France in 2008. The team is also actively involved in national and international collaborations and is a partner or coordinator of several important research grants. The team leader has written several previews (Cell, Molecular cell) and reviews (ARS, Methods in Enzymology) and one book Chapter.

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

The team recently submitted one patent related to the JBC 2013 publication.

Assessment of the team's organization and life

The team is rather small and composed of two permanent researchers (including PI), 2 technicians, one PhD student and two postdoctoral fellows but that will have completed their postdoc beginning of 2014. Three postdocs have also spent short periods in the team (less than 2 years) and only one contributed to original research articles. One postdoctoral fellow should join the team in 2014.

Assessment of the team's involvement in training through research

In the last 5 years the team has trained 4 PhD students. Two of them have published as first authors in JBC and and one of the two also contributed to a review in ARS. A third student published as second author in EMBO J and contributed to two reviews. There is no indication on the present positions of these students.

The fourth PhD student was in co-tutelle with the University of Monastir but did not sign any publication yet. Two Master students were trained. Besides training students in the lab there is no indication of involvement in teaching programs or networks.

Assessment of the strategy and the five-year plan

The proposed research project follows three directions that emerged from their previous work.

1) First they aim at understanding how compartmentation of GSH controls thiol-redox homeostasis. They propose to use an original strategy based on previously developed GSH redox-biosensors (rxYFP) and active manipulation of GSH entry inside yeast cells by expressing a GSH membrane transporter to modulate GSH fluxes. By combining this detection strategy with genetic screens, the team aims at identifying genes that are required for GSH diffusion in and out of the different cell compartments, first focusing on the endoplasmic reticulum compartment. This strategy is very original and should bring important insights on how GSH levels/activity are modulated inside the different cell compartments.

2) The second objective is to complete the understanding of the ER associated degradation pathway in mammalian cells. They propose to focus on JAMP a trans-membrane protein of the ER, known to interact with RNF5 and RNF185. They want to determine whether JAMP has a redox function and if this function is required for JAMP to modulate the ERAD pathway. They propose a straightforward approach with perfectly mastered methodologies.

3) The last objective is to complete the knowledge of how peroxiredoxins control replicative life span in yeast. In particular, the project aims at understanding how TSA1 controls H2O2-induced aggregates through a chaperone like function. This is a very promising and challenging research objective. Even though, the experimental strategy is not detailed and therefore difficult to fully evaluate, the strong expertise of the team in peroxiredoxin is a main asset.

Conclusion

- **Strengths and opportunities:**

Longstanding and excellent expertise of the team leader in the field. An original biochemical and genetic strategy to identify novel players of GSH homeostasis. Secured funding for the next two years.

- **Weaknesses and threats:**

The team is quite small in regard of the objectives as more than 3 independent directions are developed simultaneously.

- **Recommendations:**

Interactions with the other teams of the Cell Biology Department should be strengthened during the transition period to ensure perfect integration in the department.

Team

INTEGRATED APPROACHES OF ION TRANSPORT

Name of team leader:

Mr Sébastien THOMINE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	5	5
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	
N6: Other contractual staff (without research duties)	4	
TOTAL N1 to N6	13	7

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	5	5

• Detailed assessments

Assessment of scientific quality and outputs

The scientific output of the team in terms of number of publications and quality of the journals is excellent (27 in 4 years with 6 last authorships and 2 first authorships for the team leader, but also several publications in which researchers in the group are also first authors or last authors (4)). Publications are in well recognized journals in Plant Biology and Biochemistry and Biology (Plant Cell Environ., New Phyt.,Plant J.,Plant Cell Physiol.,J.Biol.Chem. FEBS J.) but also in high profile journals where team members are among the first and/or last authors. The team works on very interesting aspects of plant membrane transporters and has provided intriguing examples of the specific roles of metal transporters in sustaining plant function and their intricate regulation by cellular signals. A somehow distinct research axis is the investigation of mechano-sensitive channels, which are very probably of critical importance for plant cell function and plant development, but for which a precise role remains to be determined. Both research axes are very timely and represent exciting topics at the forefront of plant and cell biology.

Assessment of the team's academic reputation and appeal

The various invitations of team members to speak at national and international conferences nicely reflects the interest of the team's contribution to the scientific community.

The team has been able to attract a number of high profile PhD students and postdocs and young researchers which testifies to the appeal of the research topics and team leaders within the community. Most of the non-permanent staff who have left the lab have found positions in top research universities in Europe and abroad, which is another indicator of the high quality and reputation of the team's research. The team has an impressive number of invited reviews in highly reputed journals and there is a great international visibility of the team members as testified by the number of invited lectures to international conferences of many of the team members.

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

As stated above, the team clearly has a very good scientific productivity and publishes in journals of considerable impact within the scientific community. The research topics are of fundamental importance for our understanding of plant life and contribute to a better appreciation of how plants perceive and withstand environmental stresses. The team members have a track record of vulgarization efforts of their research, which is of interest to the public as it impacts on our vision of the future of agriculture and the role of plants in our environment.

Assessment of the team's organization and life

There is a good team structure with respect to permanent versus non-permanent staff and the number and scope of research topics are appropriate for the team strength if the current number of non-permanent staff can be kept.

Assessment of the team's involvement in training through research

All team members have an impressive track record of teaching through research with a high number of master and PhD students being trained in their team. The team leader has also participated as external expert in a high number of thesis committees in France, Europe and abroad.

Assessment of the strategy and the five-year plan

The research plan of the team is ambitious and creative and has clear potential to lead to great advances and novel insights into the regulation of intracellular ion homeostasis and mechanosensing. The questions asked by the team demonstrate a great appreciation of the complexities of ion homeostatic regulation in plants. The team's combined efforts to identify new players through forward genetic screens and the development of nanosensors in order to enable the analysis of mutants at the necessary resolution has great synergistic potential. It is timely and at the forefront of the current research in the field. All of the research projects are timely, very exciting and of high potential.

Conclusion

- **Strengths and opportunities:**

Great expertise and international visibility of the team leader and the other members of the group in the field. Great potential for the future department.

- **Weaknesses and threats:**

No real weaknesses. Some of the minor project parts are high risk and might be better thought through, but the committee was generally impressed by the great scientific and technological ambition of the projects.

- **Recommendations:**

The team is composed of 5 researchers with no technical support which should be taken into consideration within the department during the transition phase.

● Department of Microbiology

Overall assessment of the department

Strengths and opportunities related to the context

The Department of Microbiology is composed of 12 research groups brought together from five institutes. They represent a unique ensemble of scientific expertise that are capable of addressing important biological phenomena in a broad range of microorganisms, and that may impact our health and environment in profound ways. Several groups have excellent national and international visibility. Besides generating fundamental knowledge, research conducted in this department has also a great potential for biotechnological and medical applications, which provides opportunities to obtain important funding through contracts with industrial partners. In this area, the Microbiology Department is the leader in the I2BC institute with the highest number of patent applications and one start-up created in the reporting period. Integration of this department in the institute should not pose any problem with a multitude of opportunities for interdepartmental collaborations. Research projects of this department are well integrated in all identified transversal institute themes. Therefore, the committee fully supports creation of this department, which will bring significant added value to the institute.

Weaknesses and threats related to the context

The AERES committee has identified also several weaknesses that should be addressed in the near future. The research groups constituting this department are heterogeneous concerning their scientific production and scientific visibility, which may impact their funding situation, long-term viability and the ability to attract high-level international scientists and students. Many group leaders will retire in the near future. Some groups are critically small.

Recommendations

For the fragile groups, especially those lacking in funding, profound and creative evaluation of their weaknesses and redefinition of their research priorities is urgent. Some teams may consider adjusting their five-year plan to fit more closely with the scientific priorities of the I2BC. For the critically small groups, merging with other groups should be encouraged whenever possible from a scientific stand point. The retirement of group leaders is a threat, which provides one of the opportunities to define the general concept of the department, recruit new group leaders, consolidate existing strengths, but, even more important, to bring in missing or emerging competences. It is the mutual opinion of the committee that the priority should be in bringing innovative research directions. The new recruits should increase coherence within the department, promote further interactions with other departments, and finally increase the international visibility of the department. The leadership of the institute should develop a profound plan of how to tackle this situation, and should consider support for the recruitments in this department as priority.

Team

MOLECULAR BIOLOGY OF CORYNEBACTERIA AND MYCOBACTERIA

Name of team leader:

Mr Nicolas BAYAN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	4	4
N2: Permanent EPST or EPIC researchers and similar positions		1
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**8**	**7**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

This group has developed an original research aiming at understanding the biogenesis of the corynebacterial cell envelope. The overall organization of this structure is conserved in Corynebacteriales, an order of actinomycetes group, which includes bacterial species of tremendous importance for industry (i.e. *Corynebacterium glutamicum*) or human health (various pathogens such as Mycobacterium tuberculosis). The choice of *C. glutamicum* as a model system is a perfectly suitable strategy because this organism is genetically tractable and non-pathogenic, its general and secondary metabolism has been investigated in depth and importantly, it is highly tolerant to alteration of the outer-membrane, a feature not found in mycobacteria for instance. It is therefore a remarkable model to investigate the biogenesis of the Corynebacteriales outer-membrane. However, this strategy was original 15 years ago when people from this group initiated their work. Now several other teams use the same model and the competition is strong worldwide. Therefore the originality of the work can no longer just rely on the model organism.

During the last 5 years, the team contributed to major breakthroughs in the field: direct visualization of the mycomembrane by cryoelectron microscopy, development of a method to disrupt the corynebacterial cell envelope and to purify the outer-membrane, and a demonstration of the O-acylation of outer-membrane proteins with unique fatty acids (the mycolic acids). These are major achievements, which paved the way for further researches on the outer-membrane biogenesis in Corynebacteriales.

Despite the impact of these results, the number of publications has been low (7 as 1st or last authors). Research output was published in specialized and good, but not top-rank, journals (J. Bacteriol., Microbiology). The average citation per item is medium. In comparison, other groups reported on the same topics in much higher impact journals. The visibility of the team could be improved when the principal investigators show a more aggressive publication strategy and regularly attend international meetings on bacterial cell surfaces.

Assessment of the unit's academic reputation and appeal

The expertise of the team on corynebacterial cell envelope seems internationally recognized with collaborations with major scientists in the field from France, Germany and UK. However, the visibility is restricted to the field and does not extend to the more general microbiology domain. The team leader coordinated a national project (supported by ANR between 2008 and 2011) and was involved in another ANR consortium (2009-2013), as a partner. This is limited in regard to the major methodological developments made by the group. The two senior scientists were not involved in any international network, and have not had any invitation to present at international meetings. They have not had editorial activity in scientific journals. A single foreign Post-Doc was present in the reporting period and for a very short period of time (2 months).

This is clearly an area where the PI should have a greater activity in the future.

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

The team has not had any strong interaction with the social economic and cultural environment. No contract with industrial partners is reported. Given the major impact of several studied organisms for health and biotechnology, a greater connection with the economic environment is expected.

Assessment of the unit's organization and life

The team is a fusion of two previous groups from IGM and IBBMC working on similar topics. This seems a sound strategy, not only to increase the size of the group, but also to enhance the group dynamics to improve the visibility and attractiveness, and to add to the leadership.

The team has very limited collaboration with other groups at I2BC but will benefit from a departmental structure and a more dynamic environment. The scope of research is in lines with the I2BC scientific priorities.

Assessment of the unit's involvement in training through research

The team leader, as well as other senior group members, is actively engaged in teaching courses within the University. They are involved in several licences programs and are heading teaching units and a Magister program. The very high teaching load interferes with the development of the scientific program.

16 students (3 PhD and 13 master or license students) were trained in the lab and two published as first author.

Assessment of the strategy and the five-year plan

The laboratory has two main projects for the next five-years. First, the team will screen a mutant library to identify genes required for envelope biogenesis. This project will take advantage of the long-standing and productive collaboration with a group in Toulouse (expert in mycobacterial cell envelope constituent analysis). The second project aims at analyzing the impact of post-translational modifications of cell envelope proteins on their subcellular localization and function.

In general, these projects are interesting and reasonably ambitious. They are in lines with previous work and take advantages of the methods developed in recent years. However, the originality and risk-taking is limited and it is unclear how the integration within I2BC will boost the projects through in-house collaborations.

Conclusion

Lab members have pioneered the use of *C. glutamicum* as a model system for exploring the biogenesis of the Corynebacteriales outer-membrane. They have developed various methods and contributed to important scientific achievements. They benefit from a good network of national and international collaborators.

- **Strengths and opportunities:**

This team has strong expertise. The model organism, *C. glutamicum*, appears a fantastic system to unravel the various aspects of the biogenesis of the *Corynebacteriales* envelope. The team developed a unique and promising method to disrupt the *C. glutamicum* envelope and this method will be instrumental in the future. The background to develop an ambitious and successful project is there. In addition, the fusion of the two groups working on similar fields is an opportunity to enhance the attractiveness and the international visibility. Finally the integration within I2BC should open new opportunities for in-house collaborations.

- **Weaknesses and threats:**

The main weakness is poor visibility and attractiveness of the team. The team is involved in collaborations with strong groups but seems to rely too much on external collaboration to exploit their microbiological and biochemical tools. The group should have their own strong projects on which the team will build their national and international recognition and participation to international network. A major threat for future years is the lack of funding. No contracts running after 2013 are indicated in the report.

- **Recommendations:**

In conclusion, the tools are available but should now be used to develop ambitious projects not just relying on collaborations. The team should have a more aggressive publication strategy to report their main achievements in top rank journals. A more frequent participation to international meetings may help to improve visibility.

Team

LABORATOIRE DE GENOMIQUE ET BIODIVERSITE MICROBIENNE DES BIOFILMS (LGBMB)

Name of team leader:

Mr Michael DUBOW

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	4	4
N2: Permanent EPST or EPIC researchers and similar positions		
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**9**	**8**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

This team is composed of 5 permanent members (1 professor, 3 associate professors, 2 technicians) and 6 non-permanent members (one master student, two PhD students and two emeritus researchers). The main objective of this team is to study the largest reservoirs of biodiversity on the Earth, natural bacterial and bacteriophage populations. Particularly original is exploration of the microbial biodiversity in the extremely harsh desert environments. They also studied microbial and bacteriophage populations in sediments of the Seine River downstream of Paris, in the biofilms within the Paris drinking water distribution network, in cooling circuits of the nuclear power plants along the Loire River. Besides generating fundamental knowledge, research of this team aims at finding genes coding for the functions of potential medical and industrial applications. They have many national, but also international collaborations. They collaborated with several industrial partners: Targanta Therapeutics, Compagnie Eaux de Paris and Électricité de France.

In the future, this team envisages continuing examination of the microbial and phage biodiversity using functional metagenomic screens in surface sand from several deserts. One of the major goals is to screen cloned desert metagenomic libraries for the new enzymes and also for novel anti-bacterial and anti-fungal activities.

During last 5 years, this team published 34 articles, of which members of this team were 1st or last authors of 19 (two emeritus not working on team subjects were last authors of 3 of these 19 articles). These 19 publications were were published in specialized fundamental, applied and environmental microbiology journals, like Journal of Microbiology, Microbial Ecology, Water research, with the average IF around 3. They also published one book chapter, one patent application (team PI is 3d of 4 inventors) and one popularization of science article. Number of publication is rather big for such small team.

Given the fact that all permanent members have heavy teaching duties, it seems judicious choice to initiate multiple collaborations in order to increase their scientific productivity (nearly doubling it), as well as to increase financing opportunities (in particular collaboration with the companies).

Assessment of the unit's academic reputation and appeal

The Team participates in four French national networks and obtained a “Bill and Melinda Gates Foundation” grant. The team attracts many foreign students. The PI gave four invited lectures at international meetings during last five years.

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

During reporting period, team has collaborated with several industrial partners: company Eau de Paris, Électricité de France and Targanta Therapeutics. Collaboration with the Targanta Therapeutics resulted in the patent application (team PI is 3rd of 4 inventors).

Assessment of the unit's involvement in training through research

Five PhD students graduated in the last five years. All these students are 1st authors of, at least, one publication. Actually, there are three PhD students in the team. Altogether, the number of PhD students is particularly elevated given the number of permanent staff.

Members of this team are involved in setting up and coordinating master's training programs.

Assessment of the strategy and the five-year plan

The project is continuation of the ongoing research. There is high probability that examination of the microbial and phage biodiversity using functional metagenomic screens in surface sand from several deserts will give interesting results. One of the major goals is to screen cloned desert metagenomic libraries for new enzymes and also for novel anti-bacterial activities and anti-fungal activities. Given the team’s expertise and past success in similar projects, there is a great probability of success.

Conclusion

- **Strengths and opportunities:**

This group has developed an original research approach.

There are many collaborations with academic and industrial partners.

Big number of publications for such a small team.

The team is attractive for the PhD students.

- **Weaknesses and threats:**

The publications are in relatively low impact journals.

Small number of the permanent research staff.

The PI is very productive, other members much less.

The PI is close to retirement.

- **Recommendations:**

If the department wants to maintain this project, PI succession must be rapidly assured.

The team should have a more aggressive publication strategy in order to publish in higher-ranking journals. More frequent participation to scientific meetings is highly recommended.

Team ENDOTOXINS: STRUCTURES AND ACTIVITIES

Name of team leader: Ms Martine CAROFF

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	2
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**4**	**5**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The research activity of this group focused on the structural analysis of endotoxins. This group has a long standing and unique expertise on the use of mass spectrometry technology to depict the fine structure of LPS, which are technically challenging compounds. The activity of the team is highly technology-driven, with novel technological developments improving or facilitating the LPS analysis. However, over the last 5 years, the main achievements have consisted in the application of its expertise to characterize the LPS structure from various microbial contexts: candidate *Bordetella pertussis* vaccine strains, *B. pertussis* clinical isolates, LPS from sulphate reducing bacteria… The PI reports 15 papers and one patent from the group over the last 5 year, which is good for a small team (6 members). The studies are mostly performed in collaborations but team members are being first or corresponding authors in 10 papers. These papers were published in good, but not top rank speciality journals, like Toxins and Rapid Commun Mass Spectrom, with the average IF around 3. These papers do not show important citation rate, but the focus is specialized and the audience is limited. A significant part of the reported activities have not yet led to publications.

Assessment of the team's academic reputation and appeal

The long-standing expertise of the team on LPS analysis and mass spectrometry is internationally recognized. The PI reports 4 invited lectures in international conferences. The PI was involved in the organization of two scientific meetings (national and international) and acted as scientific counsellor of a third international meeting. The team is actively engaged in international research with groups from Canada, China and Morocco. The PI was successful in raising funds from foreign agencies and coordinated several collaborative projects. The team leader is member of the scientific committee of the Equipex project “ANDROMEDE”.

In conclusion, the PI benefits clearly from an international visibility. However, despite the PI academic reputation, the attraction appears limited (only two foreign postdoctoral fellows over the period). The team does not report any editorial activity in scientific journal.

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

The PI has been engaged in technological transfer through the creation of a Start-up in 2011. She was awarded 3 prizes for innovation. She has developed a collaborative project with a non-academic partner, the company Oséo (a PhD student with a CIFRE fellowship working on this project). In addition, the team leader works, as member of a selection committee, in association with HEC for promoting and coaching innovative companies. The PI and one team member are co-authors of a patent.

Therefore, the activity of the PI in this field of technological transfer and interaction with economic environment appears important.

Assessment of the team's involvement in training through research

During the last five years, the PI has contributed to master formation in France and in Canada. The second senior group member is also actively engaged in teaching courses at the University de Bretagne Occidentale. He is heading teaching units at L1 and L3 levels. Four PhD students and 9 masters or licenses students were trained in this group.

The laboratory is a good training environment with a steady output of students

Assessment of the strategy and the five-year plan

The laboratory has two main projects for the next five-years. First, the team wishes to pursue the work on LPS structure characterization in metabolic disease and in *Bordetella* vaccines. This project is funded by an ANR Grant and is clearly in lines with previous work. Second, the team aims at developing new methods to use LPS as a biomarker and to detect LPS in biological samples. These projects are interesting and may lead to important and valuable technological innovation. The willingness to collaborate with non-academic partners is consistent with this objective.

Overall the projects are credible and in lines with the team's expertise. Given the very small size of the group, it seems wise to focus on the strength, structural characterization of LPS, and to avoid dispersion on secondary projects such as the TLR project. If this team wants to maintain its leadership and visibility in the field, it is pivotal to focus on technological developments in order to maintain a steady flux of collaboration with groups addressing specific biological questions connected to LPS. The participation to the Andromede Equipex project is a superb opportunity fully in line with this objective.

A main concern is the retirement of the PI, which will threaten the viability of the team.

Conclusion

This lab applies its unique expertise to investigate the role of LPS in various microbial contexts thanks to international collaborations. The research projects are sound.

- **Strengths and opportunities**

This lab has pioneered the characterization of LPS by mass spectrometry and the PI is an acknowledged expert in this field. This insures a flux of collaboration which is enhanced by the openness of the PI to non-academic partnerships. The Equipex Andromede project is a great opportunity to maintain the leadership of the team in this domain. The five-year plan with a clear technology axis seems a good strategy.

- **Weaknesses and threats**

A main weakness was the very small size which threatens the viability of the team. However, the recent arrival of two collaborators working in hospital is opening interesting opportunities. The main risk associated with this technology-driven research is that constant technology improvement is required to maintain the leadership and visibility. Otherwise, the contribution to research projects may appear secondary with regard to the biological question addressed.

Finally the interaction with other teams at I2BC appears very limited, if any. In addition, a main issue is the retirement of the PI in the next period which will question the future of the team.

- **Recommendations**

Given its small size, this group has two strategic options: to reinforce its strengths through technological developments or to choose a specific biological question and develop the biological expertise to tackle it properly. From the project the first option is favored. However, the PI will retire soon. Therefore, the panel encourages the team and the department to discuss the future of the team.

Team

BIOLOGY AND BIOTECHNOLOGY OF CYANOBACTERIA

Name of team leader:

Mr Franck CHAUVAT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**4**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The group has a long-term history studying basic aspects of cyanobacterial metabolism, development and biotechnology. In particular, the team has been pioneering in the development of a genetic system for cyanobacteria that allows for the deletion and expression of genes in these organisms. These methodologies are now commonly used in the field. In recent years, the team employed genetics to study fundamental processes in cyanobacteria, among which the process of cell division and the production of exopolysaccharides. The group has discovered a critical role of glutathione in the defense against oxidative and metal ions stresses, and revealed that glutathionylation also operates in signaling and regulation.

In recent years, the community interest in cyanobacteria has increased because of their potential applications in white biotechnology and fuel production, using its ability to grow phototrophically using CO2 as carbon source. However, many of its features limit their use for large-scale application including its sensitivity to ethanol. The group has embarked on this topic and utilized metabolic pathway engineering to make cyanobacteria suitable for hydrogen and ethanol production. Mutants of a transcription factor have been obtained that allow for the low level production of hydrogen as well as increased tolerance against oxidative stress. Also the yeast pyruvate decarboxylase and ethanol dehydrogenase have been introduced into cyanobacteria, causing a partial redirection of metabolism towards the production of ethanol. These are first proofs of principle for hydrogen and ethanol production, and now need further optimization and tuning.

Considering the relatively small size of the group (permanent: 2 researchers and 1 technician; non-permanent: 2 PhDs, 1 technician), the team has a good publication record. During last 5 years, this team published 20 articles, of which members of this team were 1st or last authors of 12. These 12 publications were published mostly in the best journals of microbiology, like Mol Micobiol and J Bacteriol, but also in other journals like BMC Structural Biol and Metabolomics journals. They also published 4 book chapters. The team leader has edited a book on the genomics of cyanobacteria with contributions of international researchers, and has written 4 book chapters. The team leader regularly presents the work at national meetings, and at few instances also outside France.

Assessment of the team's academic reputation and appeal

The group obtained three ANR grants including a substantial grant on bioenergy. A good funding state was achieved during the reporting period that however expired by the end of 2013. Although there are no international collaborations listed in the report, interactions exist with groups in India and Israel. Various national collaborations exist. No editorial board memberships are reported. The group consists of various nationalities of Postdocs and PhD students.

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

The group expresses a keen interest in using genetic methods to characterize fundamental processes in cyanobacteria. In the past they have disseminated the methodology of genetic manipulation of cyanobacteria and this has been instrumental for the development of the field. Currently, these methods are also used by main competitors and the team faces the need to identify a new niche to further develop their research on cyanobacteria. In recent years, the group has stepped into the field of biofuel and hydrogen production by cyanobacteria, which is an important topic but that is addressed world-wide by large consortia of scientists. Although initial successes have been made, and some interactions exist with companies on this topic, substantial investments are needed in order to compete internationally. The group did not yet succeed to secure grants for the following period and because of their small size, there is a need to make strategic decisions on the direction(s) to follow in the future.

Assessment of the team's organization and life

The group is relatively small while working on a range of topics. The team leader is intensively involved in research activities and in the daily activities co-steers the group with the other permanent staff member of the team.

Assessment of the team's involvement in training through research

Three PhD students completed their work during the reporting period, a several master students have completed their studies in the group. A number of outreach activities are listed.

Assessment of the strategy and the five-year plan

A strong focus on biotechnological aspects of cyanobacteria is anticipated also to embark on funding opportunities and this dominates the future plans. Two main research lines are foreseen: 1) engineering of cyanobacteria for hydrogen and bioethanol production and 2) detoxification and signaling of oxidative and metal stress. These are continuations of the current research directions. Through the use of mutants and general metabolic engineering approaches, the team aims to improve the production efficiencies. Basically, an engineering approach will be used including the selection of mutants that amongst others are more robust during ethanol fermentation and that are better performers. The team will also pursue the studies on the role of glutathione in detoxification. A better understanding of the stress defense mechanism may also contribute to the development of more robust production hosts. The program is a good mix of basic and applied research, and seems largely feasible provided that a source of funding is obtained to maintain competitiveness.

Conclusion

- **Strengths and opportunities:**

Strong background and authority in cyanobacterial genetics; contemporary topic biotechnological application of cyanobacteria with good opportunities for funding and networking.

- **Weaknesses and threats:**

Small group size; lack of substantial funding; strong international competition in the field of biofuel and hydrogen production.

- **Recommendations:**

Invest in networking, team up with international groups and/or industries for European funding; identify a new niche in the cyanobacterial research with improved funding opportunities.

Team

MOLECULAR BIOLOGY OF THE GENE IN EXTREMOPHILES

Name of team leader:

Mr Patrick FORTERRE and Mr Jacques OBERTO

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	5	2
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**9**	**6**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

This group focuses on understanding the biology, genetics and evolution of extremophiles, with the major focus on Archaea. The key areas are: DNA toposiomerases from extreme thermophiles, study of the KEOPS/DEZ enzymatic complexes responsible for t6A formation in tRNAs, comparative analysis of microbial genomes, and investigation of membrane vesicles in archaeal thermophiles. The foundation for this project has been laid some years ago by the discovery by former PI and coworkers of reverse gyrase and a plethora of other 'unusual' and novel DNA topoisomerases in thermophilic archaea. It was further fueled by identification of DNA-containing membrane nanovesicles in the population of thermophilic archaea and identification of the components of the KEOPS/DEZ complex as universally conserved (and thus present in the LUCA (Last Universal Common Ancestor)) proteins. The research of many members of the team has been very original, visible and unique. During last 5 years, this team published 68 articles, of which members of this team were 1st or last authors of 41. Many of these 41 publications were published in generalist journals like, Genome Biology, Embo journal, Nucleic acids research, PLoS Genetics, PNAS. In addition, some collaborative articles were published in very high impact journals like Nature and Cell. Members of this team were also authors of 7 book chapters and two textbooks.

The group of the former PI is one of the recognized leaders in the field of evolution and molecular biology of archaeal extremophiles. The output of the future PI seems somewhat more modest, although useful bioinformatics tools for the comparative analysis of microbial genomes have been developed and made available to the scientific community.

Assessment of the team's academic reputation and appeal

The former PI of the team has a very high visibility. He has an excellent reputation and world-wide recognition. The former PI is invited to numerous conferences and meetings (often as a keynote speaker). He chairs important committees, delivers public lectures, publishes reviews in the journals of the highest impact, etc. The reputation and prestige of the former PI's research defines the overall highest standing of the team.

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

The members of the team actively participate in regional and international scientific meetings as presenters of invited talks and plenary lectures and also as authors of poster presentations. The key members of the team are actively involved in broad activities related to their professional engagements. Such activities range from participation in various councils and scientific committees, to organizing and chairing thematic groups and clubs, to organization of international colloquia. An additional service to the broad scientific community comes from the development of publicly accessible bioinformatics tools by the future PI.

Participants of the group make an excellent effort to disseminate their research to the general public. The success in this area by former PI is especially commendable; his many articles and multiple lectures increase the prominence of the group and contribute to its exposure to mass media and general public.

Assessment of the team's organization and life

The co-authorship of the previously published papers reveal a tight integration between the individual laboratories of the team. The facility for culturing thermophilic anaerobs set up at the IGM seems to be an important integrative component, which provides a platform for development of new experimental tools and can be utilized by different groups of the team involved in experimental microbiology and biochemistry.

Assessment of the team's involvement in training through research

The current members of the team have supervised 6 PhD students and 5 Masters students. Although this is a good number of trainees, it is not exceptional compared to the other smaller teams.

Assessment of the strategy and the five-year plan

The future directions of research are largely innovative and promising. Three main areas for the future studies are DNA topoisomerases in archaeal extremophiles, biochemistry and evolution of the t6A modification system, and the evolution of bacterial genomes, with a special emphasis on viruses, plasmids and membrane vesicles. The TOPO and genome evolution projects appear to be highly promising and build upon the previous success of the team in these areas. The TOPO direction may not only yield important fundamental discoveries, but may also generate interesting tools for medically-relevant studies. Similarly, the project aimed at unraveling the role of membrane vesicles in genetic transfer in *Archaea* and attempting to integrate the evolution of archaeal genomes with viruses and plasmids is very appealing. It is sufficiently daring, yet is based on the exciting discoveries and new tools developed by the group members. It organically integrates experimental research with advanced bioinformatics analyses and is expected to generate high-impact results. The KEOPS/DEZ project seems to face fairly steep competition. Although the 'alternative' activities of the components of the complex (e.g. their involvement in peptidoglycan biosynthesis in bacteria) is indeed interesting to explore, the appeal of the complex as an experimental model for unraveling biology and evolution of extremophiles as opposed to 'yet another' tRNA modification complex is not immediately obvious.

Conclusion

- **Strengths and opportunities:**

The team, their past research and their future plans are excellent and their studies will likely yield exciting discoveries with general biological significance.

- **Weaknesses and threats:**

The concern is that the previous and current success of the team is based primarily on the research and reputation of the former PI, whereas the leadership capacity of the future PI is not entirely clear at this point.

- **Recommendations:**

The team should use the time when the former and current PIs are acting as co-leaders to increase the productivity and visibility of the future PI and clearly reveal his leadership capacity. A clear plan for action following formal separation of the co-PI would increase the stability of the team.

Team

BACTERIAL CELL ENVELOPES AND ANTIBIOTICS

Name of team leader:

Mr Dominique MENGIN-LECREULX

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**8**	**8**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The research of the team is focused on the metabolism and structure of peptidoglycan, the main component of the bacterial cell wall. The work concerns basic biochemical and enzymological research. In the past period, this involved studies on the structure-function relationship of Mur ligases, the membrane enzymes MraY and MurG involved in lipid I and II biosynthesis, metabolism of the carrier lipid undecaprenylphosphate, the development of antibiotics targeted at cell wall biosynthetic enzymes and recognition of peptidoglycan by the host innate immunity mechanism. The group has made good progress in each of these topics and excels in enzymological characterization, with a well-defined expertise in peptidoglycan biology. A large body of the work is done in collaboration with national and international researchers and this maximizes the output of the group. The group has been part of an FP6 programme on antibiotics development. The team has generated an impressive list of 83 research papers including 23 where members of this team were 1st or last authors. These 23 articles were published in good international peer-reviewed microbiology and biochemistry journals, like J Bacteriol and J Biol Chem. The work is well cited. The group has a good international visibility.

Assessment of the team's academic reputation and appeal

The team has been part of a EU FP6 program on antibiotics development that now has come to an end. The team currently coordinates two national ANR programs and is involved in numerous national and international collaborations. The team leader regularly contributes lectures to international meetings and is an internationally recognized authority on cell wall biosynthesis.

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

The structural and biochemical analysis of the cell wall enzymes is highly relevant for antibiotics development, and this is a red line in the activities of the team. *In vitro* screens are carried out for new small molecules that may act as inhibitors of cell wall biosynthesis. Through interactions with structural biologists and organic chemists, the group studies the molecular basis of inhibitions and tries to find leads to improve the potency of inhibitors. So far no patents have been generated, but because of the diminished willingness to make investments in anti-infectives development by pharmaceutical companies, the team has encountered difficulties to interest industries for further development.

Assessment of the team's organization and life

The unit is well organized with each of the team members contributing a specific expertise in the field of cell wall biosynthesis including specific roles of technicians. The team has many joint publications, and in addition to the team leader, the group members frequently present their work at meetings. The number of non-permanent staff is relatively small for the staff group size. Because of the retirement of a group member, the critical expertise on mass spectrometry of peptidoglycan intermediates was transferred to another group member. The team manages many collaborative interactions in a successful manner.

Assessment of the team's involvement in training through research

Two students have completed their PhD in the reporting period, and the team has supervised various masters and doctorant students mostly from the University Paris-Sud. Postdocs provide a major contribution to the scientific output of the group. Currently there is one postdoc and one PhD student in the team. The group is not involved in a specific training network but two permanent staff members have teaching service, particularly in Masters, allowing direct contact and attractivity to students.

Assessment of the strategy and the five-year plan

The work will continue along the lines developed in recent years and most of the work planned concerns detailed structural characterization of peptidoglycan modifications and proteins. Also the work on C55-P carrier lipid metabolism will be continued with a focus on recycling. In collaboration, the antibiotics development work will be continued, but could benefit from pharmaceutical company links which requires the continued attention of the team

leader. The work on bacteriocins targeting peptidoglycan biosynthesis will be expanded towards bacteriocins of a wide range of organisms. A challenging aim is to isolate supercomplexes of peptidoglycan biosynthesis machineries including various membrane proteins. Overall, the work plan is very coherent, covering a wide range of aspects of cell wall biogenesis. It represents a logical extension of previous work and appears feasible considering the expertise of the group.

Conclusion

- **Strengths and opportunities:**

Good track record in the field of peptidoglycan biosynthesis, broad programme, very good publication output, opportunities in antibiotics development.

- **Weaknesses and threats:**

Difficulties to interest industries to invest in antibiotics development.

- **Recommendations:**

The group is very well connected with other researchers in the field and in structural biology; seek for interactions with medical microbiology (and possibly industrial) to collaborate in antibiotics development in order to focus the work on major pathogens; consider protect knowledge when promising antibiotics are found.

Team

BACTERIAL ADAPTATION TO ENVIRONMENTAL CHANGES

Name of team leader:

Mr Soufian OUCHANE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**6**	**6**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The team consists of 6 permanent staff members, 2 researchers, 3 teaching researchers and 1 technician, all of them participating to the authorship of the publications of the group. Currently, no PhD student or postdoc is present in the group. The scientific activity of the team focuses on the understanding of the mechanisms of adaptation to environmental changes in the photosynthetic purple beta-proteobacterium *Rubrivivax gelatinosus* S1. The diverse research lines can be grouped into four major topics: the control of gene expression in response to oxygen, the biogenesis of bioenergetic complexes in response to oxygen and copper, the response to copper stress and the biofilm formation and regulation. During reporting period, this team has published 7 articles in excellent journals like Mol Microbiol and J Biol Chem. Two PhD students completed their thesis examination between 2008 and 2013.

Assessment of the team's academic reputation and appeal

The members of the group have given invited conferences at international and national meetings. The team has been able to attract new scientists: a CNRS technician in 2009 and a teaching researcher in 2008. Currently no PhD student is working in the team and the team has recruited no postdoc in the last five years. The low ratio of postdocs and students may indicate a lack of funding especially the last years. Indeed, three grants were obtained (2 ANR and one grant from the IFR) but all ending in the period between 2009 and 2012. The team is member of the "Société Française de Photosynthèse" and involved in the organization of the annual meeting and is also member of the GDR "Photosynthesis". Various collaborations exist with national groups and one international group. Members of the group and especially the previous group leader were members of different expert committees or recruitment committees and involved in heavy administration duties.

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

The team members are involved in activities like the « Fête de la Science ».

Assessment of the team's involvement in training through research

In the last five years, they have supervised two PhD students and 3 master students. The PhD students published their work as first authors and this is a sign of efficient training. However, the number of PhD students is low compared to the number of permanent staff. Many master students have been trained in the group. The three teaching researchers of the group are highly involved in teaching and in administrative responsibilities at the University.

Assessment of the strategy and the five-year plan

The project is in the continuation of the on-going research includes many exciting prospects that combine the expertise of the different members of the group. They will study the assembly of bioenergetics complexes in response to oxygen, light and cofactors. So far most studies in the field have been conducted in the green algae *Chlamydomonas* and in cyanobacteria and very few is known on the assembly of these complexes and their interaction in purple bacteria. The copper tolerance in *R. gelatinosus* will also be investigated. Most of what is known on copper homeostasis in bacteria originates from studies in *E. coli* and *Enterococus hirae* and very few are known on copper in phototrophic microorganisms. The last part of this project concerns the biofilm formation and regulation in *R. gelatinus*. All three parts of the project are original, ambitious and may result in unexpected exciting results. However, the committee is worried concerning the size of the group and the largeness of the numerous projects. The group should concentrate on one or two projects only.

Conclusion

- **Strengths and opportunities:**

The quality of the work performed by the members of the team is good as shown by the good quality journals for these publications. The group has new challenging projects, with clear strategy and scientific plan.

- **Weaknesses and threats:**

The scientific production should be reinforced as well as the international visibility.

- **Recommendations:**

The team should seek for more funding and try to recruit more young PhD students and postdoc collaborators. Possibly reinforce the links with other groups in the unit and increase the number of international collaborations.

Team MOLECULAR MICROBIOLOGY OF ACTINOMYCETES

Name of team leader: Mr Jean-Luc PERNODET

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	2
N2: Permanent EPST or EPIC researchers and similar positions	3	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	2	
TOTAL N1 to N6	**7**	**5**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The team is currently composed of 6 permanent staff (one of them with significant teaching duties and another with heavy administrative duties) and 5 non-permanent staff. In addition, an expert scientist will join the group in 2015. The main focus of the team during the last period has been the study of secondary metabolism, of its regulation and evolution in Streptomycetes. In addition, the team has been involved in the study of mobile genetic elements and of the phenomenon of pupylation (prokaryotic ubiquitin-like protein modification) in Actinobacteria. During reporting period, this group has published 12 articles, of which members of this team were 1st or last authors of 6. These 6 articles were published in good specialty journals like Antimicrob Agents Chemother, but also in high impact generalist journals like PNAS and Nature Chem Biol. The team has also 2 book chapters, one patent on an anti-Mycobacterium molecule and 6 PhD thesis.

Assessment of the team's academic reputation and appeal

The team is very well recognized at the national and international level as indicated by its involvement in several collaborative projects funded by EU, French agencies or industrial partners. As a consequence, activities of the group have benefited from multiple grants (local, industrial, national and international). Two members are in the Editorial board of international microbiology journals. Members are frequently invited to give lectures or oral communications at national and international meetings. Members of the team have reached a good international reputation in their field of interest on the biosynthesis of secondary metabolites in Actinomycetes. Although the team has suffered from the retirement of 4 permanent members between 2009 and 2012, it has shown a good capacity to attract young scientists, with three PhD and a Master student that are currently part of the team. The PI of the team has been involved in the organization of national and international meetings on Actinomycetes.

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

Two members of the team have contributed to organize the participation to the international student competition on synthetic biology. The team has several collaborations and is well connected with industrial partners and the PI is co-authors of a patent.

Assessment of the team's involvement in training through research

The team is significantly involved in training. In the last five years they have supervised 8 undergraduate students, 6 Master students and 5 PhD students. One of the former PhD students of the team was awarded a prize for the best oral communication at a specialized meeting. One of the PhD students is co-supervised with the University of Sfax (Tunisia) while a former PhD student was co-supervised with the University Charles (Prague). Members of the group have participated to several PhD final examinations and advisory/recruitment committees. Two members of the team have contributed to organize the participation to the international student competition on synthetic biology.

Assessment of the strategy and the five-year plan

Four projects are planned. Three of them are within the general themes of the study of secondary metabolism, its regulation and evolution in Streptomycetes. The fourth one is on pupylation (prokaryotic ubiquitin-like protein modification) in Actinobacteria. The team proposes to explore Streptomyces secondary metabolism by: i) looking for genomic islands encoding secondary metabolites by developing a new genome mining method that does not rely on sequence similarity; ii) developing combinatorial and mutational approaches for the biosynthesis of new pyrrolimides; and iii) identifying and expressing cyclodipeptide synthases in an heterologous host to study these enzymes and their products. The project on pupylation is aimed at expanding current studies on Streptomyces to other Actinobacteria such as Corynebacteria. This project will take advantage of a scientist with experience on the biology of Corynebacteria that is expected to join the team in 2015. Overall the projects are well planned, connected with each other and with other groups. The project is likely to be successful and originate new knowledge and significant papers.

Conclusion

- **Strengths and opportunities:**

The proposed projects and team are likely to be successful and productive. Strengths of the proposal are mainly the background of the team in the specific field and their contacts with other laboratories and with industrial partners. Altogether, this represents a good opportunity to further improve the level of the scientific publications and reach the fixed goals.

- **Weaknesses and threats:**

While the PI is quite productive, other members of the group are much less active. This could be a weakness of the proposal together with the relatively small size of the group.

- **Recommendations:**

This is a relatively large group with 6 permanent members and an additional one joining in 2015, therefore an increase in the number and quality of products would be desirable and expected. In addition, attention should be paid to the funding situation since most of the grants have now ended and one 4-year ANR contract will start in 2014. The team should try to develop in-house collaborations with other groups of the Microbiology department and the I2BC institute.

Team PLANT BACTERIA INTERACTIONS

Name of team leader: Mr Denis FAURE and Mr Peter MERGAERT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	5	5
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)	2	1
TOTAL N1 to N6	**12**	**10**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	5	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	4	4

• Detailed assessments

Assessment of scientific quality and outputs

The proposed team is the result of a strategic merge of two teams previously hosted at the "Institut des Sciences du Végétal" resulting in a well-balanced and competitive new team. The team will profit from the increased critical mass and provides a stimulating dynamic environment for further development and shared facilities and support. The research theme of the team is focused on characterizing plant-bacteria interactions. One of the PIs is interested in determining how interactions occur that are involved in the establishment of the symbiotic interaction between bacteria and plants while the other PI focuses on understanding plant-bacteria communication and inter-bacterial communication.

The team has made major findings. It was shown that host plant cells produce nodule-specific cysteine-rich (NCR) peptides that penetrated into the bacterial cytosol and cause the bacteria to enter an irreversible differentiation phase. Interestingly, NCRs resemble defensin-type antimicrobial peptides (AMP) that are key effectors of innate immunity in both animals and plants. During this reporting period it was also successfully demonstrated how a plant pathogen is able to by-pass the plant GABA-defense, using another molecule produced by the plant. During reporting period, team has produced 57 articles in peer-reviewed journals and 18 book chapters. The most visible results were published in top journals and are highly visible internationally (e.g. Science, PNAS, PLoS Biology). The remainder of the group production is also of very high quality and was published in journals with good impact factors (Plant Physiol, New Phytol, J Biol Chem, Mol Microbiol, Mol Plant-Microbe Interact).

Assessment of the team's academic reputation and appeal

Both PIs of the team have a very well established international reputation with many invitations and oral presentations at international conferences. Further support of their well-established international reputation derives from editorial and expertise activities of the members of the team (Editor for PNAS, Editor of Research in Microbiology, associate Editor for the Mol Plant-Microbe Interactions, AERES committees, scientific council of the ERC). One of the PIs has been involved in the organization of several national meetings.

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

Two international patents were produced during the reporting period. One project has direct potential in agricultural and economic benefits. Members of the group have participated to communication for the general public (publications, radio programs, wikipedia articles).

Assessment of the team's involvement in training through research

The team has trained many students. Hence, 13 PhD students have defended or are doing their thesis, and 15 students have been trained for master internship. There is an assistant professor in the team, who is teaching in M2. The former PIs participated to courses in France and abroad (PhD training programs in Malaysian, European and American universities).

Assessment of the strategy and the five-year plan

The proposed project concerns a follow-up of current studies as well as an exploration of new areas. New powerful methods will be used to investigate root bacterial colonization. Plant interference with the bacterial quorum sensing will be studied by analyzing the ecological significance of the plant lactonase activity. The group has been studying bacterial lactonase, and their future work will build on their expertise and achievements in this field. Structural characterization of periplasmic sensors involded in binding plant metabolite will be pursued and will certainly benefit from the I2BC environment.

Bacterial differentiation in the Rhizobium-legume symbiosis will be studied, by the complete « omic » approach, in a new model system in which the bacteroides have three different host-dependent morphotypes. These studies will include the identification of important determinants for the bacteroides differentiation in both the plant and the bacteria. During symbiosis, plant cell undergoes replication of its nuclear genome in the absence of cell division, and this is associated to large and specific transcriptional reprogramming. Molecular characterization of this

process in M. truncatula will be a new research area for the team. The team has successfully secured finances to realize their ambitions. The new area entered will undoubtedly provide important connections with other teams at I2BC and provide biological insights of great interest to many researchers in the field and beyond.

Conclusion

- **Strengths and opportunities:**

The team has a strong background in plant-bacteria interaction and carries out excellent fundamental research; their work provides relevant general concepts for a range of host-bacterial interaction with direct application in agriculture and food safety. The merging of the two teams is coherent and strategic, and it provides a critical mass favorable for the realization of the project. The two PIs have already shared lab meetings, know each other since a long time and have shown to be able to work together in a collaborative spirit. Some research lines on plant cell differentiation have been terminated because of strategic and rational considerations, providing a better match to the I2BC Microbiology department. The team has developed a very good attractiveness resulting from work initiated under former directors, that are still very active, and from the independent work developed by the current PIs. The fruitful collaboration will be strengthened by the integration of the collaborating team in the I2BC (BBS department).

- **Weaknesses and threats:**

There is a risk of decreased interactions with groups working on plant biology because of the embedment in the Microbiology department where they will be the only ones using plants.

- **Recommendations:**

The PIs should maintain strong interactions with other groups working on plants.

They might apply for European funding, and also develop a collaborative project that profits from the synergy between the PIs.

Team

INFECTION GENETICS EMERGING PATHOGENS EVOLUTION (IGEPE)

Name of team leader:

Mr Christophe SOLA

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions		
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	2	
TOTAL N1 to N6	**4**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The IGEPE team was created in 2007 thanks to an "Excellence Chair in Microbiology" from UPS granted to the team leader. The scientific interest of the team is focused on "Systems Epidemiology", an original research field at the interface of Microbiology, Demography and Ecology. The team know-hows involve essentially genomics and bioinformatics. They developed a high-throughput and cost effective assay using CRISPR loci for in vitro diagnosis of Multi-Drug Resistant Mycobacterium tuberculosis. This technique was adapted to the detection of Salmonella and Legionella. Involved in new technologies applications, the team also developed electro-chemical detection assisted DNA chips for the identification of *M. tuberculosis* clades. These approaches were exploited by the IGEPE team to investigate the polymorphism of the CYP2D6 cytochrome in the framework of a collaborative project. Activities of the team in the field of molecular epidemiology were essentially focused on the study of the transmission rate and genetic diversity of tuberculosis in different countries. Exploiting its knowledge of CRISPR, the team developed a new algorithmic method to analyze spoligotypes (CRISPR) similarity and evolution in *M. tuberculosis* and showed it provided better results than more classical phylogenetic tree-based techniques. This bioinformatic technique is now in the way to be transferred to the study of CRISPR in Salmonella and Legionella. These studies were leading to the publication of 25 articles in international peer-reviewed journals over the period 2008-2013, most of the articles appearing in PLoS ONE and Infect Genet Evol. Over the 25 articles listed, 7 were signed as last author by a member of the team and most resulted from collaborative studies. No article in journals with IF>5 was listed.

Assessment of the team's academic reputation and appeal

In addition to the grant provided by the "Chaire d'Excellence" from UPS (140k€), the team took part in different collaborative projects in the framework of the "European and Developing Countries Clinical Trial Partnership", DIM-MALINF and with the Royal Tropical Institute and "Direction Générale de l'Armement". This was leading to a mean of 611 k€ over 6 years, including service contracts.

As previously noted, the team developed scientific collaborations with many countries and received Doctoral and post-doctoral students from Venezuela, Italy, Brazil and Pakistan. The team also collaborated with the Pasteur Institutes International Network and took part in the Global Network for the Molecular Surveillance of Tuberculosis under the direction of RIVM (Netherland). The team leader was invited to give lectures in 9 congresses between 2008 and 2013. He was co-chairman of the ICEPID-ICEPT 2012 Congress in Hungary and is Academic Editor of the journal PLoS ONE. He is also member of the expert panel of the Italian Research Ministry, of the European Center for Diseases Control and of the South African Research Foundation. In 2013, the team leader was recipient of a L. Deschien Microbiology price from the National Academy of Medicine.

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

The team created a technological platform that provides R&D, genotyping services and reagents thanks to a license purchased from Luminex®. A startup is under creation. One of the team's thesis was granted by the Merieux foundation. The team takes part in the "Fête de la Science" (France) and in the Make Science project (India).

Assessment of the team's organization and life

The size of the team is limited (2 permanent staff, 2 PhD students, 1 non-permanent Assistant Engineer). The team also receives L-level students for short periods. Only one of the 2 staff members is HDR and both are members of UPS and have thus teaching obligations (although this obligation was reduced temporarily in the case of the team leader as he was recruited in the framework of a "Chaire d'Excellence"). The indicated budget of the team over the previous years (Mean =100 k€/year) appears coherent with its size.

Assessment of the team's involvement in training through research

Two thesis have been produced by the team since 2008. There is a thesis co-advised with the Pasteur Institute of Madagascar. The 2 staff members guided a total of 5 Master students and 6 L-Level trainees. The team received 11 foreign trainees for short to long (one year) internships. Between 2007 and 2009, the team leader was Director of the Master 2 degree of UPS. Both staff members have now different responsibilities in Masters or Licence formation units.

Assessment of the strategy and the five-year plan

The team's project is in the direct continuity of its progress report. It is focused on the development of the previously described spoligotype (CRISPR) and electro-chemical detection assisted DNA chips techniques but the precise research program was not detailed. New collaborative projects to investigate the genomic diversity of pathogens (essentially Multi-Drug Resistant *Mycobacterium tuberculosis*) to understand tuberculosis epidemiology, history and evolution should be also developed and the former ones are continued. The mode of action and metabolic consequences of CRISPRs in Salmonella and Legionella should be also investigated. The creation of new diagnostic tools is also mentioned. A main concern is the limited connection of the scientific projet with I2BC scientific priorities.

Conclusion

- **Strengths and opportunities:**

Original techniques and approaches with high applied potential.

Wide collaborative network in foreign countries.

Budget adapted to the needs.

Good scientific production.

Team recently created (2007-08).

Potential for cross connexions with other teams of the microbiology department.

Expertise in a re-emerging disease in occidental countries (tuberculosis).

- **Weaknesses and threats:**

Very limited size of the team (2 permanent staff).

One HDR staff member, the team is then totally dependent on the team's leader.

The project is at the margin of the central axis of I2BC.

Limited interactions with other teams of the microbiology department.

Risk of dispersion with the creation of the start-up.

- **Recommendations:**

The project should be re-oriented on I2BC priorities.

Dispersion to secondary project should be avoided.

The second staff member should rapidly defend an HDR.

The team should recruit other permanent members or at least obtain grants allowing the recruitment of contractual investigators.

The involvement of the team's members in the start-up should be clarified to preserve the research potential to the IGEPE team.

Team

GENOMES AND POLYMORPHISMS

Name of team leader:

Mr Gilles VERGNAUD

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	3	1
TOTAL N1 to N6	**6**	**4**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The main objective of the research is microbial surveillance, investigating evolution of bacterial pathogens and studying pathogen-bacteriophage interactions.

The group includes three key personnel and four non-permanent members. Previous research has been focused, among other areas, on describing populations of specific bacterial pathogens in different locales, analysis of CRISPR elements in Yersinia and investigation of *P. aeruginosa* bacteriophages. The group is generally well published with 52 papers and 4 book chapters appearing since 2008. The spectrum of the journals, however, is somewhat narrow, with 8 papers over this period appearing in PLoS One. Although there is nothing intrinsically wrong with having one's favorite journals, diversifying the spectrum of scientific venues could help to reach a broader audience.

Assessment of the team's academic reputation and appeal

The team has high reputation. The group participates in a number of national and international collaborations including laboratories and organizations in China and Russia. The team has also organized two training courses (one national and one international) on bacterial genotyping. The members of the group have participated in several French and international scientific meetings, presenting invited lectures, oral communications and posters. The team has provided useful resources for the scientific community: the web tool for analysis of CRISPR loci generated by the group is actively used by many groups. Other databases (microbial tandem repeats, the genotyping database and the Orsay phage database) are also publicly available.

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

The group has participated in outreach activities having organized several broad-audience conferences and participating in the 'fête de la science'. The group's interaction with industry is excellent; two patents (together with the biotech start-up CEERAM) have been filed and a contract with Pherecides Pharma provides additional funding for research.

Assessment of the team's involvement in training through research

Three PhD students, several Masters students. Several papers have been published with the students. However, given the total number of publications, proportion of published articles involving student is not very high.

Assessment of the strategy and the five-year plan

The project focuses primarily on bacteriophages, their interaction and coevolution with pathogens, and exploration of their potential use for treatment of drug-resistant infections. Although phage-based therapeutic approaches went out of fashion in most countries, there are many basic biological as well as medically-relevant questions of phage-pathogen interactions which remain unclear. Identifying phages that could hypothetically be used for the treatment of infections caused by MDR strains, investigating whether antibiotic- and phage-resistance could be linked and analyzing whether 'therapeutic' phages could spread resistance via gene transduction are among the important questions that will be addressed. The planned approaches are somewhat serendipitous, but if the previous success of the team is any indication of their future progress, the project will likely generate interesting data. An additional value comes from the plans to organize and maintain the collection of clinical pathogens which could be a source of synergy with the other groups in the department.

Conclusions

- **Strengths and opportunities:**

Altogether, the team comes around as a solid and productive research group, visible and recognized in the area of microbiology.

Their work in a medically and socially important field adds value to their studies and opens interesting venues for the rest of the department and the Institute.

- **Weaknesses and threats:**

The surveillance side of the research carried out by the group does not fit snuggly in the stated theme of I2BC.

The placement of the papers in the scientific journals seems somewhat biased (8 papers in PLOS One in the 5 year period) and a broader choice of journals would seem to be beneficial.

- **Recommendations:**

The relatively small size of the team calls for the well-defined priorities in regards to the multiple projects planned for the next period.

An effort to publish the papers in the journals with the highest visibility would be also beneficial.

Team ENERGETIC METABOLISM OF STREPTOMYCES

Name of team leader: Ms Marie-Joelle VIROLLE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**6**	**4**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

This is a small group, currently composed of 3 permanent staff (the PI, a technician and an assistant professor working in the team for 80% of her time), 3 non-permanent staff (a post-doc, a PhD student and an engineer) and a visiting scientist. Main focus of the team during the last period has been the study of the energetic metabolism in Streptomycetes and of its connections with antibiotic synthesis and morphological differentiation. In spite of the small size of the group 11 papers have been produced between 2009 and 2013, mostly in specialty journals like Applied Soil Ecology and Applied Environ Microbiology. The team also produced 2 patents and 3 PhD theses.

Assessment of the team's academic reputation and appeal

The team collaborates with several other national and international groups and participates to various projects (French agencies, EU, international contracts). The PI is in the editorial board of a scientific journal and is frequently invited to give lectures at international meetings. The team has experienced the departure of 8 members between 2008-2011 but has shown a good capacity to attract scientists from abroad (some in the frame of cooperative contracts with foreign countries).

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

One member of the team is involved in teaching at various levels while the PI teaches at Master students. Several students (BTS, L3, M and M2) have been supervised by members of the group. The team is very active in collaborating with other groups in France and abroad. Some of those collaborations have originated joint papers. The team has also contacts with industrial partners that in some cases have sponsored a PhD student working in the group. The PI has co-organized 2 national and 1 international meeting and is Editor of a scientific journal.

Assessment of the team's involvement in training through research

The team is significantly involved in training. In the last five years, they have supervised several students at the undergraduate, Master and PhD level. One of the PhD students was co-supervised with the University of Sfax (Tunisia).

Assessment of the strategy and the five-year plan

The proposed project aims at developing a better understanding of the lipid metabolism in Streptomyces by using genetic and genomic approaches. This topic is particularly relevant since lipid metabolism is connected with antibiotic biosynthesis and morphological differentiation. In addition, lipids, and in particular TriAcylGlycerol (TGA), are also relevant as direct precursor of bio-diesel. Within this main frame the team proposes to: i) use in silico and omics approaches to identify all genes of Streptomycetes directly or indirectly involved in acetylCoA synthesis from glucose and/or glycerol; ii) use *in silico* and omics approaches to identify genes of Streptomycetes coding for enzymes of the lipid/TGA biosynthetic pathway and involved in the synthesis of enzymatic co-factors; iii) study the correlation of nitrogen limitation and phosphate metabolism on TGA metabolism; and iv) perform a transcriptional analysis of genes coding for regulatory proteins involved in TAG biosynthesis. Overall the project seems quite ambitious for a small team, however, the team has already shown the capacity to be productive. The proposed experiments appears straighforward and are likely to originate new knowledge and papers.

Conclusion

- **Strengths and opportunities:**

In general the proposed projects and team are likely to be successful and productive.

Strengths of the proposal are mainly the background of the team in the specific field and their contacts with other laboratories and with industrial partners. These things represent a good opportunity to improve the level of the scientific publications and reach the fixed goals.

- **Weaknesses and threats:**

Weakness of the team is the small size of the group and the lack of a plan for different experimental approaches in case the proposed one should encounter difficulties.

- **Recommendations:**

The five-year plan is quite ambitious for the small research group.

The significant funding raised should make it possible the recruitment of experienced PostDocs to successfully carry on the projects.

5 • Conduct of the visit

Visit dates:

Start: Monday January 6th 8:30 a.m. 2014

End: Thursday January 9th 6:00 p.m. 2014

Visit site: Gif sur Yvette

Institution: CNRS

Address: CNRS Campus

Programme of visit:

Sunday January 5th
Evening
CNRS Castle
19h00 - 21h00
Welcome of committee members. Dinner 1 (Committee)

Monday January 6th
Morning
Building 21, Auditorium
8h00-8h30 : Introduction *(AERES coordinators + experts committee)*
8h30-10h00*: I2BC Presentations of Director & Deputy director (experts committee + Departments heads + group leaders + representatives University, CEA and CNRS)*
10h00-10h15*: Break*
10h15-12h45*: Presentation of departments (experts committee + I2BC direction, Department heads + group leaders + representatives University, CEA and CNRS)*
12h45-14h15 : Lunch *1, CNRS restaurant (Room reserved for experts committee)*
Afternoon
14h15-14h30 : Group leaders presentations

GENOME : Room VIOLETTE	B3S-VIRO : CUBE, Ground floor	BIOCELL : AUDITORIUM	MICROBIOLOGY : Room BLEUE
Organization of the bacterial chromosome (Mr Frédéric BOCCARD) 14h30-15h10	***Bacteriophages of gram-positive bacteria*** (Mr Paulo TAVARES) 14h30-15h10	***Functions and dysfunctions of mitochondria*** (Ms Agnès DELAHODDE) 14h30-15h10	***Biology and biotechnology of cyanobacteria*** (Mr Franck CHAUVAT) 14h30-15h10
Programmed genome rearrangements (Ms Mireille BÉTERMIER) 15h15-15h55	***Bacteriophage T5*** (Ms Pascale BOULANGER) 15h15-15h50	***Biogenesis and functioning of mitochondrial oxphos complexes in yeasts*** (Ms Nathalie BONNEFOY) 15h15-16h00	***Bacterial adaptation to environmental changes*** (Mr Soufian OUCHANE) 15h15-15h55
16h00-16h15: Break			
GENOME : Room VIOLETTE	B3S-VIRO : CUBE ground floor	BIOCELL : AUDITORIUM	MICROBIOLOGY : Room BLEUE
Genome analysis (Ms Linda SPERLING) 16h15-16h55	***Integrative structural virology*** (Mr Jean LEPAULT) 16h15-16h55	***Biogenesis and function of centriolar and ciliary structure*** (Ms Anne-Marie TASSIN) 16h15-16h55	***Plant bacteria interactions*** (Mr Denis FAURE/ Mr Peter MERGAERT) 16h15-17h00
DNA bioinformatics and biophysics (Ms Marie-Claude MARSOLIER-KERGOAT) 17h00-17h35	***Rhabdoviruses*** (Mr Yves GAUDIN) 17h00-17h40	***Cytoskeleton in cell morphogenesis*** (Mr Alexis GAUTREAU) 17h00-17h40	***Molecular biology of the gene in extremophiles*** (Mr Patrick FORTERRE/ Mr Jacques OBERTO) 17h05-17h50
DNA replication dynamics in higher eukaryotes (Ms Kathrin MARHEINEKE) 17h40-18h15	***Molecular biology of Rotaviruses*** (Mr Didier PONCET) 17h45-18h25	***Imaging, endocytosis and the actin cytoskeleton*** (Ms Christien J. MERRIFIELD) 17h45-18h20	***Laboratoire de génomique et biodiversité microbienne des biofilms*** (Mr Michael DUBOW) 17h55-18h40
18h30-19h: Debriefing (Committee) CUBE, ground floor Building 21 ***19h30-21h*** Dinner 2 CNRS Castle			

Tuesday January 7th

Morning

GENOME : Room VIOLETTE	B3S-VIRO : CUBE ground floor	BIOCELL : AUDITORIUM	MICROBIOLOGY : Room BLEUE
Evolution and maintenance of circular chromosomes (Mr François-Xavier BARRE) 8h30-9h10	***Virulence and latency of Herpesviruses*** (Ms Audrey ESCLATINE) 8h30-9h10	***Cellular signaling and ubiquitination*** (Mr Grégory VERT) 8h30-9h05	***Bacterial cell envelopes and antibiotics*** (Mr Dominique MENGIN-LECREULX) 8h30-9h10
Genome Stability in bacteria (Ms Bénédicte MICHEL) 9h15-9h50	***Structural biochemistry of microtubules: motors and regulation*** (Mr Marcel KNOSSOW) 9h15-9h55	***Autophagy and development*** (Mr Renaud LEGOUIS) 9h10-9h50	***Molecular biology of Corynebacteria and Mycobacteria*** (Mr Nicolas BAYAN) 9h15-9h55
Sexual differentiation in fungi and meiosis (Mr Robert DEBUCHY) 9h55-10h35	***Structural biology of molecular switches and motors*** (Ms Julie MENETREY) 10h00-10h35	***Membrane traffic and cell coordination*** (Ms Marie-Hélène CUIF) 9h55-10h30	***Endotoxins: structures and activities*** (Ms Martine CAROFF) 10h00-10h40
10h40-11h00 : Break			
GENOME : Room VIOLETTE	B3S-VIRO : CUBE ground floor	BIOCELL : AUDITORIUM	MICROBIOLOGY : Room BLEUE
Nuclear regulation and stress (Mr Joël ACKER/Mr Olivier LEFEBVRE) 11h00-11h35	***Cytoskeleton dynamics and motility*** (Mr Christophe LE CLAINCHE/ Mr Louis RENAULT) 11h00-11h45	***Dynamics of cell compartmentation & cell imaging*** (Ms Beatrice SATIAT-JEUNEMAITRE) 11h00-11h45	***Energetic metabolism of Streptomyces*** (Ms Marie-Joëlle VIROLLE) 11h00-11h40
Transcriptional regulation of genomes (Mr Michel WERNER) 11h40-12h20	***Structural biology and radiation biology laboratory/nuclear envelope, telomeres and DNA repair*** (Mr Jean-Baptiste CHARBONNIER/ Ms Marie-Hélène LEDU/ Ms Sophie ZINN-JUSTIN) 11h50-12h35	***Cell signaling and morphogenesis*** (Anne-Marie Prêt) 11h50-12h30	***Molecular microbiology of Actinomycetes*** (Mr Jean-Luc PERNODET) 11h45-12h25
***12h35-14h00 : Lunch 2**, CNRS restaurant (Room reserved for committee)*			

Afternoon

GENOME : Room VIOLETTE	B3S-VIRO : CUBE ground floor	BIOCELL : AUDITORIUM	MICROBIOLOGY : Room BLEUE
Physiology and pathogenicity of stress (Mr Stéphane CHÉDIN/ Mr Laurent KURAS) 14h00-14h40	***Molecular assemblies and genome integrity*** (Ms Françoise OCHSENBEIN/ Raphaël GUEROIS) 14h00-14h40	***Growth and metabolism in drosophila*** (Mr Jacques MONTAGNE) 14h00-14h35	***Genomes and polymorphisms*** (Mr Gilles VERGNAUD) 14h00-14h40
Post-transcriptional regulation of gene expression (Ms Anna POLESSKAYA) 14h45-15h20	***Fonction et architecture des assemblages macromoleculaires*** (Mr Herman VAN TILBEURGH) 14h45-15h30	***Oxidative stress and cancer*** (Mr Michel Toledano) 14h40-15h20	***Infection genetics emerging pathogens evolution*** (Mr Christophe SOLA) 14h45-15h25
16h05-16h20: Break			
GENOME : Room VIOLETTE	B3S-VIRO : CUBE ground floor	BIOCELL : AUDITORIUM	
Epigenetics and cancer (Ms Annick HAREL-BELLAN) 15h50-16h30	***Protein engineering and protein modeling*** (Mr Philippe MINARD) 15h55-16h40	***Integrated approaches of ion transport*** (Mr Sébastien THOMINE) 16h20-17h05	
Mammalian epigenomics (Mr Matthieu GÉRARD) 16h35-17h10			
Senescence and genome stability (Mr Carl MANN) 17h15-17h50			
Paleogenomics (Mr Jean-Marc ELALOUF) 17h55-18h30			

18h30-19h: *Debriefing (Committee) (CUBE ground floor Building 21).*

19h30-21h:

Dinner 3 (CNRS castle)

Wednesday January 8th

Morning

GENOME :	B3S-VIRO :	
Room BLEUE	CUBE ground floor	
Proteasome: assembly, regulations and functions	**Bioenergetics, metalloproteins and stress**	**Meeting with I2BC Administrative and Technical staff**
(Ms Anne PEYROCHE)	(Mr Bruno ROBERT)	
8h30-9h10	8h30-9h15	**Auditorium**
Protein maturation, cell fate and therapeutics	**Molecular photophysics and catalysis**	9h30-10h45
(Ms Carmela GIGLIONE)	(Mr Winfried LEIBL)	
9h15-10h00	9h20-10h05	
10h05-10h20 : Break		10h45-11h30: Break
GENOME :	B3S-VIRO :	
Room BLEUE	CUBE ground floor	
Genomic, structure and translation	**Regulatory mechanisms in photosynthetic organisms**	
(Mr Olivier NAMY)	(Ms Diana KIRILOVSKY)	
10h20-11h05	10h20-11h05	
RNA structure and dynamics	**Oxidative stress and detoxification**	**Meeting with I2BC scientific staff**
(Mr Dominique FOURMY)	(Mr Pierre DORLET)	**(without group leaders and I2BC direction)**
11h10-11h50	11h10-11h55	**Auditorium**
Supramolecular assemblies and translation	**Biological high-field magnetic resonance**	11h30-12h45
(Mr Marc MIRANDE)	(Mr Sun UN)	
11h55-12h30	12h00-12h35	
Structure, function, evolution of catalytic RNA		
(Mr François MICHEL)		
12h35-13h10		
13h10-14h30: Lunch 3.		
CNRS restaurant (Room reserved for committee)		

Afternoon

GENOME : *Room BLEUE* ***Molecular bioinformatics*** *(Mr Alain DENISE /Mr Olivier LESPINET)* *14h30-15h10* ***RNA sequence, structure and function*** *(Mr Daniel GAUTHERET)* *15h15-15h55*	*B3S-VIRO :* *CUBE ground floor* ***Photosystem II*** *(Mr Alain BOUSSAC)* *14h30-15h05* ***Laboratory of membrane proteins and membrane systems*** *(Mr Francis HARAUX)* *15h10-16h00*	***Meeting with Directors of Doctoral schools*** ***Auditorium*** *14h30-15h* ***15h00-15h15**: Break* ***Meeting with I2BC PhDs, postdocs & CDDs*** ***Building 21*** ***Auditorium*** *15h15-16h30*
***15h55-16h10**: Break*		***16h30-17h00**: Break*
GENOME : *Room BLEUE* ***Signalisation et réseaux de régulations bactériens*** *(Mr Philippe BOULOC)* *16h10-16h50* ***Gene regulation in Salmonella and its phages*** *(Ms Nara FIGUEROA-BOSSI)* *16h55-17h30* ***Radioresistance of bacteria and archaea*** *(Mr Fabrice CONFALONIERI)* *17h35-18h20*	*B3S-VIRO :* *CUBE ground floor* ***Microbiology and structural enzymology*** *(Ms Solange MORERA)* *16h10-16h45)* ***Interactions and assembly mechanisms*** *(Mr Stéphane BRESSANELLI)* *16h50-17h30*	***Debriefing*** ***Building 21*** ***Auditorium*** *17h00-18h30*
***18h30-19h20**: Debriefing (Committee) (CUBE ground floor Building 21).* ***19h30-21h** : Dinner 4 (CNRS castle)*		

Thursday January 9th

Morning

Cube (ground floor Building 21)

8h30-11h30: Plenary meeting of committee, *ad hoc* interviews of I2BC director and/or department heads possible (Committee)

***11h30-11h45** : Break*

Cube (ground floor Building 21)

11h45-12h45: Meeting committee with University, CEA and CNRS representatives

13h00-14h30 : Lunch committee with University, CEA and CNRS representatives

CNRS restaurant (Room reserved for committee)

Afternoon

Cube (ground floor Building 21)

14h30-16h15: Redaction evaluation report (Mr Frédéric BARRAS+ Presidents sub-committees)

***16h15-16h30**: Break*

Cube (ground floor Building 21)

16h30-18h00 : Redaction evaluation report (Mr Frédéric BARRAS+ Presidents sub-committees)

End of site visit

Specific points to be mentioned:

The expert Ms Angélique VÉTILLARD was unable to attend the site visit.

6 • Supervising bodies' general comments

UNIVERSITÉ PARIS SUD

Comprendre le monde, construire l'avenir®

Le Président de l'Université Paris-Sud

à

Monsieur Pierre GLAUDES
Directeur de la section des unités de recherche
AERES
20, rue Vivienne
75002 Paris

Orsay, le 21 mai 2014

N/Réf. : 147/14/JB/LM/AL

Objet : Rapport d'évaluation d'unité de recherche
N° S2PUR150008279

Monsieur le Directeur,

Vous m'avez transmis le 14 avril dernier, le rapport d'évaluation de l'unité de recherche « Institut de Biologie Intégrative de la Cellule » - I2BC - N° S2PUR150008279, et je vous en remercie.

L'université se réjouit de l'appréciation portée par le Comité sur cette unité particulièrement importante pour sa recherche en Sciences de la Vie et prend bonne note de ses suggestions. Elle suivra son démarrage avec attention.

Monsieur Thierry MEINNEL, Directeur de l'unité de recherche, n'a pas souhaité apporter de commentaires.

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

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