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

Section des Unités de recherche

AERES report on the research unit

Genomes and Genetics Department

From the

Institut Pasteur

March 2011

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From the

Institut Pasteur

Le Président de l'AERES

Didier Houssin

Section des unités de recherche

Le Directeur

Pierre Glorieux

March 2011

Research Unit

Name of the research unit: Genomes and Genetics Department

Requested label

N° in the case of renewal

Name of the director: Mr Didier MAZEL

Members of the review committee

Committee chairman

Ms Ariane TOUSSAINT, Université Libre de Bruxelles, Bruxelles, Belgium

Other committee members

Mr Serge BOITEUX, CEA, Fontenay-aux-Roses, France (CoNRS)

Mr Eric BÖTTGER, University of Zürich, Zürich, Switzerland

Mr Søren BRUNAK, Technical University of Denmark, Lingby, Denmark (Institut Pasteur Scientific board)

Mr Tom COENYE, Ghent University, Ghent, Belgium

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Mr Gabriel WAKSMAN, University College of London, London, UK (Institut Pasteur Scientific board)

Observers

AERES scientific advisor

Mr Pierre LEGRAIN

University, School and Research Organization representatives

Mr Tony PUGSLEY Institut Pasteur

Ms Evelyne SAGE, CNRS Life Sciences

Ms Claire LHUILIER, CNRS Physics

Report

1 • Introduction

- Date and execution of the visit

The visit took place on March 7-9 2011, at the Institut Pasteur. Due to the large number of teams to be evaluated, during the three sessions of presentations by the teams, the committee of 12 people was split into two sub-committees. This of course allows for shortening the duration of the visit but it is unfortunate that a committee member had no chance to listen to all the presentations. Fortunately, the general discussion to prepare the reports on the teams was very positive and a consensus could be easily reached between members of the sub-committees.

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

Located at the Institut Pasteur in Paris, the Department Genomes and Genetics was created in 2006, regrouping most of the teams formerly part of the Department Genome Structure and Dynamics. The teams in the department are spread over various buildings on the IP campus, which does not seem to impact too much on the intra-department contacts and favours contacts with groups in other departments, possibly with the exception of the bioinformatics activities. The Department brings together teams working on various domains of the living world, prokaryotic and eukaryotic microbes pathogenic for humans and other animals and humans. Among those teams, two may be considered as founding teams (3 and 6), three joined in 2006 from other departments in the same Institute (1, 7, 8, 9) and four are teams emerging from this department (2, 4, 5, 20). The main lines of research are evolutionary genomics, DNA metabolism (replication, recombination and repair), regulation of gene expression and regulatory networks, and host-pathogen interactions.

- Management team

Presently headed by Didier Mazel (elected by his peers and appointed by the General Director and proposed for renewal), with Christophe d'Enfert as deputy director, the Department was headed by Antoine Danchin with D. Mazel as deputy director from 2006 to 2009. While remaining an intermediate between the Institut Pasteur upper management and the research units, the department head has recently gained more impact, being involved in decisions on the equipment budget and in the institute scientific strategic decisions and prospective. He informs department members of the scientific policy of the Institute Directors and fosters relations with other departments. A departmental council composed of the team heads and elected members from the different personnel categories meets four times a year, aside from two departmental council meetings of the team heads, a departmental committee in charge of scientific animation and a yearly departmental retreat. One scientist is in charge of the contacts with the Institute Technology Transfer Office.

The Genomes and Genetics department groups 14 research teams and 4 technical platforms, which constitute the Pasteur Genopole. Among these 14 units 9 constitute CNRS URA 2171 (teams 1-9), one is part of CNRS URA 3012 (team 17) and another of INRA USC2019 (team 18). This quite complex organisation results from the history of the Institut Pasteur research units. Their articulation with National French research organisations does not interfere with the overall management of the department. The administrative links between the Institut Pasteur laboratories and the other research organisations allows for their contribution to specific financial and human resource supports.

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	5	5
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	36,2	34
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	43	41
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	39,8	39,8
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	18	
N6: Number of Ph.D. students (Form 2.7 of the application file)	27	
N7: Number of staff members with a HDR or a similar grade	24	26

2 • Overall appreciation on the research unit

• Summary

The department has a very strong publication record and its scientific activity is clearly visible within the French genetics research landscape. The contribution of the different teams to both the publication record and the visibility is not completely uniform and some topics and research areas are stronger than others. The department has contributed 5 patents over the evaluation period, and here again some teams appear more concerned and productive than others. The Pasteur Genopole offers services to the Institut Pasteur and to some extent provides its services to external laboratories.

• Strengths and opportunities

- The strength of the department is its expertise in bacteria, yeast genetics and genomics.
- A large majority of the teams are leaders in their respective fields, some with ground breaking perspectives and imaginative projects.
- Team heads and members contribute to teaching, both inside IP and in universities and organize seminars and conferences in the department, for the Institute and the rest of the scientific community in France and abroad.
- The Department is attractive for PhD students and post-docs from France and abroad and has produced several group leaders now very successful in other institutions.
- The department management is fully appreciated by its members who are happy to work there!

• Weaknesses and threats

- Several teams are not as productive as others and not all projects are of the same quality.
- An attempt to establish a productive systems biology team was so far not as successful as it should have been. However, this line of research is clearly very important for the future of the positioning of the Department as a leader in its fields of interest.
- Several technical platforms are part of the department. They are of unequal quality. Some of them need benchmarking/audit both for the type, management and quality of services proposed to the local and outside scientific community.
- Some team leaders may be retiring in the near future. A clear strategy for continuation/discontinuation of their respective lines of research has yet to be decided.
- Although the IP and the department acknowledge the importance of transparent communication between the different management layers and the researchers, the committee noted that there is room for improvement in this area. Researchers often complained they were not informed in a timely fashion of decisions that affect day-to-day operations, while representatives of the management team complained that communications were often ignored by researchers. PhD/Postdocs did not seem fully aware of existing means for them to interact. Improvement of information transfer could rely on the use of novel communication channels (more informative websites, but also social media like Facebook and Twitter).

- Recommendations

- To proceed along the lines developed and initiated in the recent years, making sure to take as much advantage as possible of the existing strengths and if needed focus on the most original and promising projects.
- To make sure to cope with the developments of the high throughput era,
- To secure excellent bioinformatics support.
- Some geographical regrouping of the teams in the department, if requested, would be productive.
- Reorganization of the technical platforms is necessary and a more precise definition as platforms vs research teams would also be beneficial.
- To secure outstanding emerging young teams to replace team members reaching retirement age.

3 • Specific comments

- Appreciation on the results

Several teams in this department have made seminal discoveries in their respective fields. The department scientific production is of very high quality (for the evaluated period more than 520 articles published in international refereed journals 107 of which published in journals with an impact factor (IF) over 9, including 7 Nature, 2 Nat Genet, 1 Cell, 5 Science). The strong implication of the Department in genetics and genomics is reflected by 7 publications in American Journal of Human Genetics (IF 12.3), 10 in Genome Research (IF 11.3) and 16 in PLoS Genetics (IF 9.5).

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

Several members of the department have received prestigious awards from the Institut de France (Jean-Pierre Lecocq award ; EADS award, twice the CEA award, Simone & Cino del Duca award and Dagnan-Bouveret award) and other Institutions (e.g. the René Descartes award). One team leader was elected member of EMBO and another got the CNRS Bronze medal in 2008. Many department members were invited speakers at prestigious international conferences. Department members are also very active in teaching. Some teams are part of national and/or international networks and collaborations (e.g. NIH grants, EC grants).

Recruitment of young scientists was successful with four new CNRS "Chargés de Recherche" three CNRS ITA, one INRA “Chargé de Recherche” and one Institut Pasteur “Assistant”. Around 50% of the post-docs in the department come from abroad as well as a fraction of the graduate students. Overall they represent 58 people in the department.

5 patents have been issued during the 2006-10 period.

The department budget has been consistent over the years and is secured for the coming years. One department member received an ERC Starting Grant.

- Appreciation on the management and life of the research unit

The composition of the department is quite stable. It is presently composed of 14 teams and 4 technical platforms. Three teams have been closed over the past 4 years (one former PI moved to EPF, Switzerland, two other retired in 2007 and 2009, respectively). Three provisional teams have been created, since 2006. One short term research group (G5) is headed by E. Rocha recruited at the Institut Pasteur, the two others emerged from local teams.

Lines of research of each department team are distinct but they are also integrated. Advantage is taken from collaboration within the department where possible.

The scientific animation is consistent, with yearly departmental retreats, weekly seminars by invited speakers, yearly PhD/postdocs symposia, the organization of one day meetings open to the scientific community, and the contribution of department members to the organization of international conferences and courses.

Five members teach outside the IP (University Pierre-et-Marie Curie, Ecole Polytechnique), 4 direct Pasteur courses, one coordinates 27 Pasteur courses. The department participates in master courses, and some of its members have organized several international courses (e.g. joined EMBO courses, bioinformatics, diagnosis etc.).

- Appreciation on the scientific strategy and the project

As detailed in the evaluation of individual teams below, there are many highly relevant and feasible projects in this department. Several are particularly original and innovative. There is a general policy for resource allocation at IP and individual teams are clearly active and very successful at raising funds from national and international agencies. The general research strategy of the department is not in the hands of the department.

4 • Appreciation team by team

TEAM 1: Dynamique du Génome (CNRS 2171)
Team leader: Benoît ARCANGIOLI

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1,25	2,25
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	
N7: Number of staff members with a HDR or a similar grade	1	2

- Appreciation on the results

Team 1 headed by B. Arcangioli, associate professor at the Pasteur Institute for the past 10 years is a relatively small group (2 researchers from IP, 3 engineers from IP and CNRS, 1 PhD student).

Over the past 10 years the teams made several important breakthroughs using the model unicellular eukaryote Schizosaccharomyces pombe (fission yeast) to study the molecular mechanisms underlying mating-type switching. This system entails a cell fate decision in which an asymmetric cell division is created by a genome "imprinting" mechanism and may provide important clues for understanding cell fate decisions and the generation of cellular diversity during division in higher eukaryotes. The teams most important achievements include (i) demonstrating that the imprint corresponds to a programmed, site-specific, single-strand DNA break, (ii) showing that the break occurs in connection with a DNA replication fork pausing event, (iii) separating molecular events associated with the

establishment of the imprint from its developmental consequences in a subsequent cell cycle, (iv) demonstration of a role for a conserved lysine specific demethylase (Lsd1) in the imprinting process.

A more recent observation made by the team provides a possible molecular explanation for a human ataxia syndrome associated with mutation of a tyrosyl-DNA phophodiesterase (Tdp1), as well as a number of other ataxias that result from mutations affecting related DNA repair pathways. This work may have important implications for understanding a number of diseases in which reactive oxygen species (ROS) lead to genomic damage in resting (G0) cells. The really groundbreaking aspect of this work is that it provides a very tractable molecular and genetic system to study a phenomenon that has recently arisen in human disease studies but has been essentially inaccessible experimentally.

The publication record is very good with 12 papers in peer-reviewed journals. The publications are consistently in high-level journals, e.g. Nature, EMBO Journal (3 papers), PNAS, Mol Biol Cell, J Biol Chem, Cell Cycle, and DNA repair (1 paper each). Publications with first and/or last authors from the unit considered only include: PNAS (2007), JBC (2007), EMBO J (2008&2009).

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

The team leader is recognized as a major figure in this relatively small field. For a team this size, the output is good to excellent, particularly considering the quality of each individual publication. The team has had several successful collaborations with groups in France and in Japan, and most recently with a group at Cold Spring Harbor, which has resulted in a paper in Nature (2011).

Team leader has significant teaching duties: i) at Pasteur institute as director of the Pasteur Course of Molecular and Cellular Genetics (7 weeks/year), ii) EMBO course on S. pombe (3 days) every two years since 1999, iii) three students obtained their PhD during the evaluated period. He is part of the organizing committee of national recurrent meetings (Levures, modèles et outils and 3Rs meetings). He is also part of the scientific committee of Association pour la Recherche sur le Cancer (ARC), a major French funding agency

The team leader has been relatively successful in raising funds to maintain this small group, which seems for the most part to have attracted primarily French graduate students and postdoctoral fellows, in addition to a considerable number of Masters students. The team leader has local (Team 9), national (at Institut Curie in Orsay) and international (Cold Spring Harbor laboratories, USA) collaborations.

- Appreciation on the scientific strategy and the project

Further activities of the team will focus on three relatively distinct but interrelated areas of research: (1) a genetic and biochemical analysis of the imprinting pathway, (2) mapping and analysis of DNA replication pause sites on a genome-wide scale (in collaboration with CSHL and Team 9, (3) genetic and chemical biology analysis of genome stability in quiescent cells.
The first project focuses on Lsd1, and proposes to identify targets by a mass spectrometry approach. It is unclear from the information given whether there is a high likelihood of success, given that the target molecules may be present in very small quantities in the cell. Genetic suppressor studies, as well as novel approaches to search for imprinting mutants are much more compelling projects, and take advantage of the groups' expertise in devising and carrying out clever genetic screens. Preliminary results here look promising.
The replication fork pausing project addresses several important questions in genome biology (DNA and RNA polymerase collisions, mechanisms underlying "fragile sites" and genome plasticity. The third project, genetic and chemical biology analysis of DNA damage in quiescent cells, is extremely interesting from both the basic biology perspective as well as the potential for the development of pharmaceuticals. High throughput chemical screening offers a credible possibility to generate lead compounds for eventual pharmaceutical testing in mammalian systems (impact on neuron degeneration).
The projects are sound and ambitious and they cover different fields of research and technologies. Consequently, manpower and financial support should be adapted, which is not obvious at the moment.

- Conclusion :

— Summary

The team leader is a very creative scientist who is making important and novel contributions in two areas of genome biology, using a powerful model system. Significantly, both of these areas have important implications in fundamental human biology: stem cells and asymmetric cell division on the one hand, and genome stability in quiescent (post-mitotic) cells on the other hand. Publication records are excellent considering the size of the group.

— Strengths and opportunities

Strengths of this team include creative experimental approaches, excellent use of a model system to uncover basic mechanisms with broad implications in higher eukaryotes.

— Weaknesses and threats

The size and composition of the team are of concern for the success of the projects. Today, only two scientists are in charge of the project: the group leader and a research fellow (60 years old) who recently joined the group without a strong background in the S. pombe field. Furthermore, there are no post-doctoral fellows in the laboratory and no secure funding to recruit them rapidly.

— Recommendations

The team leader needs to quickly follow through with his stated plans to find additional financial support and manpower to realize his ambitious program.

TEAM 2: Biologie des bactéries intracellulaires (CNRS 2171)

Team leader: Carmen BUCHRIESER

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	4	5
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2,25	2,25
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

In the past 10 years Dr. Buchrieser has build up an impressive publication track record that is expanding exponentially. As research assistant and young assistant professor Dr. Buchrieser has participated in various microbial genome sequencing and comparative genomics projects that were published in the early years of this millennium. The Nature Genetics paper of 2004 providing evidence in the Legionella pneumophila genome for exploitation of host cell functions then marked her establishment as an independent researcher in the field of bacterial genomics. Moreover, this landmark publication gave direction and focus to her subsequent research activities that led to the initiation of the current Provisional Research Unit that soon will come to the end of its term. This ground breaking work on genome sequencing and comparative genome analysis in Legionella pneumophila unexpectedly led to the identification of a large number of bacterial proteins with eukaryote-like properties that Dr. Buchrieser is currently studying on the molecular and cellular level in relation to the specific subversion of host cell functions during infection. Moreover, the L. pneumophila genome sequence facilitated functional genomics approaches, i.e. genome-wide transcriptional profiling studies that allowed Dr. Buchrieser to investigate basic aspects of virulence gene regulation in the bi-phasic infection cycle of Legionella. This also facilitated the identification of the first small non-coding regulatory RNAs in L. pneumophila. The work on quorum sensing regulation (LqsASR) and two-component regulators (LetA/LetS) included fruitful long-standing collaborations with a laboratory in Zurich, Switzerland, and at the University Ann Arbor, Michigan. While keeping up her strength in genome sequencing and comparative and functional genomic analysis as evidenced by her recent publications on the identification of a worldwide distributed epidemic L. pneumophila clone and the characterization of the Legionella longbeachae genome to uncover unique strategies to cause Legionnaires' disease, she has thus greatly expanded the methodological approaches of her laboratory towards a powerful integrated genome-based functional approach.

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

Based on Dr. Buchrieser's past track record and proposed research projects she is well positioned to further develop her profile of a leading scientist in the highly active Legionella field. Contributing to this is the high visibilty of Dr. Buchrieser (numerous invited lectures at conferences and seminar presentations in the reporting period) and the fact that she has taken an active role in shaping the Legionella field, most notably by organizing in 2009 the international Legionella conference in Paris. Dr. Buchrieser has also set-up a network of long-standing collaborations with other leading scientists in the Legionella field, including one at the University of Michigan, (USA), two in

Germany, at the University of Munich and at the Robert Koch Institut (Berlin) and a last one at the University of Melbourne (Australia). Dr. Buchrieser has also been highly successful in recruiting funding for her work on Legionella, including grants from national agencies (i.e. ANR), European sources (i.e. EuroPathoGenomics Network of Excellence, Marie Curie Research and Training Network INTRAPATH), but also other national agencies (Welcome Trust, NIH).

- Appreciation on the scientific strategy and the project

The projects proposed for the coming four years in the frame of a permanent Unit are based on findings and results obtained from previous and ongoing studies and the further development of the successfully established integrated genome-based functional approach. The establishment of Next Generation Sequencing as cutting edge technology for comparative genomics, population genomics and functional genomics is a logical and consequent step. This will be relevant for the generation of draft sequences of additional Legionella strains (further to the 24 strains currently sequenced in collaboration with the Sanger Centre) that are required to establish a robust whole-genome-based phylogeny for the genus Legionella as a necessary basis for any in-depth evolutionary analysis. This will allow Dr. Buchrieser to address central questions on the emergence of Legionella as human pathogen and to study the underlying molecular mechanisms, i.e. on the genus level to identify the genetic specificities of L. pneumophila and L. longbeachae that resulted in the predominance of these two species in causing human legionellosis, and on the strain level to identify the genetic factors that allowed the L. pneumophila clone Paris to spread globally as human pathogen. Emphasis will be given on how the encoded repertoires of eukaryotic-like proteins determine predominance for human infection on the species and strain level. Another application of next generation sequencing, RNAseq, will be a much needed technology for Dr. Buchrieser for the proposed subprojects on the genome-wide analysis of regulatory networks. This technological advance combined with genetics and physiological studies will allow her to get an integrated understanding of the regulatory mechanisms and networks involved in host adaptation. Further to the study of the known regulatory factors (LetS/LetA, CsrA, Hfq, RpoS, FliA, the ncRNAs RsmY and RsmZ) the proposed analysis of KaiBC – that are based on preliminary evidence are involved in Legionella virulence - gives promise to the identification of new regulatory principles provided the fact that the homologues in Cyanobacteria encode a circadian oscillator. Finally, the proposed analysis of the molecular and cellular function of eukaryotic-like proteins of Legionella in host cell infection is highly interesting and the focusing on the class of F-box containing proteins that have in one case already shown to interfere with eukaryotic ubiquitination signaling pathways and sphingomyelinase that possibly interferes with the autophagy pathway give promise to new findings in basic cell biology that a relevant beyond the specific context of Legionella infection.

The objectives for the proposed research are clear and the individual projects and subprojects appear sound, competitive and feasible. We have not detected any major flaw in the proposed projects and are convinced that this integrated approach combining genomics, transcriptomics, bioinformatics and experimental approaches including genetics and cell biology will continue to provide new and exciting insights how the opportunistic pathogen Legionella establishes an intracellular replication niche in macrophages in the human lung based on the evolved interaction with amoebae in soil.

- Conclusion :

— Summary

Taken together, the research of Dr. Buchrieser is of highest international standards and the proposed research projects are sound and competitive. She is clearly a leader in the Legionella field and an established and internationally recognized scientist in the field of bacterial genomics. She clearly is an asset for the department “Genomes et Genetique” and for Institut Pasteur as a whole.

— Strengths and opportunities

In the highly competitive Legionella field the integrated genome-based functional approach represented by Dr. Buchrieser’s lab is original, unique, and highly productive. Dr. Buchrieser’s has competence in cell biology and uses an integrated approach. This puts her into the unique position to explore on the molecular and cellular level, virulence properties and factors of Legionella discovered in her group on the basis of comparative and functional genomics analysis. This integrated genome-based functional approach is quite unique in the highly developed Legionella field worldwide and makes Dr. Buchrieser one of the leading scientists in this field. In the broader field of bacterial genomics and pathogenesis Dr. Buchrieser is in our judgment among the very top scientists of her age group in Europe. We thus rate her past and present activity as work of the very highest international recognized standards.

— Weaknesses and threats

The committee has not identified any major weakness or flaw associated with the past, present and prospect future work of this group. The only criticism may relate to the fact that the proposed project, although timely, sound and promising, is in most part a continuation of the successful experimental approaches already followed up presently, although the inclusion of next generation sequencing opens up new avenues for innovative research.

— Recommendations

A long term securing of Dr Buchreiser's team in this department would be an asset for the Institut Pasteur. The increase of her group size (from currently 8 to about 12 members) would ensure continuity of specific technical and methodological expertise as a basis for her integrated experimental approaches, including support in next generation sequencing as key technology for her research in the coming years.

TEAM 3 : Génétique Moléculaire des levures (CNRS 2171)

Team leader: Bernard DUJON

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	3	3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	-
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3,5	3,5
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	-	
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	
N7: Number of staff members with a HDR or a similar grade	4	3

- Appreciation on the results

The team leader Bernard Dujon is a professor at the university (UPMC), director of the URA2171CNRS at the Pasteur institute, and a member of the French Academy of Sciences. The unit "Génétique Moléculaire des levures" was created 1987 and renewed 2001. The unit is currently composed of 10 members: 4 researchers (CNRS, Pasteur, UPMC), 3 engineers/technicians and 3 post-docs/PhD students. It includes an "associated group" composed of 4 persons. It should be noted that Team 3 has seen significant turnover in the evaluation period (2006-2010); several researchers moved, many of them creating their own groups at Pasteur Institute or elsewhere: (UPMC, University Paris-XI, new Team 20). In addition, two past members of the team 3 were recruited at the CNRS (Marseille) and UPMC (UMR7238), respectively.

Nevertheless, the productivity of the unit was excellent with 31 peer-reviewed articles. Publications with first and last authors from the unit considered only include: Mol Biol Evol (2006), J Cell Biol (2006), Plos Genet (2006&2008), NAR (2008&2010), Nature Struct Mol Biol (2009), PNAS (2) (2010). In addition, the team leader published reviews in prestigious journals such as Trends in Genetics (2006) and Nature Reviews Genetics (2010). The major research topics during the evaluation period were: i) The comparative evolutionary genomics of yeast. Based on the Genolevure network and international collaborations within GENOSCOPE, the complete sequencing of a sizable number of evolutionary distant yeasts allowed the genome evolution of Saccharomycotina to be reconstructed (Genome Res 2009 & Nature Rev Genet 2010). This has been pioneering work in the field of molecular evolution. ii) Mechanisms of genome stability, particularly the instability of repetitive sequences (Nat Struct Mol Biol 2009), and the identification of megasatellite sequences in C. glabrata. iii) The architectural organization of chromosomal domains in the nucleus and the connection between nuclear pore attachment and repair of double-strand breaks in subtelomeric regions (J Cell Biol 2006 & PNAS 2010). This topic has now become part of the newly formed Team 20 iv) The project on the stability of nuclear and mitochondrial DNA conducted by the "associated group" who revealed a NHEJ-like process in E. coli (PNAS 2010).

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

The team leader is a prominent and renowned scientist at the international level. He is a member of the French Academy of Sciences and received prestigious scientific awards. He makes major contributions in genetics and genomics of yeasts. He is frequently invited to important scientific events and conferences and published review

articles in the best journals like Nat Rev Genetics 2010. A most significant contribution is the formation and dissemination of a great number of talented scientists who are now running their own laboratory at Pasteur Institute or elsewhere. The team has major ongoing collaboration through the Génolevure network that has been recently renewed at the CNRS and the GENOSCOPE for NGS facilities. The team has sufficient financial support from national and international agencies to finalize the genomics and yeast genetics aspects of the project.

- Appreciation on the scientific strategy and the project

The project outline for the coming 5 years is divided into three parts between the team leader and two additional PI. The project of B. Dujon is largely a continuation of the ongoing work on the molecular evolution of yeasts including new branches. The second project proposes to address the dynamics of micro- and mega-satellite DNA, including the study of genomic instability at DNA repeats and the characterisation of structures at stalled replication forks (EM in collaboration with Institut Gustave Roussy). These two projects were considered as technically sound and scientifically solid but not overly original and innovative. The third project, proposed by the "associated group", aims at studying the impact of DSB repair impairment on senescence in human cells, DSB repair in adult stem cells and differentiated cells, and mitochondrial DNA transfer to the nucleus with its biological consequences. One major concern associated with this project was feasibility and thus competitiveness, given that the work is to be carried out in an environment of yeast genetics, which is suboptimal, both conceptually and from an infrastructural point of view. Yet, the PI quoted several pending publications (submitted and in preparation).

- Conclusion :

— Summary

The production of Team 3 during the evaluated period was abundant and of high scientific quality. The team leader is an outstanding scientist at the international level. He promoted the development of excellent young scientist and research teams. An example is the creation of Team 20.

— Strengths and opportunities

- The impact of B. Dujon in the fields of genetics and genomics of yeast at the international level.
- Well established collaborations and significant financial supports.
- Teaching to recruit new students and possibility to raise money for research and salary.

— Weaknesses and threats

- The projects appear to have weaknesses in originality and innovation. Although the general direction is clear, a lack of a greater vision is notable.
- For the « associated group », the feasibility and, thus, the competitiveness of the project on human stem cells is uncertain. While the research topics seem compatible (both addressing aspects of DNA stability), the panel questioned the usefulness of combining yeast and mammalian cell work in one infrastructural unit.

— Recommendations

- Some concern about the future for the fields of genetics and genomics of yeast because of the leaving of leading scientist (not replaced).
- The PI of the « associated group » in charge of the stem cells project should very rapidly produce significant contributions in the field (papers in preparation) to put herself in a position to apply for the creation of an independent unit at Pasteur Institute.

TEAM 4 : Evolution et Génomique Bactérienne (CNRS 2171)

Team leader: Philippe GLASER

- Staff members

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

- Appreciation on the results

This team's research focuses on the genus Streptococcus, addressing issues of diversity and evolution mostly using sequencing techniques. The team has provided two important contributions in the field of horizontal gene transfer, by (i) showing that chromosomal regions several hundreds kb-long could be transferred between S. agalactiae strains, and (ii) discovering a new type of conjugative elements in Firmicutes. This group addresses important issues of evolutionary relationships within the genus Streptococcus and how this relates to pathogenicity. Overall, the work is of high quality. It has clear biomedical significance and in that sense is important and has significant impact.

The scientific production is reasonable, given the size of the group (6 persons). The group published 8 papers on its own research, 1 in PNAS and 7 in good specialised journals such as Mol. Microbiol. or J Bacteriol. In addition, due to the strong link of the team with the departmental sequencing and transcriptomic platforms, members of the group contributed to 17 publications. The head of the group also contributed to one review on Group B Streptococci in 2006 in Nature Review of Microbiology, and is participant in two patents.

In summary, the production is not stellar, but the group has a solid publications track record.

The group has established important intra-mural and extra-mural collaborations with excellent groups.

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

Dr. Glaser and to a lesser extent another team member are regularly invited to meetings and conferences (11 invitations, among which 4 abroad). Dr Glaser organised the 2008 Genomes meeting at Pasteur, he is involved in several scientific boards, such as ANR and DIM (France), ERA-NET (Europ), and regularly participates in evaluation committees for AERES. He has also the responsibility of the genopole at Pasteur. In summary, the group has a clear international visibility.

The ability of the team to recruit high level students and post-docs is difficult to assess from the report. Most of members of the group have joined in 2008-2009. But others are being recruited, notably on a new ANR grant with Team 2.

However, the group is only moderately successful in attracting funding. Current funding includes 1 ANR grant funding 1 postdoc. In « past » funding, no major grant is listed.

The group is part of a small international network.

- Appreciation on the scientific strategy and the project

The project aims at identifying genetic loci involved in the virulence of Streptococcus agalactiae and S. pyogenes, as well as the genetic features responsible for host adaptation by comparing S. agalactiae and S. gallolyticus, by combining sequencing and transcriptomics techniques. It will also continue the molecular dissection of the new mobile genetic element they have identified. This project is well conceived but somewhat unfocused and is a logical follow-up of what the group is known for. The emphasis on pathogenicity is a positive development. The programme will yield reasonably strong results and should be supported. The committee would like to encourage the team leader to think beyond the narrow confines of his specialty.

- Conclusion :

— Summary :

This is a moderately strong group with an international reputation. The planned research programme is strong, mostly based on sequencing but broadening in scope.

— Strengths and opportunities :

This is a group that exploits well its local environment. Collaborations within IP and strong connections with some of IP's excellent groups working on related projects and diseases are assets that are being exploited to the full.

— Weaknesses and threats :

After pioneering genomic research on Streptococci, the group has been cruising along using similar tools : it is now time to refresh and use a truly interdisciplinary approach to research. Notably the functional aspects are almost totally absent from the research programme and the team leader should be encouraged to branch out.

— Recommendations :

This reasonably productive group should be allowed to continue as it stands, with a strong connection to the sequencing activity.

More international outlook would be a positive development.

The team leader should be encouraged to branch out on more functional studies.

TEAM 5 : Génomique Évolutive des microbes (CNRS 2171)
Team leader: Eduardo P C ROCHA

- Staff members

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

- Appreciation on the results

The team's activities are centred around the in silico analysis of gene mobility, genome organization, evolution and population dynamics in prokaryotes. The vision/approach is very broad, based on multiple genome, nucleotide and protein sequence analysis and various phylogenetic analysis on multiple genomes and metagenomic sequences, using data available in public databases.

The results are obviously perceived very positively by the scientific community involved e.g. in ecology, population dynamics and niche colonization. The group has an excellent publication record (41 articles) in both high ranking general journals (1 in Nature, several in PLoS Genetics) or highly ranked journals in the fields of microbiology and evolution (Mol Biol Evol, Molec Microbiol). In addition the team has produced several reviews in the best specialized reviews such as MMRB, FEMS Microbiol Rev, Curr. Biol. Ann Rev Genetics).

The team was established at the Institut Pasteur recently as a short term team ("G5 group"), hence the stability of the team is hard to evaluate. At present the group has 1 CR2 CNRS scientist, 3 IP post-docs and one PhD student. Three PhD thesis (one of which co-directed) were defended in the group, since 2008 and the students are now for post-docs in high standard labs.

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

All these points are difficult to address due to the young age of the team. However the team head has a quite long career and reputation in the field of prokaryotic evolutionary genomics. The group has some intra and inter-departmental and national collaborations and many international collaborations. Participation to national and international conferences seems to be limited as well as participation in teaching.

The group presently lives on the G5 package. Two pending grant applications if granted would secure the group's budget for the coming years.

- Appreciation on the scientific strategy and the project

The project is extremely broad and as a result, it is difficult to judge its feasibility. The questions addressed, despite their obvious interest, are too wide and not necessarily focusing on the most important/ interesting points that need to be addressed in the field of gene mobility and its incidence on bacterial genome and population dynamics. In addition the project does not well document the robustness of the methodologies to be used or ways to assess that robustness.

There are plenty of financial resources available in the field as well as lot of cutting-edge projects to be addressed.

- Conclusion :

— Summary :

Good results, extremely well valorised in terms of publication, have been obtained from a large set of projects addressing very general questions. This "scientific wandering" has the drawback that questions are not pushed far enough. The risk exists that with more and more and larger and large projects in the field of prokaryotic genome plasticity, such broad approaches loose value. Hence there is a definite need for more focussing and more robustness.

— Strengths and opportunities :

The team has good records in bioinformatics and should continue to exploit it.

Molecular biologists are asking for collaborations that offer plenty of space for cutting-edge projects.

— Weaknesses and threats :

Translation of experimental results in the field of genome plasticity and population dynamics is lacking as is the production of results that can be experimentally tested.

Lots of experimental data on molecular aspects of the mechanisms of gene mobility in prokaryotes exist and they need to be mined to find important and precise questions to be addressed with bioinformatics approaches.

— Recommendations :

The recent contribution of this team in collaboration with a group expert in conjugation, of an in silico analysis and classification of proteins belonging to conjugation systems and the related type IV secretion systems, provides a good example of how a collaboration with specialists in a given field does bring about such a focusing. A deeper understanding of experimental data and closer collaborations with experimentalists to come up with testable predictions are essential for the future success of the team.

TEAM 6 : Génomique des Interactions Moléculaires (CNRS 2171)

Team leader: Alain JACQUIER

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	5	5
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	3	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3.5	3.5
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	
N7: Number of staff members with a HDR or a similar grade	3	3

- Appreciation on the results

This relatively large team (currently 13 members) works on RNA biology using the budding yeast Saccharomyces cerevisiae and has been particularly productive. The team is highly integrated, but divided into three sub-teams: one developing and applying genetic interaction screens, one studying ribosome biogenesis, and one focusing on "cryptic" transcripts genome-wide.

The work addresses two key and topical issues in cell and genome biology. Ribosome biogenesis is an essential and extremely energy-intensive cellular process that underlies cell growth, and there is an increasing awareness of its importance in overall cell regulation as well as in many different disease states. This is therefore a fundamental area of research with broad implications. The second subject, cryptic RNAs, is an exciting new field of clear significance with a very open horizon. Preliminary results from a newly designed genetic interaction screen, indicate a high potential for important future discoveries and for stimulating cooperation within the team. During the evaluation period, the productivity of this unit was excellent with 16 peer-reviewed papers documenting original work, among those 5 in high impact journals including Nature (2009), PNAS (2008), Mol Cell (collaboration, 2008), Genes Dev (collaboration 2007), and J Cell Biol (2006).

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

This team has made a major impact in the gene regulation field through their breakthrough discovery of "cryptic" RNA expression in the budding yeast S. cerevisiae. This work has opened up new perspectives on gene regulation, chromatin structure and mRNA metabolism, several of which the team is actively pursuing. This work alone would be sufficient to place the team at a very high international standing within the field. At the same time, the team continues to make significant progress in understanding the complex molecular events involved in ribosome biogenesis (primarily dissociation and recycling of 60S maturation factors), as well as, in collaboration with others, transcription of ribosomal protein and rDNA genes. No data were provided regarding presentations or organization of international meetings, but it is clear from the published record that the team has very high visibility internationally in both the transcription and ribosome biogenesis fields.

- Appreciation on the scientific strategy and the project

Three excellent general aims, one focused upon further development of the screening platform, the other two focused on two novel biological problems (cytoplasmic mRNA quality control and cryptic transcription), are extremely timely and of high general interest in the broad field of gene expression. Experimental strategies appear excellent and the team has a comprehensive command of the required techniques/technologies.

- Conclusion :

— Summary :

The team has made major impact on CUTs (cryptic RNAs), and have at the same time competed quite successfully with much larger teams in the development of advanced genetic screening platforms. It has also made significant contributions to the understanding of ribosome maturation.

— Strengths and opportunities :

The research of this team is highly original and innovative, both conceptually and experimentally. Recently discovered functional links of between cytoplasmic mRNA degradation pathways and ribosomal biogenesis provide a unique opportunity to focus future projects on nuclear and cytoplasmic RNA quality control mechanisms

— Weaknesses and threats :

It is hard to point to any weaknesses, since this is a team of uniformly high quality. One area of potential risk, however, is the genetic screening work, which will produce enormous amounts of data.

— Recommendations

A clear strategy for focused data analysis, validation and design of follow-up projects will be necessary to avoid dispersion of resources.

In the past the team has had a composition perhaps too biased towards senior scientists, but this situation seems now resolved, in part because the team has been allowed to expand.

TEAM 7 : Plasticité du Génome Bactérien (CNRS 2171)

Team leader: Didier MAZEL

- Staff members

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

- Appreciation on the results

Over the period evaluated, the activity of Team 7 proceeded along two main lines: i) studies of the molecular mechanisms of site-specific recombination (integration and excision) of the integron cassettes and ii) evolutionary genomics and genome organization and plasticity in the genus Vibrio (many members of which host integrons). The common theme bridging these two research lines is the deciphering of the evolutionary mechanisms responsible for the emergence of virulent strains of Vibrio, whether pathogenic for humans or marine animals.

The team has a prominent position in the field of site-specific recombination and has contributed very important data related to Vibrio and bacterial gene organization and plasticity.

Most prominent contributions of the team over this period were: i) the 3D structure of an IntI protein bound to the self-paired attC-bs established in collaboration with a group at Institut Pasteur (NAR 2007, Nature 2006), which provides hints into key structural features that explain the particularly low specificity of attC-IntI recognition; ii) the elucidation of the particularity of the IntI cognate cassette site attC to be recognized by IntI on a structure generated for SS DNA and the cellular pathway controlling this process (EMBO J. 2010); iii) The demonstration that IntI expression is under the control of the SOS response, that the SOS response in Vibrio is induced by conjugation so that cassettes mobility can now be connected to mechanisms that generate SS DNA, like conjugation and transformation (Science 2009, PLoS Genetics 2009, PLoS Genetics 2010).

Along the second line of research, the team, in collaboration with the sequencing platform PF1 and the Genoscope, sequenced a third Vibrio genome (Env. Microbiol. 2009), providing a further assessment of the overall genome organization in the genus (large pan-genome vs limited core genome) with two chromosomes, one (Chr2) bearing many more variability than the other (Chr1). This division of genetic information increases growth rate and hence appears to contribute to the expansion of pathogenic clones (PLoS Genetics 2008).

Publication records are outstanding (26 papers in peer reviewed journals). Publications with first and/or last authors include: Mol Microbiology (2007), NAR (2007&2010), PLoS Genet (2008, 2009 & 2010), EMBO J (2010), Science (2009). In addition, D. Mazel published in highly ranked microbiology review journals such as Nature Reviews Microbiology (2006) and Annual Review of Genetics (2010).

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

Teaching activity limited but 4 PhD's finished in the 4 years covered by this evaluation, and 5 master students accommodated as well as two short term visiting students from Harvard and California State University.

Publication records are outstanding including 2 invited reviews in best microbiology review journals, visibility and achievements of the team as well with invited participation in international meetings. The team has multiple collaborations within Institut Pasteur, national and more importantly international with prominent labs in the field. This resulted e.g. in funding within 2 EC grants. The team is clearly successful in securing funds and its budget is secured for the 4 coming years.

D. Mazel was awarded the J.P. Lecoq award from the Académie des Sciences (2006) and the Pasteur award Vallery-Radot (2010). He was/is involved in the organization of several international conferences, is often solicited as a reviewer by various journals, is an editor of Res. Microbiol., is regularly invited to talk at international conferences and to give seminars in France and abroad. One post-doc was recruited as CR2 CNRS in 2008.

In addition, Didier MAZEL is Associate Professor at the Pasteur Institute, and since two years, director of the "Genomes and Genetics" Department. He is proposed to be the future director of the Department after its renewal for the period 2012-2015.

- Appreciation on the scientific strategy and the project

The results obtained in the past 4 years certainly justify the continuation of the ongoing work along two lines i) integron related gene mobility, regulation and molecular mechanisms, characterization of the IntI-attI interactions that are so far completely unknown, further elucidation of the function of genes carried by integron cassettes and their relevance to pathogenicity ii) Vibrio genome organization in two chromosomes, its incidence on growth and relevance to pathogenicity. These themes of research are on the agenda of several national and international granting agencies and this team is in a position to benefit from these.

While the integron project remains at the top of the research in the field, the lines chosen to develop Vibrio genome analysis appear less convincing (construction and growth rate analysis of strains with various combinations of the number of chromosomes (1 or 2) and nature of replication origins and termini). Although the experiments proposed take advantage of existing and performing genetic tools, this two chromosomes organization is not restricted to the Vibrio genus and hence this type of questions may demand a broader approach considering other bacterial genera, and hence would benefit from more focusing on the role of chromosomal organization on clonal expansion and pathogenicity.

- Conclusion :

— Summary

Excellent team with outstanding publication records and visibility, which will be maintained if efforts are concentrated on the lines of research in which the team is the strongest and has the most original perspective.

— Strengths and opportunities

The group has a recognized leading position in its field of research, several national and international collaborations and hence is in a prominent position to keep finding appropriate funding and recruit brilliant new members.

— Weaknesses and threats

There may be a risk of entering a less exciting route of exploring Vibrio genomes one after the other without pinpointing the most interesting features to be investigated.

— Recommendations

To concentrate on what the team does best, integron genetics/genomics and related mechanisms of mobility.

To make sure to get most of the Vibrio case in comparison to what is/will be done on other bacteria with more than one chromosome.

TEAM 8 : Biologie Systémique (CNRS 2171)

Team leader: Benno SCHWIKOWSKI

- Staff members

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

- Appreciation on the results

This is a moderately productive bioinformatics group developing software for the analysis of proteomics data and other types of data. The group has contributed to a visualization methodology called Cytoscape, that appears to be very popular (although no statistics are provided). However, Cytoscape is essentially only a visualization platform and thus, effective contribution to research in high throughput data analysis is moderate given the number of years this group has been at Pasteur.

Output is moderate, primarily in low impact or very specialist journals, some in higher impact but specialist journals in the field (2 Mol Cell Proteomics). This is not necessarily surprising as the activity is primarily a methods/platform development group and this kind of research, useful to a wide community of researchers, often tends to be published in specialist journals.

This group is part of a world-wide network of groups working on methods development. Given the paucity of data coming out of the Proteomics platform at IP, the group has naturally turned to the outside world,. What is certainly striking is the lack of integration of the group within Pasteur, which could have been more extensive given that many groups at IP produce large amounts of data from high- and low-throughput experiments.

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

Invitations to international conferences and symposia are not listed separately and the panel has found it difficult to extract the information. However, there appears to be some, indicating international recognition. Moreover, the group is developing Cytoscape in collaboration with a wide consortium of institutions worldwide.

The group has postdocs and students, funded by a large grant where Schwikowski is not a PI, but yet plays a substantial role.

There appears to be no grant associated with the group as PI, although there are collaborative grants where the group appears to play some significant roles. These fund two postdocs. The group is part of several consortia of international collaborators that have been awarded large grants, from e.g. the US NRNB, GlycoHiT (EC-FP7). Several such applications are being submitted. The group is actually very isolated at IP: there is no serious proteomics activity going on at IP. So IP is sterile ground for a group like this one.

No concrete results of the research activity and socio-economic partnerships were described in the report.

- Appreciation on the scientific strategy and the project

It is the sentiment of the committee that the scientific project is unclear, and not building on a strong track record.

This team probably needs a different environment: the group is poorly served by its environment at Institut Pasteur. Alternatively, it is advised that the group should adapt its strategy to the local environment and integrate better within Institut Pasteur.

- Conclusion :

— Summary

This is a moderately productive group doing moderately useful work on developing software to analyse high throughput mostly proteomics and other types of data. The productivity is moderate to poor and the projects ill-defined. The real biological question is missing. More focus and a real connection with experimental biologists are urgently needed.

— Strengths and opportunities

The group has a strong background in computational biology and the availability of computing power.

It has the capacity and the technical know-how to develop a more productive group by integrating within Institut Pasteur, and not waiting for a change in the Institute's strategy (or lack thereof) regarding proteomics.

— Weaknesses and threats

The group has not taken advantage of the scientific environment that Institut Pasteur has on offer. It is fair to say that the institute has not invested in proteomics as it should have, but a viable group should be able to adapt.

The major weakness is the absence of connection to a biological project.

Although the team leader has made some effort recently by connecting with a laboratory at the Institut Pasteur, it is not clear yet how it is going to work.

— Recommendations

It is recommended that the group attempts to plug in more into Institut Pasteur and develop a biologically-relevant systems biology project.

TEAM 9 : Physique des systèmes biologiques (CNRS2171)
Team leader: Massimo VERGASSOLA

- Staff members

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

- Appreciation on the results

This group has produced very original work on the basic decision making mechanisms during motility in different organisms (bacteria to insects). They employ a combination of mathematical modelling, biophysics, and experimental validation of model predictions. During the past years they have also established fruitful local collaborations and developed novel methods for identifying non-coding RNA regulators in Listeria monocytogenes or analyzing membrane dynamics. All this work shows a very tight collaboration between theoretical predictions and experimental validation. The group has a very impressive publication record with articles in general high impact journals (Nature, PNAS), a range of excellent specialized journals (Fluid Mechanics to Nucleic Acids Research and Bioinformatics).

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

The group leader and members of the group are invited to numerous conferences (close to 50 in the reporting period), they have organized three conferences, and the infotaxis work has been popularized in numerous “non-scientific” journals. The group thus shows excellent international visibility. This is also reflected in the fact that team members can attract very productive post-docs and researchers.

- Appreciation on the scientific strategy and the project

The research project is well thought of and focuses on the motility of free-living organisms, chemotaxis in bacteria and eukaryotes, and olfactory search strategies in insects. The group leader focuses the project on a topic where the group is clearly a world leader and where preliminary studies show the feasibility of the proposed research. In addition to this focus on motility, the group is open to seize opportunities that present themselves, as with a recent project related to biofilm formation. All these ambitious and innovative projects combine biophysics, mathematical modelling and experimental validation of the model predictions.

- Conclusion :

— Summary

The group has produced very interesting work combining theory, biophysics, and other experiments. The projects are a continuation of recent activities. They include ambitious, innovative extension of topics for which the group is a world leader.

— Strengths and opportunities

One particular strength of the group is the very tight connection between experiment and modelling. Combined with interesting and novel ideas, this promises the success of a very original and timely research project. The group has established an excellent interface between biology and physics at the Institut Pasteur and has shown that they can very successfully collaborate with generic biology groups at the Institut Pasteur.

— Weaknesses and threats

The proposed research is in the very competitive field of chemotaxis. However, they have already made great impact, they focus on a particular niche in the field, and they are on their way to become the leading group in the field.

— Recommendations

The committee supports this group without reservation and agrees with their plan to focus on projects studying the motility of free living organisms.

TEAM 12 : Pathogénomique Mycobactérienne

Team leader: Roland BROSCH

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	5	5
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3.25	2.25
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	
N7: Number of staff members with a HDR or a similar grade	2	2

- Appreciation on the results

Roland Brosch is leading a very active temporary unit, created in 2008, addressing mycobacterial pathogenicity and genomics. This unit grew out of the group of a well-known scientist, who left Institut Pasteur in 2007. The group has built up an impressive track record and has made landmark contributions to the field. The unit is actively participating in several international collaborations. Research lines of the unit include: i) Comparative and evolutionary genomics to understand how Mycobacterium tuberculosis evolved as a pathogen and to address the extraordinary evolutionary success of this pathogen, ii) Molecular analyses of secretion systems, in particular ESX/Type VII a key player in mycobacterial pathogenicity, iii) TB vaccine and TB drug development, iv) Mycobacterial lipids and their role in pathogenicity. This latter research line is carried out by another PI, who forms an independent group within the team.

Overall the team's research is highly relevant and of significant impact.

The group is very productive and has published more than 50 high quality papers in the last 5 years, including papers in high impact journals such as PNAS, PLOS Pathogens, Genome Research, Science, and Nature Genetics. Roland Brosch's work is highly cited, his group has filed two patents and they have supervised three master II students and several post docs.

The group has an extensive network of collaborations mainly within France and Europe. They continue to collaborate with the former PI, who is now at EPFL at Lausanne, with another scientist, former staff member, who is creating her own group at the Institut Pasteur in Lille and with a former postdoc, who is now researcher at the University of Pisa in Italy.

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

Roland Brosch is a highly visible scientist who is highly regarded in the field. Since 2006, he has been invited numerous times to international symposia and congresses and to present lectures at research institutions. Roland Brosch and the other group leader have both been awarded with the "Prix Canetti" in 2007 and 2010 respectively.

The team has been very successful in raising funds. They participate in all major EC projects on TB (4 EC-FP7 projects), which is extraordinary. In addition they participate in 5 ANR projects.

At the national level, the group is collaborating with various teams of the Institut Pasteur, the Génoscope in Evry, IPBS at Toulouse, to name just a few. The group has excellent participations in international scientific networks, has strong collaborations with foreign partners such as the Sanger Institute (Hinxton, UK), and the Netherlands Cancer Institute in Amsterdam.
The group is involved in vaccine development and testing of novel anti-mycobacterial compounds, such as promising active molecules belonging to the class of benzothiazinones. In the field of lipid research, potent anti-inflammatory compounds have been identified.

- Appreciation on the scientific strategy and the project

The proposed research for the next 4 years is sound and mainly a continuation of the research lines from previous years. The field of evolutionary genomics will be developed further by using gene knock-in's and knock-out's and next generation sequencing will be used to study the evolution of today's tuberculous bacillus. The work on TB drug development and on mechanisms of action of mycobacterial virulence lipids will be continued, as will be the study of the type VII secretion system with the aim to identify potential drug targets and develop vaccine candidates.

The proposed research is highly relevant and interesting, although the vision for the future could have been more clearly expressed.

- Conclusion :

— Summary

An active and dynamic group with high visibility in the field, working on a highly relevant topic. The group has an excellent track record and extensive collaborations both in France and abroad. The research proposed for the future is a continuation of present research lines addressing evolutionary genomics of Mycobacterium, type VII secretion, TB drug and vaccine development and mycobacterial virulence lipids. Overall, this is an excellent group and the committee strongly supports the transformation of this team in a more permanent research unit at the Institut Pasteur.

— Strengths and opportunities

- Young team working on a highly relevant topic with a high visibility in the field and an impressive track record in Mycobacterium research.
- A group that is excellent in raising external funds and that is strongly embedded in international collaborations.
- The PI, Roland Brosch is an esteemed scientist within the Mycobacterium research community.

— Weaknesses and threats

- The group is active in a highly competitive research field, which makes it a challenge to stay at the top in the coming years.
- There is a strong collaboration with the former PI, and it is important that Roland Brosch and his group continue to develop independent research lines.

— Recommendations

To stay at the top in the highly competitive field of Mycobacterium basic research focus and a clearer vision for the future would be appreciated.

TEAM 15 : Génétique Mycobactérienne

Team leader: Brigitte GICQUEL

- Staff members

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

- Appreciation on the results

The Team Génétique Mycobactérienne has a long-standing history in mycobacterial research. During the past decades, Brigitte Gicquel has made highly relevant, original and innovative contributions to the field with significant impact. She has an excellent track record. Research topics studied in the group include i) host responses after tuberculosis infection; ii) early responses after BCG vaccination; iii) biosynthesis of cell wall structures produced by Mycobacterium tuberculosis; iv) identification of M. tuberculosis genes involved in virulence and host adaptation. The group has an excellent track record: it is very productive with 67 publications in the last 5 years, including publications in high impact journals such as PloS Medicine, Human Genetics, EMBO Journal, PNAS, Immunity, Journal of Experimental Medicine and PLoS Pathogens. From 2006 until 2010, five PhD thesis were performed within the unit.

Brigitte Gicquel is very well connected in the scientific community; she has a large number of stable collaborations. Her work is highly visible and linked with many international as well as national partners and partners on the Pasteur campus. She has been and still is actively involved in running TBVAC, the European initiative towards tuberculosis vaccine development.

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

Brigitte Gicquel and her group have received numerous invitations to international conferences and meetings. The group has organized symposia in China and Tunisia. Brigitte Gicquel is committed in disseminating research and she plays an important role in establishing firm connections with countries suffering most from tuberculosis, countries which would benefit mainly from new developments to control this disease.

The research group has attracted many scientists from abroad including post-docs or senior scientists from Slovakia, India, Italy, New Zealand and South Korea and PhD students from Mexico, Portugal and Madagascar. Brigitte Gicquel has always been especially supportive to her former PhDs and post-docs, and she has built up ongoing collaborations with them. The group has been very successful in raising grants from the EC, NIH/NIAID, ANR and other funding agencies.

The group has strong collaborations in France and inside and outside Europe. There is a fruitful collaboration with Institut Pasteur institutes in China, South Korea and Tunisia. The group is efficiently using the Institut Pasteur network in other countries to disseminate results. The group has been very strongly involved in TB vaccine development through the TBVAC initiative.

- Appreciation on the scientific strategy and the project

Brigitte Gicquel wants to focus her research on microevolution within M. tuberculosis with a particular focus on drug resistance. She plans to support an assistant professor, member of her team, to establish an independent group working on host responses to TB infection with particular emphasis on host-pathogen interaction, identification of genetic susceptibility factors and host biomarkers. At this point and besides basis research, Brigitte Gicquel wishes to start a group of expertise which will help to implement new molecular tools in TB labs in emerging and developing countries, involving technology transfer, organization of symposia and training workshops and establishing collaborative projects. The committee is in full support of this vision and would like to encourage Institut Pasteur to find means to provide resources for this valuable endeavour.

- Conclusion :

— Summary

This is a highly visible and productive group with a longstanding history in Mycobacterium research. The research proposed for the future is focused on drug resistance and host responses to TB infection. In addition, Brigitte Gicquel is strongly interested in implementing newly developed molecular tools in TB labs in emerging and developing countries.

— Strengths and opportunities

- The group has a strong expertise in mycobacterial genetics.
- The group is highly visible with numerous collaborations in North and South countries.
- Various new successful research groups have emerged from the Unit.
- There is a strong interest in technology transfer to developing and emerging countries who will benefit most from new developments in the field.

— Weaknesses and threats

- M. tuberculosis is a difficult organism to work with and it is mentioned in the report that is very difficult to do 3-year PhD studies in this field without sufficient technical support.
- There is apparently a lack of sufficient technical support by Institut Pasteur after the departure of key scientists who successfully established their own research groups.
- There is no full support for the activities of the group in disseminating their results.

— Recommendations

The committee supports the plans for an independent group that will focus on host responses, while the group headed by Brigitte will work on drug resistance and technology transfer.

TEAM 17 : Génétique Évolutive Humaine

Team leader: Lluis QUINTANA-MURCI

- Staff members

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

- Appreciation on the results

With the possibility of massive sequencing, the study of natural variation in human populations is an excellent strategy to learn about human demography and the diversity of the human immune system. The group is pursuing this strategy with great success. Studying the forces that drive human genome variability could indeed lead to the identification of complex disease genes. This topic clearly has its place at the Pasteur institute and the group has oriented their projects in this direction.

They have used sequencing data from "neutral" loci to estimate the demography of human populations between about 100,000 years ago and today. These analyses are based on various evolutionary and demographic models and propose novel interpretations of human evolution.

The group has many stable collaborations, an excellent publication record (almost 90 publications in the reporting period), and very sound results, published in high impact journals such as Nature Genetics, Science, and PNAS.

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

Collaborations are important for successful research in human genetics and the group has established numerous local, national and international collaborations with over 20 identified sites. The results are highly regarded and the team members have been invited to over 60 conferences. The team leader has received five academic awards in the reporting period and has been extremely successful in obtaining research grants (14 grants in the reporting period ranging from 30 k€ to 330 k€). In summary, the team is highly attractive and visible, and their publications have a considerable impact in the field.

- Appreciation on the scientific strategy and the project

The research project aims at how genetic variants affect phenotypic variation and why they have been selected during evolution. The project is clearly structured into two sub-projects: one concerning human demography and the second one focusing on genetic variations related to the immune response, i.e., to identify immunological phenotypes under genetic control that have been targets of selection. This topic extends past work of the group and is very complementary to studies of infectious disease carried out at the Pasteur institute. One novelty is to identify the interesting loci by analyzing mRNAs and miRNAs in 400 individuals. The group has demonstrated that they are very competent in analyzing and interpreting these types of data and the project will certainly yield interesting and novel results.

- Conclusion :

— Summary

The team is a leading group in human genetics. They have produced highly interesting results in the past reporting period and the proposed project is essentially a continuation and extension of this work. The projects will certainly yield results, given the excellent track record of the group.

— Strengths and opportunities

The team has a very solid background in human genetics and their current project could strengthen even further collaborations or synergies with groups at the Institut Pasteur. The numerous established collaborations and the access to sequencing and technological facilities, as well as the demonstrated capacity to treat and interpret complex genetic data ensure essentially that the proposed project will be a success.

— Weaknesses and threats

The weakness of the research is the inherent difficulty of experimentally testing predictions of the genetic analyses and thus to remain descriptive. The group may want to explore new collaborations in order to expand the project, essentially classical human genetics, to include experimental tests, for example of the function of the genes involved in immunity against infectious disease.

— Recommendations

The very sound research projects in human genetics should be continued and potentially extended to novel functional studies (in collaboration). Securing sequencing capacity will be essential for this type of work to be fully successful.

TEAM 18 : Biologie et Pathogénicité fongiques

Team leader: Christophe d'ENFERT

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	5	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	
N7: Number of staff members with a HDR or a similar grade	2	2

- Appreciation on the results

The research activities of Team 18, Unité Biologie et Pathogenicité Fongique, headed by Christophe d'Enfert, are entirely focused on the characterisation of processes involved in the pathogenesis of the dimorphic fungus Candida albicans. Topics addressed during the 2006-2010 term include i) the study of the genetic diversity of this organism, ii) the study of Candida albicans biofilm formation and the associated antimicrobial resistance, and iii) the characterization of the signaling pathways involved in the switch between the yeast form and the hyphal form. In addition, the team has been involved in the development of resources for the Candida research community, including the CandidaDB database.

Over the last period this team has produced 26 highly cited papers, most of which are published in good specialists journals within the field (including Molecular Microbiology, Eukaryotic Cell and Antimicrobial Agents & Chemotherapy). No papers are published in journals with very high impact factors, which is not unusual in this research field.

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

Members of this team have been invited or selected to give over 30 oral presentations at national and international meetings. The leader of the team has been on the scientific board and/or local organizing committee for several meetings of the International Society of Human and Animal Mycology (including the Paris 2006, Tokyo 2009 and Berlin 2012 meetings). The team leader has been the driving force behind the highly successful FEBS Advanced Lecture Course on Human Fungal Pathogens for which he was the chairman in 2005, 2007 and 2009 and co-chairman in 2011.

The way the team is set-up (4 permanent scientists on a total of 12 people), there is ample room to accept post-docs and PhD students and the group appears to actively recruit members who obtained their degree abroad (e.g. University of Minnesota).

This team has been relatively successful in securing funding, not only in France (e.g. ANR) but also on the European level (e.g. Marie Curie International Training Network, Wellcome Trust). Funding is also provided through collaborations with industry (F2G, L'Oréal).

Christophe d'Enfert is well known and appreciated in the European Candida community and his team is actively collaborating within several national and European research networks. His collaborators include researchers from the USA, the UK and other European countries. As mentioned, he is playing a leading role in international training programs, including the Marie Curie training networks and the FEBS Advanced Lecture Course on Human Fungal Pathogens.

In terms of socioeconomic valorisation, the group has contributed to 4 Invention Disclosures since 2006, and two of these were followed by patent applications.

- Appreciation on the scientific strategy and the project

Future activities of this team will be focussed on 4 areas: (i) improving the tools for Candida albicans genomics, (ii) genome dynamics and evolutionary genomics of Candida albicans, (iii) formation of biofilms on abiotic and biotic surfaces and (iv) regulatory processes involved in hyphal morphogenesis.

Considering the expertise of the team leader and his team, there is no doubt that reaching the majority of the aims listed in the project proposal is feasible. The continuing efforts to develop genomic tools like the ORFeome library, a collection of barcoded overexpression plasmids and a collection of barcoded overexpression strains appears particularly promising. These tools have the potential to become very relevant for research pertaining to Candida albicans virulence and the early access to these tools (that will later be distributed to the community through a collaboration with the Fungal Genetics Stock centre) provides this group with a huge advantage.

However, at the same time several of the other goals outlined appear less innovative and/or cannot be considered "cutting edge". In addition, much of the work proposed along this line is a continuation of the work already being initiated or carried out. While the fact that this team wants to tackle various issues is fully appreciated, it would be difficult for this team to be among the top researchers in all of them, especially considering the international competition in this area. The team is more likely to obtain groundbreaking results in the field of biofilm formation on biotic surfaces and in the field of morphogenesis, rather than in the continued study of genomic diversity.

- Conclusion

— Summary :

Team with excellent publication records, international visibility (community services) and internationally appreciated research activities

— Strengths and opportunities :

The group is embedded in many national and international research networks, able to continue to obtain sufficient funding from different sources, well respected in the research community and has immediate access to new tools

— Weaknesses and threats :

To maintain leadership position in the field may be difficult by continuing to work in all the same areas without being able to propose cutting-edge innovating projects in some of them.

— Recommendations :

This team should more focus its research activities on a limited number of projects for which it is likely to be able to obtain/maintain a leading position. The field of biofilm formation on biotic surfaces and the field of morphogenesis, are very promising and hence the team leader is hardly encouraged to focus on these more promising topics.

TEAM 20 : Spatial regulation of genome functions

Team leader: Romain KOSZUL

- Staff members

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

- Appreciation on the results

This is a new team comprised of former members of the Dujon team (including a senior CNRS scientist) together with one ARC postdoc and one Ph.D. student. The recent award of an ERC starting grant to the team leader will permit expansion of the group to include 2 additional postdocs plus an engineer. This is therefore a "young" team; the team P.I. has become independent just this past year.

Both Koszul and the CNRS senior scientist now have considerable experience in advanced imaging and analysis techniques that allows one to visualize specific chromosomal loci in live yeast cells, and in the case of Koszul in "HiC" analysis of genome-wide chromosome collision events. This group also gains significantly from a collaboration with a team at Institut Pasteur. In addition, Koszul has a wealth of experience, and a very strong publication record, from his postdoctoral period in a Harvard laboratory, where his work focused on force transduction by actin cables through the nuclear envelope to meiotic chromosomes in yeast. The CNRS senior scientist has also been very productive over the past 5 years while she was still a member of the Dujon team.

The recent work of the two principal team members is clearly of high quality, and state-of-the-art technically. This is documented by publications in prestigious journals, including Cell (2008), PLoS Genet (2008), J Cell Biol (2006, 2010), Nat Meth (2008), and PNAS (2010)

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

This is a recently created team. Thus, it is not appropriate to assess these criteria, although the two senior scientists are individually well-known and recognized in their respective fields.

- Appreciation on the scientific strategy and the project

Five objectives are outlined, altogether forming a coherent and highly original research program with a potential for a major impact in the field. The technologies to attack the individual projects seem to be at hand. They are clearly cutting-edge and will require considerable efforts towards further development and refinement. Given the expertise of the principal team members, and the well-established collaboration with an in-house physics/bioinformatics team, there is strong promise for success.

- Conclusion :

— Summary :

This is a very promising young group, combining creativity, expertise and spirit in an original and innovative research program that has a potential for ground breaking discoveries.

— Strengths and opportunities :

The team seems a perfect match, providing together the scientific and technical skills required for tackling the complex problem of spatio-temporal chromatin organization and its impact on genetic transactions.

— Weaknesses and threats :

The research program, with five technically challenging projects, appears very ambitious. For a starting group, there may be a serious risk of dispersion of resources if all five objectives are addressed in parallel. Even if two new postdoctoral fellows are quickly recruited (during 2011) it might still be inadvisable to pursue all 5 aims immediately.

— Recommendations :

The P.I. should be encouraged to set clear priorities and to focus on bringing at least one project to the publication stage in the coming year.

Team 11: PF1 Génomique

Team leader: Christiane BOUCHIER

Note: This team is a support group or platform. It is evaluated for its added value for the department and the Institut Pasteur overall scientific organization. There will be no assessment of research activity.

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	6	6
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	0
N7: Number of staff members with a HDR or a similar grade	0	0

- Relevance

The platform PF1 (Team 11) is a sequencing platform that clearly serves a need within the Institut Pasteur. It has been involved in 17 Sanger and 16 Illumina sequencing projects as well as in sequencing activities connected to the Collection de l'Institut Pasteur. There is no doubt about its added value for the department and Institut Pasteur in general. However, at least partially due to the lack of insight into the actual costs associated with this service, it is difficult to assess its performance in comparison to outside contractors. Many teams in this and other departments at Institut Pasteur use genome sequencing services external to Institut Pasteur for their projects and it is not clear whether this is because of cost or type of service offered.

Besides the services being offered at present, this platform should act more as a sort of “go-between” between researchers from Institut Pasteur and outside contractors (like the Beijing Genomic Institute), and the platform would in this way obtain experience not present in the individual groups.

- Quality

Most projects are carried out in collaboration with research groups from Institut Pasteur but a small number of projects are carried out with French research groups outside Institut Pasteur.

- Response time

No clear procedure for the selection of projects seems to be in place. This may be justified by the fact that so far the platform has been in the position to accept all the projects. Researchers at Institut Pasteur seem to feel that the speed of the service could be improved, although a thorough analysis of user satisfaction has not been presented. In view of the evolution of sequencing needs for the department and Institut Pasteur, efficient user-platform interface and cost-benefit analysis will become unavoidable.

- Research level

As the majority of projects are carried out in a collaborative way, researchers associated with PF1 are co-authors on a large number of papers (53 papers in peer-reviewed international journals for 2006-2011).

- Benchmarks

No data on user satisfaction have been provided.

PF1 identifies a lack of bioinformatics support and a lack of technicians to do some of the wet lab manipulations, as bottlenecks for further growth. At the same time they realize that the bioinformatics facilities are being reorganized and that this may present an opportunity to increase interactions and share expertise.

TEAM 13: Logiciels et Banques de Données

Team leader: Bernard CAUDRON

Note: This team is a support group or platform. It is evaluated for its added value for the department and the Institut Pasteur overall scientific organization. There will be no assessment of research activity.

- Staff members

	Past	Futur
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	11	
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	
N7: Number of staff members with a HDR or a similar grade	0	0

- Relevance

The platform Logiciels et Banques de Données (Team 13) is involved in installing software and in database maintenance, two basic needs for all bioinformatics activities on the Institut Pasteur campus. The team is also involved in website development and provides assistance in programming. Until 2008, the team organized a 4-month class 'Informatique en Biologie' dedicated to biologists wanting to learn programming. This class was of very high level and provided an opportunity for scientists to learn Python. This team also maintains the Mobyle platform, a user-friendly interface that provides access to a large number of programs. However, many of these programs (maybe even the majority) are obsolete and should no longer be offered to the users. Mobyle also offers functionality for data integration and workflows, but again, the approach does not seem competitive and users may be better advised to use BioMart, Taverna, or other tools for these tasks. The team should evaluate the relevance of its services vs. efforts carried out elsewhere (EBI, NCBI and other smaller, more specialized bioinformatics web interfaces).

- Quality

The group has no user committee, and hence a clear picture regarding the quality of the service, or the users' satisfaction is hard to establish. It collaborates inside Institut Pasteur, but has also opened internationally with the Mobyle platform that is a public site (with help address). The group size may be too large with respect to the competitivity of the work carried out. No indication of the number of visits to the websites was mentioned.

- Response time

No clear procedure for the selection of projects is available, and no information concerning response time was available. However, the team keeps email tracks of 400 solved problems internally and 1200 internationally. Interaction with the Genomics Platform seems to be frequent. At present, a working group meeting twice a month with the other platforms around the needs for NGS is in place.

- Research level

The group has no real activity of publishing, apart from its work on Mobyle.

It is not constructed around projects and funding shared with biologists, and rather has a generic service activity.

- Benchmarks

Benchmarking of the most relevant softwares provided through Mobyle is essential to improve the quality of the service. The group should make sure that it does not invest resources in areas where it cannot compete and where the software development leads to duplication of effort made elsewhere.

TEAM 14 : PF2 Transcriptome et Epigénome

Team leader: Jean-Yves COPPÉE

Note: This team is a support group or platform. It is evaluated for its added value for the department and the Institut Pasteur overall scientific organization. There will be no assessment of research activity.

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	6	6
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		1
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	0
N7: Number of staff members with a HDR or a similar grade	0	0

- Relevance

The Transcriptome and Epigenome platform (PF2, Team 14) of the Genopole is dedicated to the development and use of high throughput approaches for transcriptomics and epigenomics studies. While PF2 has in the past used a wide range of different array technologies (in-house-made spotted and commercial microarrays), it is presently mainly using high-throughput next generation sequencing (NGS) (first the Illumina Genome Analyzer, GAIIX ; recently replaced by the Illumina HiSeq2000). It is clear that there is a need for such a platform in the current setting at the Institut Pasteur.

- Quality

The majority (>80%) of the activities of PF2 are in the form of scientific collaborations, while <20% is in the form of service. PF2 does not initiate its own research projects. Formation/training of platform members is continuous and provided through the training department of Institut Pasteur (paid by Institut Pasteur) or paid by the platform budget.

- Response time

There is a well-outlined strategy for project selection. Whether or not a project is accepted depends on (i) the biological question (which must be in the main areas of research in IP) and (ii) feasibility. These two criteria are discussed during early informal contacts between the researchers and bioinformaticians/biostatisticians in the team. Following these preliminary discussions, a formal application can be filed which can then be send out to up to two external referees. Approx. 20% of the projects are turned down in the very early stage (during preliminary informal discussions), mainly because of doubts concerning feasibility. This strategy has the big advantage that very few of the initiated projects fail but it may lead to an increase in the time needed before results are obtained, which again may be a problem especially for smaller-scale pilot studies. A revision of the review procedures seems to be in place, especially taking into account the need of being able to carry out smaller scale pilot studies with in a reasonably short time frame.

- Research level

As the majority of projects are carried out in a collaborative way, researchers associated with PF2 are co-authors on a fair number of papers (34 papers in peer-reviewed international journals for 2006-2011). In addition, PF2 often interacts with other platforms that use the same types of technologies (both inside and outside IP). For example, inside Institut Pasteur, PF2 collaborates with the teams 13 and 16 (platforms) for topics in which there is shared interest.

- Benchmarks

Since 2007 1800 Affymetrix arrays, 400 Agilent arrays and 50 Nimblegen arrays have been processed in the framework of 150 collaborative projects. NGS has been used in nearly 40 projects since 2008, in > 90% of the cases for RNA sequencing.

Users from Institut Pasteur just pay for reagents & consumables. Much time is taken to provide optimal support, training and advice on data interpretation to users. PF2 tries to interact closely with users to setup wet lab protocols according to the users' need and to develop the most appropriate analysis tools.

No actual data on user satisfaction have been provided and, from contacts with researchers at the Institut Pasteur, it appears that the level of data analysis provided by this platform is not always meeting the expectations.

There is a clear vision of what issues will need to be tackled in the near future. For the wet lab these include the development of 3rd generation sequencing, an increase in multiplexing, optimisation of procedures to allow the reduction in the amount of starting material required, and direct sequencing of RNA. For the dry lab, further development of NGS data analysis will require new tools (including a user friendly analysis pipeline, visualisation tools and genome browsers). While the PF2 PI has an outspoken positive view about the future, he identifies the shortage of statistical capacities in Institut Pasteur in general and in PF2 in particular as a possible limitation for the future. Continued support from and interactions with other bioinformatics groups in Institut Pasteur were also identified as crucial for further growth.

TEAM 16: PF4 Intégration et Analyse Génomiques

Team leader: Ivan MOSZER

Note: This team is a support group or platform. It is evaluated for its added value for the department and the Institut Pasteur overall scientific organization. There will be no assessment of research activity.

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	6	
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	
N7: Number of staff members with a HDR or a similar grade	1	1

- Relevance

PF4 provides essentially genomic analyses, annotation pipelines and data integration, all focused on bacterial genomes, except for a collaboration with Team 18 on Candida albicans. It maintains a public web site on these annotations that is user-friendly and successful, with 100,000 visits for Genolist per month. It also developed tools for MLST analysis and phylogeny. The annotation pipeline was set up for the needs of the units sequencing their favorite microbe, in the 2000's, and has expanded since then on more or less the same frame. In view of the change of scale of the present sequencing projects, it needs to take a new start and re-think its logics. This re-orientation is already in movement, with the national will to share efforts on the processing of high through put data, via ReNabi. PF4 has taken a position to work in the fields of NGS, comparative genomics and data visualization, which is a challenge, and implies extensive new developments. This effort needs to be conducted in networks at a larger scale to avoid redundancy with other such facilities. Whether PF4 should or not extend its activity toward lower and higher eukaryotes is a question that needs to be addressed. A closer synergy between the platform and research teams may be beneficial to the development of e.g. more specific annotation tools for mobile genetic elements, a major interest for this department (Team 5, "Génomique évolutive des microbes", could for instance provide the systematic analysis of the conjugative elements they developed recently to develop a dedicated annotation tool for these elements, Team 7 "Plasticité du Génome bactérien" for integrons, etc.).

- Quality

No information of the user satisfaction is available. The platform runs 57 collaborative projects.

- Response time

Projects do not appear to be selected likely because all can be accepted. It was recognized that this procedure could lead to an "overload", in turn leading to a reduced quality of the service provided. The platform works clearly in the frame of projects written in common with the biologists, with specific packages for PF4, and sometimes financing of post-doctoral fellows. It also takes M2 students. This certainly gives the team some dynamics.

- Research level

The team is clearly engaged in methods development. It published its Genolist environment in the database issue of NAR, which makes it visible.

- Benchmarks

Whether PF4 should develop all tools in-house, or rather refer to other platforms and connect with other interfaces appears not to be an issue yet in the team. The committee strongly encourages the PF4 leader to take now some distance and reconsider the way the platform should function in the future to remain competitive in the new landscape of high throughput sequencing.

OVERALL CONCLUSIONS AND RECOMMENDATIONS FOR THE PLATFORMS

- The lack of detailed data regarding user satisfaction makes it difficult to accurately assess the needs of the researchers in the department and precludes the formulation of specific recommendation; this committee would advise to gather these data and use them to guide future strategic decisions.
- Procedures to select/prioritise projects are not implemented in all platforms; in the platforms where such procedures are being used they may be too rigid.
- A recurring theme (shared by platform leaders and team heads) is that there is a lack of bioinformatics/biostatistics support within the department (and maybe within Institut Pasteur in general) ; despite the efforts of the platforms, there is still a gap between what they can deliver in terms of data analysis and what researchers would like to have.
- At the same time the committee noticed that the available expertise in bioinformatics is not used in the most optimal way and that a necessary restructuring of bioinformatics facilities may be on the way. Several team leaders expressed the wish to recruit bioinformaticians inside their own team. While this may be the preferred solution in some cases, the committee fears that hiring “isolated” bioinformaticians and place them among biologists ignorant of computer sciences is not the ideal solution.
- The committee noted that there is a strong awareness on the ever increasing needs for data analysis, but much less on the continued need to support basic hardware (servers, data storage units, …) and software. The committee strongly recommends not ignoring this latter important aspect.
- Overall the committee found that a clear vision on how bioinformatics activities should be organised and/or coordinated is missing and identified this as an important threat to future success.
- Finally, a decision on whether to keep all or part of these activities in house and/or to outsource them should be made; however this committee understands that the necessary information (including a financial audit) to tackle these questions is currently not available.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
URA2171 - GÉNÉTIQUE DES GÉNOMES	**A+**	**A+**	**B**	**A**	**A+**
DYNAMIQUE DU GÉNOME [JACQUIER-ARCANGIOLI]	A+	A	Non noté	A+	A+
BIOLOGIE DES BACTÉRIES INTRACELLULAIRES [JACQUIER-BUCHRIESER]	A+	A+	Non noté	A	A+
GÉNÉTIQUE MOLÉCULAIRE DES LEVURES [JACQUIER-DUJON]	A+	A+	Non noté	A	A+
EVOLUTION ET GÉNOMIQUE BACTÉRIENNES [JACQUIER-GLASER]	A	A	Non noté	A	A
GÉNÉTIQUE DES INTERACTIONS MACROMOLÉCULAIRES [JACQUIER-JACQUIER]	A+	A+	Non noté	A+	A+
PLASTICITÉ DU GÉNOME BACTÉRIEN [JACQUIER-MAZEL]	A+	A+	Non noté	A	A+
GÉNOMIQUE ÉVOLUTIVE DES MICROBES [JACQUIER-ROCHA-PIMENTEL]	A+	A	Non noté	A	A
BIOLOGIE SYSTÉMIQUE [JACQUIER-SCHWIKOWSKI]	A	A	Non noté	B	B
PHYSIQUE DES SYSTÈMES BIOLOGIQUES [JACQUIER-VERGASSOLA]	A+	A+	Non noté	A+	A+
DÉPARTEMENT GÉNOMES ET GÉNÉTIQUE	**Non noté**	**Non noté**	**Non noté**	**Non noté**	**Non noté**
PATHOGÉNOMIQUE MYCOBACTÉRIENNE INTÉGRÉE [MAZEL-BROSCH]	A+	A+	Non noté	A	A+
BIOLOGIE ET PATHOGÉNICITÉ FONGIQUES [MAZEL-D'ENFERT]	A	A+	Non noté	A	A
GÉNÉTIQUE MYCOBACTÉRIENNE [MAZEL-GICQUEL]	A+	A+	Non noté	A	A+
RÉGULATION SPATIALE DES FONCTIONS GÉNOMIQUES [MAZEL-KOSZUL]	Non noté	A	Non noté	A+	A+
GÉNÉTIQUE ÉVOLUTIVE HUMAINE [MAZEL-QUINTANA-MURCI]	A+	A+	Non noté	A+	A+

C1 Qualité scientifique et production

C2 Rayonnement et attractivité, intégration dans l'environnement

C3 Gouvernance et vie du laboratoire

C4 Stratégie et projet scientifique

Statistiques de notes globales par domaines scientifiques

(État au 06/05/2011)

Sciences du Vivant et Environnement

Note globale	SVE1_LS1_LS2	SVE1_LS3	SVE1_LS4	SVE1_LS5	SVE1_LS6	SVE1_LS7	SVE2 _LS3 *	SVE2_LS8 *	SVE2_LS9 *	Total
A+	7	3	1	4	7	6		2		30
A	27	1	13	20	21	26	2	12	23	145
B	6	1	6	2	8	23	3	3	6	58
C	1					4				5
Non noté	1									1
Total	**42**	**5**	**20**	**26**	**36**	**59**	**5**	**17**	**29**	**239**
A+	16,7%	60,0%	5,0%	15,4%	19,4%	10,2%		11,8%		12,6%
A	64,3%	20,0%	65,0%	76,9%	58,3%	44,1%	40,0%	70,6%	79,3%	60,7%
B	14,3%	20,0%	30,0%	7,7%	22,2%	39,0%	60,0%	17,6%	20,7%	24,3%
C	2,4%					6,8%				2,1%
Non noté	2,4%									0,4%
Total	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

*** les résultats SVE2 ne sont pas définitifs au 06/05/2011.**

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

- **SVE1 Biologie, santé**
  - **SVE1_LS1 Biologie moléculaire, Biologie structurale, Biochimie**
  - **SVE1_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes**
  - **SVE1_LS3 Biologie cellulaire, Biologie du développement animal**
  - **SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie**
  - **SVE1_LS5 Neurosciences**
  - **SVE1_LS6 Immunologie, Infectiologie**
  - **SVE1_LS7 Recherche clinique, Santé publique**
- **SVE2 Ecologie, environnement**
  - **SVE2_LS8 Evolution, Ecologie, Biologie de l'environnement**
  - **SVE2_LS9 Sciences et technologies du vivant, Biotechnologie**
  - **SVE2_LS3 Biologie cellulaire, Biologie du développement végétal**

Eduardo P. C. Rocha
URA CNRS 2171
Head of Microbial Evolutionary Genomics 31/03/11

The AERES evaluation of the GEM group is based on assessments that are often inexact. For example, the report mentions "1 Nature, several Plos Genetics" as high impact publications of original work of the group which obscures and downplays its track record which includes 16 articles in journals with impact factor at least as high as Plos Genetics as first and/or last author, of which 13 include original results. Two of the supposedly review publications (MMBR and Curr Biol) correspond to major original works in the period abundantly cited in the past activities report. Within this list of publications, two articles merited accompanying perspective comments, in Plos Genetics and Current Biology, and six were highlighted by F1000. This achievement for a very small team, between 2 and 6 members in the period under evaluation, is dismissively epitomized "Good results, extremely well valorised in terms of publication".

No mention is done of the group implication in the scientific community, e.g. scientific organisation of two editions of the national conference of bioinformatics (JOBIM), direction of the CNRS GdR Molecular Bioinformatics, participation in numerous program committees, organisation of symposia and participation in numerous conferences. There is also no positive reference in the report for the multidisciplinary nature of the group's work that includes comparative genomics, molecular evolution, evolutionary ecology, population genetics, protein structure, biostatistics and algorithmic science. All references to the broad and far-reaching scope of this multidisciplinary work are implicitly or explicitly negative.

Finally, the main scientific criticisms raised against the group are the generality of the questions/results and the lack of experimental work. One is intriguing on why answering general questions might be intrinsically worst to answering particular ones. The second criticism disregards the essentially evolutionary focus of the group. Evolutionary biology has developed into a major explanatory framework of biological sciences by its ability to produce theoretical models and test them in rigorous statistical ways using empirical data. The GEM group does both and the validity of its approach is recognised by the community as shown by its publication record and by the invitations to speak in reference international conferences in microbiology, bioinformatics, genomics and evolutionary biology. While the major goal of evolutionary biology studies is not to be translated into experimental approaches, the group has effectively developed in the period 2006-2010 collaborations with 14 different wet labs resulting in a total of 16 publications. The AERES report positive mention to the recent collaboration with experimentalists on conjugation is appreciated, but one is left bewildered with its reported novelty considering that this has always been the group's way of working. We have collaborated with many first-rate experimentalists in the last five years and we will continue to do so in the future to answer questions both broad in range and relevant in impact.

Eduardo Rocha

ALAIN ISRAËL
DIRECTEUR DE L'EVALUATION SCIENTIFIQUE
INSTITUT PASTEUR

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Paris, April 4th 2011

Comments on the evaluation report by the AERES Site Visit Committee.

Our team is very satisfied by the very positive evaluation of its activities and projects made by the AERES Site Visit Committee and thanks its member for their time spent examining its activities.

Best regards,

Alain Jacquier

ALAIN ISRAËL
DIRECTEUR DE L'EVALUATION SCIENTIFIQUE
INSTITUT PASTEUR

Commentaires de l'équipe 7 (Plasticité du génome bactérien, CNRS URA2171, D. Mazel)

We read the committee report and would like to thank the committee members for their critical evaluation of our projects. Although we understand the evaluators' concern regarding our project dealing with understanding the architecture of the two chromosomes in *Vibrio* and not in other bacterial genera carrying multiple chromosomes (BMC), we think that this comment is mostly due to the fact that we did not emphasize well enough the two preeminent reasons which amply justify the pursuit of these studies in *V. cholerae* and not in a species from a different genus. The first is that all species in the whole *Vibrio* radiation (*Vibrio, Aliivibrio*, and *Photobacterium* species, more than130 species) have 2 chromosomes, whose evolutionary history parallels their 16S phylogeny – suggesting that it is both a very ancient trait and that it confers a strong selective advantage. The second is that it is clear from the literature that *V. cholerae* is now the paradigm for segregation studies in BMC, and thus that our studies will find a strong echo in the community.

Didier Mazel

ALAIN ISRAËL
DIRECTEUR DE L'EVALUATION SCIENTIFIQUE
INSTITUT PASTEUR

We thank the AERES committee for the time and effort they invested in the evaluation of our group. The report touches upon several aspects of the complex environment of our group at Institut Pasteur. The restricted review format made it difficult to communicate relevant details for an accurate assessment. The commission members had only limited access to the overall situation on the campus that is relevant to the content of the report. We comment here on the key issues raised in the report.

Integration with the Pasteur campus

> *"What is certainly striking is the lack of integration of the group within Pasteur, which could have been more extensive given that many groups at IP produce large amounts of data from high- and low-throughput experiments."*

We agree that close collaboration with experimentalists producing high-throughput data is highly desirable for our group. But:

- Many, if not, most high-throughput data-producing biologists on campus currently generate DNA sequence data. Our research topic is the integrative analysis of postgenomic data.
- Of the other biologists, some generate e.g. imaging, transcriptomic or genetic interaction data that is straightforward to analyze "by eye" or within their lab using existing tools (no scientific collaboration needed).
- Many others require bioinformatics 'engineering assistance'. Currently, our research group does assist two experimental groups on campus in analyzing their ChIP-chip data, in the hope of downstream scientific collaboration. But this type of collaboration is typically neither funded, nor sustainable for long without the possibility of first-author scientific publications.

The mere existence of large-scale data therefore does not automatically imply collaboration (or even "integration") opportunities for our group.

Productivity

> *"Output is moderate, primarily in low impact or very specialist journals, some in higher impact but specialist journals in the field (2 Mol Cell Proteomics).*

Our proteomics method developments focused on computational methods to improve coverage of current proteomics approaches. We believe that improving coverage is an issue of key importance for computational regulatory network models, on which our current projects focus. Five publications around this topic were published in the top journals of the field of proteomics (by ISI impact factor, 2xMCP, 2xProteomics, 1xJPR), and with leaders in experimental proteomics. Other methods we developed address similar key obstacles to integrated transcriptome analysis. Given that integration on the Pasteur campus has been difficult, publications in the best specialists journals may not have yielded the highest possible impact in the short term, but our methods typically lead to high impact in the long run. Examples are the original Cytoscape paper (2003, Genome Research, 1242 citations per ISI) and our pathway/data integration paper (Ideker et al., 2002, Bioinformatics, not listed in ISI, cited 397 times according to Google Scholar). We believe that active computational methods research and expertise are nonnegotiable ingredients for future integrative biology projects at Pasteur.

> *"Cytoscape is essentially only a visualization platform and thus, effective contribution to research in high throughput data analysis is moderate…"*

We disagree with this assessment about the role and impact of Cytoscape. The Cytoscape platform provides network import and export, the integration of multiple types of experimental data on a network, integrated data and network visualization, and network filtering and query tools. 18 out of the top 20 hits from "googling" " 'Network biology software' " refer to the Cytoscape project. ISI Web of Knowledge lists 418 citations of the original Cytoscape paper in 2010 alone. After starting Cytoscape in 2002, our lab

continually expanded the software into (what we believe is) the world's leading software platform for network biology. Dozens of database, visualization and analysis plug-ins are available — some of them from other groups at Pasteur — and many research groups worldwide are developing new ones. NIH is has been funding our group for this project continually for over 10 years, and recently granted another us and our collaborators five million US$ for Cytoscape. Even if the AERES subcommittee was not familiar with the field of large-scale network biology, the impact of this "only-visualization" platform cannot be judged as "moderate".

Strategy and project

> *"The productivity is moderate to poor and the projects ill-defined. The real biological question is missing. More focus and a real connection with experimental biologists are urgently needed."*

The committee visit allowed us to present two out of three current modeling projects. These projects address the construction of regulatory network models from large-scale datasets, to respond to specific biological questions raised by our internationally recognized experimental collaborators (one of them at Pasteur). This report section reiterates the need for integration, but does not cite any reason why the projects are considered to be "ill-defined". We fail to understand this assessment, and also why a biological question and real connections with experimental biologists are judged to be missing.

Recent developments give us reason to hope that we will be able to expand our links with experimentalists at Pasteur.

- To improve its capacity for integrative biology projects, the campus has reorganized its proteomics and bioinformatics infrastructure, and looks to improve the coordination of platform resources. We expect that this will allow biologists to address deeper questions beyond the 'bioinformatics engineering' using large-scale data, which our group can help solve.
- A new building on campus is dedicated to integrative biology.
- Our group is a full partner in two local data-rich and well-funded integrative biology LabEx projects that will soon start.

Our conclusions

- The Pasteur Institute offers, in many respects, an excellent research environment, but the conditions for successful large-scale biology projects to which a group such as ours can contribute are only being established at this time. We disagree with the view that this was an opportunity that our group already had in the past.
- The report does not appropriately assess the productivity of our methods-oriented work, much of which tends to have high impact, but over a longer time period.
- Our projects are well-defined collaborations with (currently internal and external) internationally recognized experimentalists, and our group has the potential to provide the campus with critical computational expertise and capabilities in the coming years.
- We agree fully that additional collaborations with the excellent local experimentalists must continue to be a key objective of our group, and look forward to helping the Pasteur campus realize the potential of integrative biology.

Benno Schwikowski

Alain ISRAËL
Directeur de l'Evaluation scientifique
Institut Pasteur

Plate-forme Génomique
Département Génomes et Génétique

Team 11 PF1 Génomique

Team leader : Christiane BOUCHIER

Note : This team is a support group or platform. It is evaluated for its added value for the department and the Institut Pasteur overall scientific organization. There will be no assessment of research activity.

No comment regarding the report

ALAIN ISRAËL
DIRECTEUR DE L'EVALUATION SCIENTIFIQUE
INSTITUT PASTEUR

Institut Pasteur

Paris, March 31, 2011

Génopole – Plate-Forme 4
Intégration et Analyse
Génomiques

Département
Génomes et Génétique

AERES 2011 Committee

Ref. *IAG/IM-11/03*

From *Ivan MOSZER*

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SUBJECT : ***Comments to the AERES report for Team 16***

We would like to emphasize that the PF4 platform contributed to 34 publications in international peer-reviewed journals in the 2006-2010 period. We deplore that this figure was not mentioned in the report, as we think that this fairly high number of publications is one good indicator of the success of the many projects we were involved in, and this indirectly testifies that users of the platform were satisfied about our collaborations, even in the absence of a formal user survey.

About the statement: "This effort needs to be conducted in networks at a larger scale to avoid redundancy with other such facilities": we want to stress our significant implication in the National Network of Bioinformatics platforms (ReNaBi), the head of PF4 being in charge of the coordination of the largest of the 6 multi-site platforms (APLIBIO – 8 sites in Ile-de-France).

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Paris, 29/03/2011

Dear Committee Members,

First of all, I would like to thank the committee members for having participated in this evaluation process and for their constructive and critical feed back. We have read the AERES report and we have no comments to make in reply to the evaluation report concerning our laboratory.

Sincerely,

Lluis Quintana-Murci

ALAIN ISRAËL
DIRECTEUR DE L'EVALUATION SCIENTIFIQUE
INSTITUT PASTEUR

Observations pour l'équipe 18 (Biologie et Pathogénicité Fongiques – INRA USC2019, Christophe d'Enfert)

Although we agree with the comment that the proposed work is a continuation of the present work, it should be noted that a previous evaluation of our group by an international panel end of 2008 stated « The proposed research program falls into five areas : genomics, genetic diversity and genome dynamics, biofilms and the mechanisms of antifungal resistance, and the regulation of morphogenesis. These do not need to be reviewed in details at this stage, but are all exciting components making full use of current scientific opportunities and fitting well together ».

Christophe d'Enfert

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Directeur de l'Evaluation scientifique
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