Stabilité génétique et oncogénèse

Rapport Hcéres

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

Section des Unités de recherche

Evaluation report

Research Unit :

Genetic stability and oncogenesis

of University Paris 11

February 2009

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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

February 2009

Evaluation report

The research unit :

Name of the research unit : Genetic stability and oncogenesis

Requested label : UMR CNRS

N° in case of renewal :

Head of the research unit : M. Filippo ROSSELLI

University or school :

University Paris 11

Other institutions and research organization:

Institut Gustave ROUSSY

CNRS

Dates of the visit :

12 and 13 January, 2008

Members of the visiting committee

Chairman of the commitee :

M. Christophe CAZAUX, Institut de Pharmacologie et de Biologie Structurale, Toulouse

Other committee members :

Mme. Françoise DANTZER, École supérieure de biotechnologie de Strasbourg

M. Bernard ROUSSET, Institut National de la santé et de la recherche médicale (INSERM), Lyon

M. Charles THEILLET, Institut National de la santé et de la recherche médicale (INSERM), Montpellier

Mme. Sylvie SAUVAIGO, Laboratoire "Lesions des Acides Nucleiques, SCIB/DRFMC, CEA Grenoble

M. Thierry FEST, Université de Rennes 1

Mme. Dana BRANZEI, Institute of Molecular Oncology Foundation (IFOM), Milan, Italy

M. Serge BOITEUX, Commissariat à l'énergie atomique (CEA) Direction des sciences du vivant, Fontenay aux roses

CNU, CoNRS, CSS INSERM, représentant INRA, INRIA, IRD.....) representatives :

M. René TOCI, CoNRS representative

Mme. Geneviève BARLOVATZ, CNU representative

Observers

AERES scientific representative:

M. Charles DUMONTET

University or school representative:

M. Dominique EMILIE, University Paris 11

Research organization representatives :

Mme. Martine DEFAIS, CNRS

M. Eric SOLARY, IGR

Evaluation report

1 • Short presentation of the research unit

Total number of lab members: 54, including

- Full time researchers: 15, including 1 emeritus
- Researchers with teaching duties: 5
- Postdoctoral fellows: 12
- ITA and IATOS: 15
- PhD students: 7, all with a fellowship

- Number of lab members with a HDR: 12, 5 are currently PhD advisors
- Number of lab members with a PEDR: 0
- Number of students who have obtained their PhD since January 2005: 7
- Average length of a PhD during the past 4 years: 4 years
- Number of "publishing" lab members: 20 out of 20

2 • Preparation and execution of the visit

The committee visited the laboratory on January 12 and 13 2009. The documents were provided in advance. However the experts would have appreciated to find additional information in these documents such as for each group, the number and names of the researchers in charge of each project and the objectives presented; ii) for each group, the number of PhD and posdoctoral students; iii) for each permanent researcher the number of invited conferences, the participation to editorial boards, etc. Some of these documents were requested and provided during the visit.

On site, the visit was quite properly organized, despite the fact that talks by group leaders were heterogenous (some lacking introductive parts, others a description of interactions with other groups of the unit, etc.). The committee had time to discuss with group leaders after each 40 min-presentation. It also had time to visit students in the labs and to discuss in plenary sessions and separetely with researchers, technicians and administrative staff.

3 • Overall appreciation of the activity of the research unit, of its links with local, national and international partners

Historically, this reseach unit originates from the merge between one UMR and one UPR, dedicated to translational/clinical and basic comprehension of DNA repair mechanisms, respectively. Two years ago, a previous assessment stated that the unit should focus its attention on a unique (same main) research theme.

The new director has followed this recommandation since the unit currently hosts 6 teams working on very connected topics (oxidative damage, DNA damage checkpoint, "repair" DNA polymerases, etc.). The groups working in other fields of research, more focused on human genetics, moved to other labs. Conversely two groups joined the unit, bringing a useful expertise in the biochemistry of DNA repair and also an interesting mouse and cellular model to study the connection between genetic instability, gene expression and DNA repair (B lymphocytes).

The productivity of the unit is ranging from good to very good, even though most of the papers are in collaboration (the relative number of first/last positions is fairly low). The committee appreciated the overall quality of the projects presented.

Technical support in the unit is significant, the technicians/researchers ratio (near 1) being interestingly high. This is a major asset for the future even though the mean age of the technicians and senior scientists is high (more than 50 years).

Because of this high mean age of the lab members, students and post-docs are critically needed in the Unit. Indeed, if the unit has undoubtedly been successful in attracting experienced group leaders, the number of new young scientists (including PhD students and permanent or post-doctoral researchers) is quite low. It should be emphasized that 4 out of 6 groups have researchers who are close to retirement.

The Unit has not still invested important resources in dedicated equipments. The committee suggests a larger sharing of financial supports in order for example to update the proteomic platform. Additional technology platforms (imaging, transcriptomics, animal facility) are available on-site at IGR.

The people in the lab appreciate the number and quality of seminars as well as the number of lab meetings. Members of the labs also agree with the management of the director and his strategic decisions. For the more "stable" forthcoming years, the committee agrees with the director who wants to increase the number of laboratory and scientific councils in order to preserve the unity of the lab.

The current director must be aknowledged for the successful reorganization of the lab.

4 • Specific appreciation team by team and/or project by project

Team : FANC/BRCA pathway and Cancer

At present this team is composed of four senior scientists, four technicians, two post-doctoral fellows and one doctoral student. The leadership of this group is highly dynamic and has two main research focuses, on Fanconi anemia (FANC) proteins and on BRCA 1. There are two prominent research figures in this group, the one of the team leader, directing mainly the research on Fanconi anemia, and the one of a professor leading the sub-team on BRCA1 research. However, the topics are interconnected, and the group leader is very supportive and clearly committed to manage the complete research program of the group.

- The program which was presented corresponded to two main projects, each following 3 or 4 lines of research:
- Understanding the role of FANC proteins in interstrand crosslink repair and redox homeostasis
- Phenotypic characterization of breast heterozygous BRCA1 cells and the role of BRCA1 on chromosome X inactivation.

The team has published a good number of publications in quality journals in the past five years, and although many are collaboration studies, the group has published several papers with the principal investigator in leading positions in very good journals such as EMBO Journal, Blood and Oncogene.

The visit by the committee confirmed that there are good skills, expertise, and original questions in this team to enable successful future research. However, since the team follows two main topics and the number of people dedicated to each of them is relatively small, the committee encourages the group leader to focus his efforts on the projects where preliminary data exist and where the potential of outstanding results are highest. The committee appreciated the enthusiasm of the group leader, which has obtained grants from ANR and Ligue Contre le Cancer ("labellisation"), to identify novel factors, targets, or miRNA regulated by the FANC pathway, but also remained cautious in regard to the number of personel that may be engaged in such screens. The research on BRCA1 appears to pursue three different lines, and although they all address important questions of the role of BRCA1 in genomic stability, given the limited resources available, the group may benefit from being encouraged to concentrate its forces on one or two aspects of research at the present stage.

Conclusion: Very good scientific data and original, interesting questions were presented by this team. Considering the recent achievements of this group, the committee agreed that the academic perspectives for the group are high. However the number of the questions and projects pursued appeared very high in comparison with the number of people available and therefore it was recommended that the efforts be concentrated on the most original aspects of the projects.

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

Team : Translesional (TLS) DNA polymerases and cancer

At present this team is composed of 2 senior scientists, one technician, one post-doctoral fellow and two doctoral students. The team exists as an independent team since 2004 (ATIP CNRS). The team leader has published a dozen publications, all in quality journals but often in collaboration with her previous postdoc mentor at Brighton (UK). The research of this young team is centered on the molecular switch between replicative and Y-family TLS DNA polymerases in the course of a DNA damage bypass. Only one paper (EMBO J) has been published in last position by the principal investigator, this low productivity being explained by the time necessary to initiate ambitious projects such as:

- the biological significance of post-traductional modifications of PCNA in human cells
- the regulation opf TLS DNA polymerases by the Rev1 chaperon protein
- the DNA replication control after UV in XP-V cells

The visit by the committee confirmed that the leadership of this group is very dynamic and creative, and it is clear that recently completed studies should be published soon in good journals. However, depending on the limited resources available as well as the competition in the area, the principal investigator might be encouraged to concentrate her forces on one or two given aspects of research at the present stage.

Conclusion: Given the recent achievements (e.g. the unexpected involvement of the TLS DNA polymerase Pol iota in repair of oxydative DNA damage, or the sumoylation of PCNA in cells deficient in TLS), and the quality of the projects, opening the possibility to identify in a next future a "SOS-like" eukaryotic pathway, the academic perspectives for the group are high. Moreover the group has several collaborations inside or outside the lab, which facilitate more detailed biochemical analysis likely to reinforce in vivo findings. However the work by this small group might profit from a greater focus on the most original aspects of the subject.

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

Team: DNA repair and Cancer

At the time of the visit, the team is composed of 3 senior scientists, three technical staffs and one PhD student working in the lab for three months. The presented program corresponds to 3 projects;

- targeted gene therapy aimed at correcting XPC gene deficiency in epidermal cells from XP cells
- genetic profiling study (transcriptome and CGH-array) of primary melanoma aimed at defining genetic signatures of adverse disease outcome
- genetic study on large cohorts aimed at determining SNP variants in DNA repair genes associated with lung and head neck cancer

Only project 1 is fully developed in house, project 2 is mainly externalized on the genomic and bioinformatics platform of IGR and project 3 is a collaboration with the CNG in Evry, a large european study group and an Inserm Unit at St Louis Hospital in Paris. It should be emphasized that the principal investigator in charge of project 3 is part time affected in the team and part-time in the Inserm Unit in Saint Louis Hospital.

The committee also noted the position of the team in UV-sensitive genetic syndrome (XP, TTD, CS) detection according to a protocol that his lab set up and is one of very few in the world to master and conduct. For this reason it was granted by the ministry of health the approval to act as a diagnostic platform for these genetic diseases. These diagnostic tests are performed on a routine basis by a lab technician payed by the IGR. This diagnostic activity allowed the lab to set up a unique collection of primary skin fibroblasts from tested patients (>900 samples frozen in liquid nitrogen).

The scientific program presented appeared as an adjunction of largely disconnected projects, with one (project 3) being developed outside of the lab and which could be continued without intervention of either the "DNA repair and cancer" team or the unit.

All 3 projects were considered scientifically sound, worth pursuing and, as concerned projects 2 and 3, interesting preliminary data. Although it was clear to the committee that project 1 (targeted correction of XPC) was just starting, there was a consensus judging it promising and the collaboration with the biotech Cellectis for the use of meganuclease to target gene insertion of great potential.

The structure of the team is a reflection of the organization of the scientific program with its 3 projects, The team concentrates its human potential on the in-house project 1 with 4 people devoted to it, project 2 is by one researcher who coordinates work of the different platforms and interacts with clinical partners, while project 3 is essentially worked out at the CNG and Hospital St Louis and led by the same researcher. The benefit of the latter to keep a 50/50 implication at IGR and the Inserm Unit at St Louis Hospital was not obvious and may be reconsidered with benefit.

The proposed position of the team leader and his skills in managing projects did not strike as being obvious. It seemed to the committee that this senior staff researcher is more commited to develop his own project than to manage the complete research program of the team.

Conclusion: Although some excellent science and very original aspects were presented, this team appeared fragile and lacking maturity. This can be attributed to a lack of integration of the scientific projects and of preparation of the leadership. Projects 1 and 2 should be kept in the general program of the laboratory but with different positioning. The leadership should be reconsidered.

Team: Reactive-oxygen species (ROS) and radio-carcinogenesis

The team is composed of six senior scientists (three are full-time researchers and three are part-time, in charge of clinical or biological departments at Institut Gustave Roussy), two technicians and three PhD students.

In the recent years, the team members have made important contributions in the thyroid field on both fundamental (molecular analyses of the hydrogen peroxide generating system) and clinical (diagnosis and treatment of thyroid cancer) aspects; it must be emphasized that a member of the team is a world leader in thyroid cancer diagnosis and treatment (as attested by his publications).

During the last two years, the team has developed experimental approaches to analyse the implication of NAPDH oxidase and reactive oxygen species (ROS) in DNA damage induced by oncogenes or caused by irradiation; one of the prominent results deals with the observation (by using a non-tumorigenic thyroid cell line) of a X-ray irradiation-induced, possibly ROS-mediated, RET/PTC gene rearrangement (one of these gene alterations occurring in human thyroid carcinomas). These and other interesting in vitro data are in the course of publication.

The projects of the team associate, in a well-defined and scientifically well-grounded continuum, cognitive, translational and clinical research. The cognitive project is centered on molecular analyses of the relationship between ROS production and DNA damage on the one hand and changes in radiosensitivity in relationship with HIF-1a activation on the other. The translational part mainly aims at: i) analysing the thyroid cell responses to kinase inhibitors (used in cancer treatment), in terms of changes in mRNA and miRNA expression profiles; ii) the identification of biological markers for the follow-up of treated patients. The objective of the clinical research (based on large cohorts of patients at IGR and national and international collaborations) is the improvement of the detection (imaging modalities) and treatment (targeted therapy) of thyroid cancer metastases.

Conclusion: The research projects of the team are original, centered on pathophysiological questions and closely related to the projects of other teams and in accordance with the general orientation of the unit, as recommended by a previous assessment 2 years ago. At least two intra-unit collaborative studies are already planned. The team leader has already shown her capacity to manage scientific programs and the research work of PhD students. The members of the team have the competence to achieve their goals and produce publications not only from translational/clinical data but also from more fundamental approaches.

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A	A	A	A	A

Team: Genome plasticity in B cells

This starting group associates 2 senior scientists, one engineer and at the time of the visit two undergraduate students (Master 1). The principal investigator was working in INSERM U783 (Necker-Enfants Malades) before moving to IGR in January 2009.

The research proposed is aimed to: (i) decipher how the B cell machinery coordinates and regulates DNA repair processes following activation-induced cytidine deaminase (AID) expression, (ii) investigate the role of AID in B cell tumorigenesis. The methodology used combines transcriptome analysis, proteome analysis and microRNAs profiling on germinal B cells isolated from wild-type and AID-deficient mice.

The committee agreed on a general consensus that the leadership of this group is highly dynamic, and shows good skills and expertise in the field of B cell homeostasis.

The questions investigated are of fundamental importance to understand how DNA repair processes respond to AID-induced DNA damage in B cells, and as such were considered as promising and relevant for the fields of genome stability and immunology.

However, the program is essentially based on technical approaches and fishing experiments that can delay the scientific production of the team in terms of publications. In addition, it appeared difficult for the committee to evaluate the position of the group leader and his scientific program compared to the interests developed by the group from which the leader is coming in INSERM U783.

Therefore, the PI might be encouraged to think on an additional focused, original and short-term project that will help to build his scientific production as well as the national and international notoriety of the team.

At first, this team will benefit from the financial support of the unit. It appeared clear to the committee that efforts have to be made in terms of grant applications.

Conclusion: Given the experience and competence of the team leader in the science proposed and the long-term relevance of the research program, the committee agrees that the scientific goals might be achieved. However, the viability of the group will rely on the ability of the principal investigator to: (i) financially support his projects, (ii) build up his scientific production as last author, (iii) increase the size of the group through the recruitment of PhD and or post-doctoral researchers. Efforts have to be made in these directions.

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

Team: DNA repair

Currently in the unit « Molecular interactions and cancer » (UMR 8126), this group wishes to join the unit for the next contract period (2010-2013).

This team, which is composed of 3 full time researchers (1 emeritus) and 3 pos-doctoral fellows, is the continuation of a long time existing research team on DNA damage and repair. It has developed its own original research, in particular with the identification of a new DNA repair system, different from the ones already known (Nucleotide Incision Repair, NIR). This finding, although not developed in other labs neither in France nor abroad, could be important from a functional point of view. Hence biochemical and regulatory mechanisms that underlie the latter repair system should be further elucidated and this topic must be pursued.

The project of this team to join the Unit is judicious and justified for different reasons:

- it will permit the forthcoming Unit to reinforce its expertise and the available molecular biology tools in both the DNA repair and DNA biochemistry fields and thus gain in visibility
- the coherence of the research topics of this team with those of the unit are evident, and efficient collaborations already exist between this team and the other teams of the Unit. According to the committee, interactions on different topics such as reactive oxygen species and diseases linked to DNA repair (Fanconi anemia) might be fruitful.

Conclusion: The team leader conducts his team and his research with maturity and efficiency. However he suffers from a lack of visibility and international recognition despite the high quality and originality of his work. He also faces difficulties to recruit doctoral and post-doctoral students. Hence the team might have an issue in terms of amount of human resources. To gain in visibility and recognition this lab should go towards complementary in vivo approaches that would help consolidate its research and assess the biological importance of NIR. Efforts should also be made to be more visible by Doctoral Schools.

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A	A	A	A	A

5 • Appreciation of resources and of the life of the research unit

Human Resources:

The unit is composed of 54 persons including 20 permanent researchers from CNRS, INSERM and University. The number of ITA/IATOS is satisfying, assuming that the unit has access to facilities at the IGR level (animal house, genomics and proteomics). The number of PhD students and post-doctoral positions appears limiting. The unit benefits from very good financial support by national and international institutions.

Life within the unit

Unit has a scientific council deciding of the scientific strategy, i.e, creation and support of new teams, recruitment of permanent researchers. The teams have frequent meetings where students can expose their recent results. In addition, external seminars are organized.

Conclusion:

The human and financial resources of the unit are satisfying and allow the development of good research projects in the future. We did not notice personal or economical conflicts that could impair the scientific life in this unit.

6 • Recommendations and advice

Strong points :

The project presented is coherent, since the six groups all work in the fields of oxidative stress, DNA repair, cell cycle regulation in connexion with human diseases such as Fanconi anemia and cancer (skin cancer and thyroid cancer). Most of the teams have ongoing collaborations and common projects. This point was critical, since the heterogeneity of the scientific project had been underlined by the previous visiting committee by CNRS. Therefore, we congratulate the project leader for taking into account these recommandations. Besides being coherent, the scientific project is also of high quality and competitive at the international level. In addition, the group leaders are relatively young (40-50 years old). The quality of the research is assessed by numerous publications in good journals. Most of the teams benefit of financial supports by national and international institutions. The project leader stated that the unit has enough resources in the next years in order to support emerging teams. At the IGR, the teams benefit from technical facilities (animal house, genomics, proteomics...) that are due be reinforced soon. This issue is essential for the success of several projects in the unit.

Weak points:

We notice many collaborative publications where first and last authors are not from the unit. We think this is a critical issue that must be corrected in the next four years. The recognition of some of the proposed group leaders is not clear at the international level. We think the situation should improve, if the proposed projects are finalized. However, the committee was very much concerned by the governance of the DNA repair and cancer team. Furthermore, the success of the group working on B cells will require special support. Finally, we noticed the absence of promising young scientists (30-35 years old) susceptible to become group leaders in the near future.

Recommendations and advice:

The committee evaluates very positively the project for this Unit because of its coherence and scientific quality. The possibility to merge the group “DNA repair and cancer” with a leading group of the unit was recommended. Generally speaking, we believe that most of the groups will progress in the four next years.

We encourage the group leaders to cooperate with the director to propose attractive conditions to recruit more PhD students and post-doctoral researchers. An active policy to encourage graduate and undergraduate students to join the unit should be adopted by the University. Researchers and teachers-researchers should also give more classes at the Master 1 and 2 levels with the aim of attracting students interested by genetic instability and cancer. A priority should be to identify promising young reseachers able to candidate for permanent positions.

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

UNIVERSITÉ
PARIS-SUD 11

Le Président de l'Université Paris-Sud 11

à

Monsieur Pierre GLORIEUX
Directeur de la section des unités de recherche
AERES
20, rue Vivienne
75002 Paris

Orsay, le 7 avril 2009..

N/Réf. : 102/09/GCo/LM/LS

Objet : Rapport d'évaluation d'unité de recherche
N° S2100012408

Monsieur le Directeur,

Vous m'avez transmis le vingt trois mars dernier, le rapport d'évaluation de l'unité de recherche « Stabilité génétique et oncogenèse » - FRE 2939, et je vous en remercie.

L'université prend bonne note de l'appréciation et des suggestions faites par le Comité.

Les points à améliorer seront discutés avec le directeur d'unité dans un esprit constructif pour l'avenir de la recherche à l'université.

Vous trouverez en annexe les éléments de réponse de monsieur Filippo ROSSELLI, Directeur de l'unité de recherche.

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

Guy COURRAZE
Président

UNIVERSITE PARIS SUD 11 - Présidence - 91405 ORSAY CEDEX

P.J. : Commentaires de Mr ROSSELLI

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IFR 54

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Villejuif, March 30, 2009

To whom it may concern

On behalf of my colleagues, I would like to thank the members of the AERES committee for their overall positive evaluation and helpful suggestions. I am especially pleased to observe that the committee found our scientific project to be coherent, of high scientific quality and competitive at the international level. The suggestions that are made are in complete agreement with what we have in mind in terms of scientific issues and future development.

I want to remind you and emphasize that, like mentioned in the review, the unit comes from a period of more than four years of successive reorganizations (Fusion of two units: 2004/05; Prolongation of the FRE: 2006/07; Present project: 2008/09) that has not provided the good environment to perform a long term research for the various teams and enough stability to their students and post-doc. Indeed, although build a project and prepare an evaluation represent an important task for people in a lab, these repeated activities are extremely time-consuming with obvious consequences on the normal work of the teams.

"The productivity of the unit is ranging from good to very good, even though most of the papers are in collaboration (the relative number of first/last positions is fairly low)." and "We notice many collaborative publications where first and last authors are not from the unit. We think this is a critical issue that must be corrected in the next four years."

We agree that researchers in the teams have many publications from collaborative studies without being « leaders » of the research. Nevertheless, more than 50% of publications are realized in-house. Our collaborative score reflects 1) the previous period of re-building of the Unit, it was easier to have external collaborations than to work directly on in-house project; 2) the positive and historical implication of many researchers in collaborative studies with national and international laboratories; 3) the importance of our

expertise in DNA repair, replication and cell cycle checkpoint controls that is absolutely required to complete studies focused on other biological end-points such as apoptosis, differentiation and cancer progression; 4) finally, we are a research unit located in a Hospital Campus and all our teams are more or less implicated in projects from bench to bed side which are principally managed by physicians. In any case, in light of the objectives presented and agreed by the committee, we hope to significantly improve the quantity and the quality of the in-house publication score in the next future.

"Technical support in the unit is significant, the technicians/researchers ratio (near 1) being interestingly high. This is a major asset for the future even though the mean age of the technicians, and senior scientists is high (more than 50 years)."

We agree with the committee that the technicians/researchers ratio is presently good. Unfortunately, this situation is rapidly moving: next year we will loose 2 IE and 1 AJT for sure (NOEMI and retirement), and probably 2 more technicians.

"Because of this high mean age of the lab members, students and post-docs are critically needed in the Unit. Indeed, if the unit has undoubtedly been successful in attracting experienced group leaders, the number of new young scientists (including PhD students and permanent or post-doctoral researchers) is quite low."

The mean age of the senior scientist, with a lack of people under 40, is a real major problem for the future. The last young scientist was recruited 5 years ago with an ATIP grant. Since 2006 three of the teams associated to the Unit presented candidates to CNRS and INSERM without success. These candidates were kept in the final list but in an unfavourable position to get a permanent position. Nevertheless, we are glad to emphasize that other laboratories awarded people formed in our teams. Two of our post-doctoral fellows were finally recruited on permanent positions at University Paris XI and Paris VII, and another at Barcelona University (Spain) to work on a similar project. In light of the well known present situation, we will do our best to rapidly bring new blood into our unit hoping that University and EPST could better support our research area and laboratory in the next future.

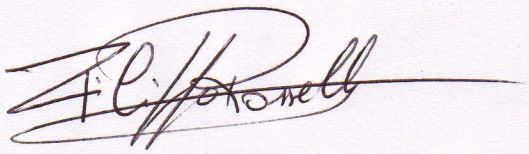
All the group leaders agree with the committee recommendation to increase the number of young scientists in the laboratory, including M2, PhD and post-doctoral students. However, I want to emphasize that the fact to maintain the number of non-permanent young scientist at a reasonable low level was a choice, dictated by the in-progress situation of the unit during the last years. For the more "stable" forthcoming years, I will encourage researchers in the teams to engage teaching in more classes at the M1 and M2 levels, and to have a more effective politics to recruit post-doctoral fellows.

"...the committee was very much concerned by the governance of the DNA repair and cancer team."

Following the constructive discussion with the committee on this particular point, we agree to merge the teams 1 and 3 under the management of the director for the next 4-years plan.

Finally, I would personally thank the committee for the general appreciation of my effort to reorganize the laboratory during the last two years.

We will certainly continue the course we set out and will continue to build the laboratory on the basis of scientific quality.



Dr. Filippo Rosselli

Response to the report by the AERES visiting committee concerning the group "DNA repair" by the head of the group.

First of all, I appreciate that the AERES commission supports my decision to join the new unit and also my research. AERES commission evaluates positively the quality and productivity of research conducted in the group "*DNA repair*". I do agree that we should use complementary *in vivo* approaches which are now under way, *ex vivo* for example. However, I would like to address several comments made by visiting committee concerning my group.

I disagree with the following comment on page 8 of the report Team: DNA repair, Conclusion: "*However the group suffers from a lack of visibility and international recognition ….*".

Several lines of evidences support that the topics of the team "DNA repair" are very well recognized by the scientific community:

(i) At the national level the group "*DNA repair*" is recognized since in 2004 when the C.N.R.S. has recruited Alexander Ishchenko as *Chargé de Recherche 1*. Furthermore, the team has been recognized and funded by *Fondation de la Recherche Médicale* as "*Equipe FRM*" in 2008 as well as by numerous grants from INCa, ARC, EDF CNRS-GDRE182 etc. These facts strongly confirm the visibility and scientific recognition of the group and the importance of its research topics.

(ii) Most importantly, at the international level, in the last five years the group has obtained several international grants from European Community FP6 OXEXRISK and FP7 RISC-RAD, National Centre for Biotechnology of the Republic of Kazakhstan and French-Polish Scientific Cooperation. These international grants argue against "*a lack of visibility and international recognition*" of the group.

(iii) The results of the group are regularly presented at French and International meetings. The head of the group was an invited speaker to the Gordon Research Conference and to NIEHS Triangle Park NC. The papers published by the group on the new alternative repair pathway have been positively cited more than 200 times (data from "*Web of knowledge*" website) including numerous citations in the most recent review papers in the field of DNA repair.

Page 8 of the report Team: DNA repair, Conclusion: "*He also faces difficulties to recruit doctoral and post-doctoral students*".

The group has presently three post-doctoral fellows and never had problems in recruiting them (6 postdocs came during the last 6 years). We do agree that we don't have yet *stricto sensu* PhD students. However, we accommodate every year PhD students from France and abroad from Russia, Poland, Spain and Kazakhstan for varying periods of time performing part of their thesis in my group.