



Génétique et biologie des cancers

Rapport Hcéres

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

Department for the evaluation of
research units

AERES report on unit:

Genetics and Biology of Cancers

Under the supervision of the following
institutions

and research bodies:

Institut Curie

Institut National de la Santé Et de la Recherche
Médicale

Université Paris Descartes

Centre National de la Recherche Scientifique

January 2013



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

Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head

Pierre Glaudes



Grading

Once the visits for the 2012-2013 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).

This score (A+, A, B, C) concerned each of the six criteria defined by the AERES.

NN (not-scored) attached to a criteria indicate that this one was not applicable to the particular case of this research unit or this team.

Criterion 1 - C1 : Scientific outputs and quality ;

Criterion 2 - C2 : Academic reputation and appeal ;

Criterion 3 - C3 : Interactions with the social, economic and cultural environment ;

Criterion 4 - C4 : Organisation and life of the institution (or of the team) ;

Criterion 5 - C5 : Involvement in training through research ;

Criterion 6 - C6 : Strategy and five-year plan.

With respect to this score, the research unit concerned by this report and its in-house teams received the following grades:

- Grading table of the unit: **Genetics and Biology of Cancers**

C1	C2	C3	C4	C5	C6
A+	A+	A	A	A	A+

- Grading table of the team 1: **Genetics and biology of paediatric cancers**

C1	C2	C3	C4	C5	C6
A+	A+	A	A	A+	A+

- Grading table of the team 2: **Analysis of Signal Transduction**

C1	C2	C3	C4	C5	C6
A+	A	A	A	A	B

- Grading table of the team 3: **Stress and cancer**

C1	C2	C3	C4	C5	C6
A+	A	A	A+	A	A

- Grading table of the team 4: **Genetics and biology of hereditary breast cancers**

C1	C2	C3	C4	C5	C6
A	A+	A	A	A	A



Evaluation report

Unit name: Genetics and Biology of Cancers

Unit acronym:

Label requested: UMR_S/Institut Curie

Present no.: UMR_S 830

Name of Director
(2012-2013): Mr Olivier DELATTRE

Name of Project Leader
(2014-2018): Mr Olivier DELATTRE

Expert committee members

Chair: Mr Marc BILLAUD, Université Joseph Fourier, Grenoble

Experts:

Mr Olivier BERNARD, Université Paris 11
(representative of CSS Inserm)

Mr Daniel BIRNBAUM, Aix Marseille Université

Mr Yvan DE LAUNOIT, Université de Lille

Mr Patrice DUBREUIL, Aix Marseille Université

Mr Philippe FORT, Université Montpellier 2

Mr Thierry FREBOURG, Université de Rouen

Ms Florence PEDEUTOUR, Université Nice Sophia Antipolis
(representative of CNU)

Mr Didier TROUCHE, Université Paul Sabatier, Toulouse



Scientific delegate representing the AERES:

Mr Daniel OLIVE

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

Mr Arnaud DUCRUIX, Université Paris Descartes

Ms. Marie-Joséphine LEROY-ZAMIA, Inserm

Mr Daniel LOUVARD, Institut Curie



1 • Introduction

History and geographical location of the unit

The Inserm/Institut Curie U830 was created on January 1st 2007 and was located in the building Pavillon Trouillet-Rossignol at the Paris site of the Institut Curie. This unit derives from the merging of two former units : the Inserm/Institut Curie U 509 (Molecular Pathology of Cancer; director Mr Olivier DELATTRE) and the Inserm/Institut Curie U528 (Signal Transduction and Oncogenesis; Director Mr Jean de GUNZBURG). One of the goals of this fusion was to associate groups developing complementary research lines on molecular bases of human cancers and on animal modeling of oncogenic processes. At its creation, the U830 was composed of 6 independent teams and was directed by Mr Olivier DELATTRE. Mr Alain AURIAS who was the Head of the group working on adult sarcomas retired in 2010. Ms Françoise MOREAU-GACHELIN who heads the team "Leukemogenesis and spi transcription factors" will also retire in 2013. Thus, among the 6 pioneer groups of the U830, four apply to the renewal application of this Unit, ie :

Team1 : "Genetics and biology of paediatric cancers" (Dir : Mr Olivier DELATTRE)

Team2 : "Analysis of transduction signals" (Dir : Mr Jacques CAMONIS)

Team 3: "Stress and cancer" (Dir. Ms Fatima MECHTA-GRIGORIOU)

Team 4: "Genetics and biology of hereditary breast cancers" (Dir: Mr Marc-Henri STERN)

An International call to recruit a junior group leader was launched in 2010. However, the two candidates that were selected out of 60 applicants did not join the U830 eventually. Since the teams of the U830 have to face a laboratory space constraint, especially Teams 3 and 4, it has been decided to postpone a new call for a junior position. Indeed, the U830 is distributed on 3 floors and approximately 900 m² are available for more than 70 persons working in this Unit. Since 3 clinicians working in the U830 on a "Contrat d'Interface Inserm" should join the "Translational Department" of Institut Curie, it is expected that more space lab will be available in 2013. In this context, 2 clinicians, currently working in the U830 have been selected to create a "translational" group in the frame of the recently created SIRIC (Sites de Recherche Intégrée sur le Cancer de l'Institut Curie directed by Mr Olivier DELATTRE). Therefore, these 2 clinicians will move their research activities to the Hospital part of the Institute. Thus, in its new configuration, the U830 will be composed of the 4 groups aforementioned to which a new team headed by a junior group leader, who has yet to be hired, will be associated during this five-year contract.

Before coming into the details of the evaluation, the Committee emphasizes that this report is strictly focused on the U830 teams that apply for the contract renewal. However, the Committee members wish to express their collective esteem to the the researchers who left the U830 for their scientific achievement. Their dedication and remarkable contributions to the biomedical research shall be praised.

Management team

The current Director is Mr Olivier DELATTRE (DRCE, Inserm) and he will be renewed in his functions for this 5-year Contract. The former Deputy Director was Ms Françoise MOREAU-GACHELIN and she will be replaced at this position by Ms Fatima MECHTA-GRIGORIOU. A steering committee composed of the group leaders meets once a month to discuss administrative, organizational and scientific topics. In addition, a "Unit Committee" shall meet once a year and includes group leaders, representatives of staff scientists, students, technician and administrative personals. All collective issues regarding the organization of the Unit (collective tasks, responsibility for equipments...) are discussed during this Committee. In addition, scientific meetings to which all the U 830 members are invited to attend are organized once a week. Finally, two agents in charge of the Health and Security issues have been nominated and work on the 3rd and 6th floor of the building hosting the Unit. The budget policy of the Unit was not explicitly described in the application.

AERES nomenclature

SVE1 LS2, LS4, LS7



Unit workforce

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	5 (3 at 50%; 2 at 30%)	4 (2 at 50%; 2 at 30%)	4
N2: Permanent researchers from Institutions and similar positions	6	6	6
N3: Other permanent staff (without research duties)	11	11	11
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)			
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	22	21	21

Percentage of producers	100,00%
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Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	11	6
Theses defended	16	8
Postdoctoral students having spent at least 12 months in the unit*	7	4
Number of Research Supervisor Qualifications (HDR) taken	6	7
Qualified research supervisors (with an HDR) or similar positions	6	7



2 • Assessment of the unit

Strengths and opportunities

1. The overall quality of the scientific production of the U830 is first-rate and the contribution of the teams to the various topics studied is nationally and internationally renowned.
2. Most of the scientific projects are well-thought, address cutting-edge questions, are based on skilful groups and supervised by group leaders with a recognized leadership.
3. Opportune collaborations between groups of the U830 that have led to the development of two transversal research programs.
4. Excellent interactions of the U830 teams with the clinicians of the Institut Curie allowing the organisation of collaborative projects and programs that create the conditions of a strong synergy.
5. Competitiveness in funds raising at a national level, but also at an International level (participations of several teams of the U830 to 6 EC programs).
6. Outstanding platforms at the Institut Curie (imaging, functional genomics, animal facilities...) are made available to the members of the U830. In addition, one of the lab scientists is at the initiative with a colleague at the Institut Curie of the creation of BioPhenics, a cell-based high throughput screening platform.
7. The U830 teams will have access to the Next-Generation Sequencing (NGS) tools with the creation of the Equipex ICGex (Equipement de biologie intégrative du cancer pour une médecine personnalisée), a program coordinated by Mr Olivier DELATTRE.

Weaknesses and threats

1. The groups are heterogeneous in terms of structure, and in most cases (besides the case of Team 1), are not balanced between scientists with permanent positions (CD, DR and professor-researchers (MCU, PR, MCU-PH, PU-PH) and ITA, post-docs and students. In this respect, Fatima Mechta-Grigoriou's support to the application at CNRS/Inserm of a post-doc from Team3 who has been granted an "ANR jeune chercheur" goes in the right direction.
2. The visiting Committee noticed the underrepresentation of professor-researchers of Paris 5 University in the U830 that should be improved.
3. As already underscored, the U830 is confronted to a limitation of lab space that restricts the capacity to attract new groups and hampers the reinforcement of the U830 scientific dynamics.
4. The high-throughput technologies and genome scale analyses require the recruitment of bioinformaticians to treat large volume of data. Bioinformatics has become a stumbling block for all laboratories working in the "omics" field. The director and group leaders of the U830 have clearly stated that the full development of their research programs relies on the hiring of scientists with this kind of expertise.
5. The management procedures in the Unit should be optimized. Discussions of the visiting committee with members of the personal have revealed that the information related to the scientific strategy of the unit and on other questions that directly concern the daily work of the personal is not always shared.



Recommendations

The Committee has been impressed by the overall quality of the U830 teams which have demonstrated their scientific proficiencies during the former contract. However, considering the excellent reputation of the U830 as well as the privileged scientific surrounding of this Unit (nearby Units at Institut Curie and on the site of La Montagne Sainte-Geneviève), the Committee considers that the U830 did not harness on these assets to recruit scientists with permanent positions (CR/DR positions or MCU/PR) or new group leaders. This constatation is the basis of the major recommendations of the Committee detailed below.

Accordingly, the Committee supports the attempt to recruit a junior group leader. Even if the strategy to limit the coming of a novel group for space constraints reasons is wise in a medium-term (a situation that should be clarified during the course of 2013), the Unit should take advantage of its attractiveness to hire a new group leader as it was initiated but discontinued.

During the on-site visit, the Committee has been informed by the Director of the Research at the Institut Curie and by the representative of Paris 5 of their policy regarding their institutional association, especially in the frame of the former and future 5-year contract of the U830. However, the Committee felt that, whatever the historical conditions of this partnership are, they should not prejudice the group leaders of the U830 in their effort to recruit professors nor refrain their involvement in teaching activities at Paris 5. Strengthening the bonds between the U830 and Paris 5 is advocated by the Committee members and would create opportunities for positions to inside or outside post-docs as it would contribute to the stabilization of the existing groups.

The recognition of the U830 as well as the possibility to apply for fellowships at the Institut Curie (or french agencies/charities) should create incentive conditions to attract post-docs with a very good track record that would be eligible for a CR position.

The Committee has appreciated the synergies between groups of the U830 that have led to the setting up of transversal projects. The Committee strongly encourages the director to foster these initiatives and group leaders/scientists with permanent positions to go further in that direction that is a valuable catalyzer of the unit dynamics.

An effort shall be made to improve the sharing of information between the "steering committee" and the rest of the unit. Following this line of thinking, the gathering of the "Unit Committee" once a year is a too infrequent periodicity and should be call to meet at least twice a year.



3 • Detailed assessments

Assessment of scientific quality and outputs

The U830 covers several fields of research in oncology, namely the study of the genetic and biological bases of pediatric cancers, as well as inherited breast and ovarian tumors. In addition, both the signalling networks involving the Ras small G proteins and the contribution of the chronic oxidative stress to the transformation processes are the focus of the U830 scientific projects. If we consider that these topics are the subject of an intense competition at an international level, it is truly remarkable that the 4 teams were all successful in their undertakings, producing original data and making several seminal discoveries that were published in the top journals in biology. During the past 5 years, members of the U830 have published 276 articles (this number is the summation of papers in which the U830 investigators are the main contributors as well as associated papers); forty of these articles have an impact factor superior to 10. If the main publications of the group are referenced, Team 1 has published 28 articles including papers in Cancer Cell, Nature, Nature Genetics, J Clin Oncol, Cancer Res, Oncogene; Team 2 has published 5 articles including Mol Cell, Plos Biol, EMBO J; Team 3 has published 3 papers in Cell Metabolism, EMBO Mol Medicine, Nature Medicine; Team 4 has published 18 articles including Blood, Cancer Res, J Clin Oncol.

Assessment of the unit's academic reputation and appeal

During the 5-year contract, team leaders of the U830 and other members of the teams attended national and international conferences as invited speaker : Team 1 : 80 invitations to give seminars in France and abroad; Team 2: 4; Team 3 : 19; Team 4 : 23. All team leaders review articles for scientific journals including Nature, Cell, Cancer Cell, New England Journal of Medicine, Am J Hum Genet... They also participate to the scientific committees of french and foreigner agencies/charities (ARC, Ligue Nationale Contre le Cancer, ANR, FRM, AICR,...) but also to the scientific councils of several Centres/Institutes (Fondation Jean Dausset, Centre Léon Bérard, Institut Paoli-Calmettes, board Oncogénétique de l'INCa...). Mr Olivier DELATTRE is the director of the SIRIC, the Coordinator of the ICGex program and he is also involved in the development of the Translation Research Department at the Institut Curie.

Heads of the groups and staff members of the groups are regularly invited to give seminars at national/international conferences (>130 invitations all unit members included during the 5-year contract) and they participate also to international consortia (6 EC programs associate U830 teams), coordinate several national research programs (INCa, INCa-DHOS, ANR, 2 Programmes Incitatifs et Collaboratifs (PIC) and are involved in the Cancéropôle Ile-de-France. All team leaders as well as members of these groups have received prizes and distinctions (Académie des Sciences; Académie de Médecine, Simone and Cino del Duca Prize, Prix du Ruban Rose, Eurocancer, Grand Prix Charles Oberling) that attest of the recognition by the national/international communities of the scientific reputation of the U830. Moreover, several members of this Unit have been involved in the organization of scientific meetings : International Course on breast cancers, Institut Curie, 2011; annual breast cancer day by Institut Curie, 2011, Colloque "Petites protéines G", Mouans-Satoux, 2008; co-organisation of regular meetings on "Dynamique, Instabilité Génétique et Oncogénèse; organization in 2012 of 3 gatherings of International Consortia on the genetics of breast cancer. Finally, another indicator of the U830 appeal is the recruitment of post-docs and according to this criteria the U830 is well-positioned since 21 post-docs joined the Unit during this contract.

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

Several members of the Unit gave interviews to the french television (TF1, France 3) as well as to local channels, videos and news papers. Four patents have been filed during the 5-year contract.



Assessment of the unit's organisation and life

Mr Olivier DELATTRE is highly experienced in the direction of a laboratory, has a charismatic leadership and has made several breakthroughs in the genetic bases of pediatric cancers. Furthermore, being both a MD and a PhD, he is highly committed in the structuration of biomedical programs.

The organization of the unit is based on independent groups, each headed by a team leader. The decision-making body is the steering Committee that includes the Director, the Deputy-Director and the group leaders that gather once a month. A "Unit Committee" meets once a year and includes group leaders, representatives of staff scientists, students and ITA personals. All collective issues regarding the organization of the Unit (collective tasks, responsibility for equipments...) are discussed during this Unit Committee. Scientific meetings are also organized once a week and all members of the U830 are invited to attend these seminars.

During the encounter of the Committee with staff scientists, ITA and post-doc/students, the comments expressed on the conditions of work and on the scientific life were generally positive. However, as already emphasized in this report, the researchers felt that several important decisions that directly impact on the functioning of the Unit and consequently on the organization of the work were not adequately shared between the steering committee and the personal of the Unit. Thus, an effort should be made to rationalize the transmission of the information within the U830 and the Committee proposes that the Unit Committee meets more frequently. Alternative like a written report following each steering committee that would be addressed to the whole Unit should be thought after.

Finally, the emergence of young investigators towards leadership (autonomous demands of funding, tutoring of students, co-authorship policy with the articles) is promoted in the U830, a fact confirmed by their independent oral presentations during the on-site visit.

Assessment of the unit's involvement in training through research

22 PhD students successfully defended their thesis during the 5-year contract which is an indicator of the good quality of the tutoring of the students in the U830, especially if we consider that 9 scientists of the Unit have their HDR (3 members of the U830 obtained their HDR during this 5-year contract). Furthermore, the majority of the students published from 1 to 35 publications during their thesis. In addition, 16 M1 and 22 M2 students did their training period during this contract and 11 students (Ecole d'Ingénieur, others...) worked also in the Unit during these 5 years. The majority of the U830 staff scientists are also involved in teaching activities in Masters : Master Paris 6 (Biologie Moléculaire et Cellulaire), Master Cancérologie Paris XI...

Assessment of the five-year plan and strategy

The director and the steering committee have decided to discontinue the projects focused on adult sarcomas and leukemogenesis because of the retirement of both involved team leaders. The rationale of this decision is to use the lab space available to favor the extension of two existing groups (Teams 3 and 4) and to recruit a junior group leader. In addition, two clinicians who presently work in Team 1, will constitute an independent translational research group in the frame of the recently created SIRIC. These choices concerning the future composition of the U830 are sound and received full support from the Committee as expressed in the Recommendations.



Furthermore, two translational projects internal to the U830 have been established between Team 3 and both Team 2 (autophagy) and Team 4 (stress, genetic instability and cancer). Also, the scientific activity of Team 1 will be refocused on the study of the genetic and biological bases of pediatric tumors and the program on sporadic breast tumors will be terminated. Similarly, the research of Team 4 will be dedicated to hereditary breast cancers and the program on T-cell prolymphocytic leukemia will be wound up. Finally, Team 2 will pursue his line of research on the role of Ral GTPases in oncogenesis while Team 3 will continue the project on the relations between stress and cancer development but with a marked orientation on the study of tumor microenvironment and ovarian neoplasia. Overall, the Committee found that these five-year plans are well-founded, consistent with the expertise of the Unit and are expected to reinforce the innovative contribution of the U830 to basic research but also to the translation of scientific findings into the clinics. In this respect, The U830 is at a favourable position to succeed in its endeavour due to the scientific skills of the teams but also because of the propitious location of the Unit that has access to collaborative clinical departments of the Institut Curie as well as to state-of-the art genomic tools. However, even if this evaluation is globally very positive, the Committee would like to draw the attention of the Director and the group leaders to circumscribed concerns on strategical choices that are detailed in the evaluation Team by Team and ought to be addressed.



4 • Team-by-team analysis

Team 1 : Genetics and biology of paediatric cancers

Name of team leader: Mr Olivier DELATTRE

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	3	2	2
N2: Permanent EPST or EPIC researchers and similar positions	3	3	3
N3: Other permanent staff (without research duties)	5	5	5
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	11	10	10

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	5	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	2	3



• Detailed assessments

Assessment of scientific quality and outputs

The team directed by Mr Olivier DELATTRE is composed of 27 members including 11 with a permanent position. The research of the team is mainly focused on the genetic determinism and biology of Ewing sarcoma, rhabdoid tumours and neuroblastoma. Within these fields, the team has yielded, over the last years, seminal contributions such as (i) the identification of the origin of the Ewing cells corresponding to mesenchymal stem or progenitor cells; (ii) the characterization of the genetic risk factors associated to Ewing sarcoma in population from European origin; (iii) the identification of somatic and germline mutations of the *ALK* gene in neuroblastoma. The scientific importance of these contributions is highlighted by publications in the top journals such as 2 articles in *Cancer Cell*, 2 in *Nature Genetics*, 1 in *Nature plus* 7 articles in high impact factor journals, such as *Journal of Clinical Oncology*, *Cancer Research* and *Clinical Cancer Research*.

Assessment of the unit's academic reputation and appeal

The team has an established international reputation in the field. Mr Olivier DELATTRE is considered as an international expert in Ewing sarcoma, rhabdoid tumours and neuroblastoma. This reputation is illustrated by his active participation to numerous international scientific committees and reviewing for very high impact journals, such as *Nature* or *Cell*. The attractiveness of the team is also illustrated by the regular recruitment of post-docs, invitations to international meetings and its active participation to 6 European projects.

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

Mr Olivier DELATTRE is strongly involved in several national scientific committees of national institutions such as INCA, Inserm, ANR or of French Comprehensive Cancer Centres which, therefore, benefit from his scientific inputs. The link of the Unit with the translational department of Institut Curie allows a transfer of basic knowledge to the clinics. Mr Olivier DELATTRE played a key role in the success of Institut Curie in national funds raising (Equipex, SIRIC).

Assessment of the unit's organisation and life

The scientific and personal leadership of the team leader was unanimously recognized by all of his team.

Assessment of the unit's involvement in training through research

The team has a sustained activity in the training through research: the team has trained 10 master students and 11 PhD.

Assessment of the five-year plan and strategy

The team will focus its projects on pediatric tumours, Ewing sarcoma, rhabdoid tumours and neuroblastoma in the continuation of the previous work, by combining high throughput genetic analyses to characterize network deregulated in these tumours and functional studies based on cellular and genetically modified mice. The project is solid, will benefit from the high quality technological platforms in Institut Curie and international collaborations.



Conclusion

- Strengths and opportunities:

- Scientific excellence,
- International reputation,
- International expertise,
- Permanent success in national and European French raisings.

- Weaknesses and threats:

- The limited number of researchers with permanent positions considering the number of topics,
- The difficulty to offer permanent positions to young scientists due in part to the limited space in Institut Curie,
- The difficulty to recruit permanent highly qualified bioinformaticians whose expertise will be critical for the success of the scientific projects.

- Recommendations:

- Recruitment of scientists with permanent positions,
- Maintenance of tight links with clinicians in order to maintain the quality of patient recruitment, the possibility to perform efficient pre-clinical investigations and to ensure an efficient transfer of the knowledge for the patient benefit. The position of the “translational research group” and its connection with the unit and the translational department of Curie should be clarified,
- Considering the excellence of the group, the bonds with the university should be strengthened.



Team 2 : Analysis of Signal Transduction

Name of team leader: Mr Jacques CAMONIS

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	3	3	3
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	4	4	4

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	1	1



• Detailed assessments

Assessment of scientific quality and outputs

The group has gained a strong international reputation on the decipherment of Ras-like signaling pathways, mainly using biochemical tools for the detection of protein interaction and by using the drosophila model for functional studies. Considering its small task-force [8 people : 2 PhD students, 2 post-docs, 3 technicians], the group has demonstrated a very good level of scientific production: 21 research articles published between 2008 and 2012, many of which in rank A journals [J. Cell Biol.; Mol. Cell; Cell; Cell Reports; Nature Methods; PLoS Biol.; EMBO J.]. The committee has unanimously acknowledged the high scientific quality of this team.

Assessment of the unit's academic reputation and appeal

The group is internationally recognized in the Ras field. Group members have been invited to national and international meetings. The group leader participates to the scientific committee of the ANR Biotechnologies agency and co-heads the Biophenics platform at the Curie Institute. The group has been well funded for the considered period as it has obtained regularly major national research grants and salaries from governmental agencies and from charities. However, there is no funding granted beyond 2013, and the group suffers from a deficit of experienced researchers with a permanent position.

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

As a founder member and scientific expert, the group leader has greatly contributed to the success of the biotech Hybrigenics.

Assessment of the unit's organisation and life

The group is highly involved in helping the career development of students and post-docs. Two post-docs have got permanent positions as assistant professors in France and Portugal.

Assessment of the unit's involvement in training through research

The group has housed 9 trainees, 7 PhD students and 5 post-docs since 2007. The group leader gives courses at the M2 level.

Assessment of the five-year plan and strategy

In the next years, the group leader wants:

- to deepen the analysis of Ral activity, in particular in the Hippo pathway, in cell migration and in autophagy, and besides,
- to develop further the high-throughput Biophenics platform towards automatic detection and measurements of phenotypic changes associated with si-RNA or drug treatment. The latter project is of high importance for the scientific community of the Curie Institute and beyond.

Although the projects proposed are in the field of expertise of the group, the committee expressed some concerns about the adequation between the number of projects and the team task-force. Also, the identification of the goals that are going to be investigated during this new contract were not always completely convincing. Thus, there is a clear need in the nearest future to identify the major scientific aims, to prioritize the defined projects and to stabilize the group with the recruitment of scientists with permanent positions.



Conclusion

- Strengths and opportunities:

The team is led by a very dynamic PI who has gained an international reputation on protein interaction and developed many long-term and fruitful collaborations. The PI also co-heads an efficient Automated Cell-based High Throughput Screening Platform (Biophenics).

- Weaknesses and threats:

The team has been funded by many contracts (as coordinator ANR, ARC, PIC, foundation de France and INCa and as partner PIC), most of which will stop in 2012. This may be a concern although the high quality of the scientific production should warrant funding for the next years.

Several postdoctorants got permanent positions elsewhere and have thus left the lab. Together with the departure of the scientists in charge of analysis of Ral signaling in *Drosophila*, this may be a threat for the stability of the team and the success of the proposed projects.

- Recommendations:

The group should adapt its projects to the size of its task force.

The recruitment of a permanent researcher would improve stability of the group.



Team 3 : Stress and cancer

Name of team leader: Ms Fatima MECHTA-GRIGORIOU

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	2	2	2

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	1	1



• Detailed assessments

Assessment of scientific quality and outputs

The team has been created in 2006 following obtaining an Avenir grant by the group leader. Until recently, Team 3 remained a small group of 4-5 people. New space has recently been dedicated to this group, allowing it to increase its size to 8-10 people. The group studies the pathophysiological consequences of chronic oxidative stress. Despite its small size, the group made very significant discoveries and, consequently, achieved an excellent publication record, with regular own publications in excellent journals such as Cell Metabolism, Nature Medicine and EMBO Molecular Medicine, as well as a number of collaborative publications. The committee has unanimously recognized both the quality and interest of the work produced.

Assessment of the unit's academic reputation and appeal

The group is clearly among the national leaders in its field, and has gained a very strong international reputation. The group leader is regularly invited to national and international meetings. She participates in several french scientific committees, both from governmental agencies (INSERM or CNRS committees) and from charities (ARC). A few students from the group obtained national prizes. The group is well funded and obtained regularly major national grants from governmental agencies and from charities. As a weakness, it has to be noted that the group did not attract experienced researchers with a permanent position from a french governmental agency.

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

The group leader has been involved in many events linked to scientific popularization and diffusion to a general audience. The group leader obtained an incitative grant from the Curie Institute, together with a Physicist, to develop a common facility to perform a deep analysis of the tumour microenvironment. There are discussions going on with private companies to secure this facility at the end of the 3 years of funding. The group has filled one patent.

Assessment of the unit's organisation and life

This is clearly a major strength of the group. The group leader is highly involved in helping the career development of students and post-docs working with her. Of note, most of the PhD students and post-docs obtained a high-impact first author publication from their work in the group. The scientific and personal leadership of the head of the group was praised by all members of her group.

Assessment of the unit's involvement in training through research

The group has recruited 4 M2 students, 4 PhD students and 4 post-docs since 2007. Most of the PhD students and post-docs obtained a high-impact first author publication from their work in the group. The group leader has been in charge of an european course on Breast Cancer. She gives courses at the M2 level (about 4 hours per year). Other members of the group, including PhD students and post-docs also participate in M1 courses (2 for 5hours/year), and 1 is "moniteur" at the L2 level.



Assessment of the five-year plan and strategy

In the next few years, the group leader wants to develop her activity in two main directions: firstly, she intends to pursue along the lines opened by her recent publication on the two types of ovarian cancer (the “oxidative stress” and the “fibrosis” types), developing fundamental studies to better understand the differences between these two types of ovarian tumours (through global proteomic or metabolomic analyses, but also through studies on selected proteins (MAP3K8) or at the biology/Physics interface on the role of mechanical constraints). The team leader also plans to develop applied research dedicated to the development of drugs or pronostic tools specific to patients with an ovarian cancer with a “fibrosis” or “oxidative stress” profiles. Secondly, she wants to go on working in the field for which the research group has a proven strong expertise, which is the mechanisms of oxidative stress regulation and how it is linked to tumor outgrowth.

There is no doubt that the questions the group leader wants to tackle down are relevant oncological questions. The second part of the project on oxidative stress corresponds to the group proven expertise and will undoubtedly lead to major findings. In addition, the orientation to applied research is well thought, valuable and received full support by the Committee. However, while the Committee has been convinced by the global phenotypic approaches previously used by the group to discriminate between “fibrosis” and “oxidative stress” ovarian tumours, including proteomic and metabolomic approaches, there were concerns about the benefit for the group to come back to classical “gene-based” strategies relying on individual markers (such as MAP3K8) of ovarian cancers. Moreover, the committee was unsettled by wide spectrum of proposed projects (although all very interesting and well-thought), stressing a need to prioritize the projects in the near future.

In summary, the project proposed by this group is of very good quality, imaginative and deserves to be supported.

Conclusion:

- Strengths and opportunities:

- The expertise and track record of the group in their research field,
- The ability to perform imaginative research,
- The quality and originality of the various research projects,
- The opportunities provided by the Curie Institute environment both for fundamental and applied research,
- The qualities of the collaborations set up by the group both at the Department, at the Curie Institute or outside.

- Weaknesses and threats:

- The lack of researchers on permanent positions in the group,
- The small size of the group to be competitive on many different research projects.

- Recommendations:

- The research plan would benefit from prioritization of the various projects,
- The recruitment of a permanent researcher from the CNRS or the Inserm would improve the group efficiency.



Team 4 : Genetics and biology of hereditary breast cancers

Name of team leader: Mr Marc-Henri STERN

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	2	2	2
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	2	2	2
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	5	5	5

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	2	2



• Detailed assessments

Assessment of scientific quality and outputs

The team of Mr Marc-Henri STERN has a staff of 10-14 people, with 5 with a permanent position. Team 4 studies inherited breast cancer. More particularly, this team has characterized a consistent series of BRCA breast cancers by using pre-NGS genomic analyses and established a new BRCA-associated parameter of genome status called Large Scale Transitions, which could be used in clinics to identify familial cases to sequence further and perhaps could predict therapeutic response to PARP inhibitors and platinum salts. They have recently identified other BRCA genes by NGS strategies in non-BRCA1/2 patients. Another research project is focused on oxidative stress and DNA repair: mostly focused on ATM role in both processes (although the strategy is not clearly explained, the in-unit collaboration with team 3 will be of great help). Altogether, this research permits this team to publish their data in good quality journals such as Cancer Research, Blood, JCO, Human Mutation... The field is challenging and competitive and the team is doing well. The scientific outputs are excellent given the fact that the team has been working “full speed” on breast cancer only recently.

The committee has unanimously praised both the quality and interest of this team, more particularly the very high potency of translational research.

Assessment of the unit's academic reputation and appeal

The team is clearly among the national leaders in the field of inherited breast cancer. International scientific reputation is very good for MH Stern, excellent for another team member. The team has attractiveness due to the Curie Institute and scientific environment. Members of the team have interesting collaborations (i.e. Reis-Filho's NGS study published in J Pathol 2012), they are regularly invited to national and international meetings and are members of french scientific committees, both from INSERM and from charities (Ligue contre le Cancer, ARC...). The team is relatively well funded, for example from ARC (fixe) or INCa (translationnel). Similarly to other teams of this research unit (besides Team1), this group has not yet attracted experienced researchers or recruited young scientists with a permanent position from a french governmental agency or from the University.

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

The team has deposited a European Patent on “the methods for detecting inactivation of the homologous recombination pathway (BRCA1/2) in human tumors.

Assessment of the unit's organisation and life

The team leader is highly involved in helping the career development of students and post-docs working with him : the PhD students obtained a high-impact first author publication (Cancer Res, Blood...) for their work in the team. The scientific and personal leadership of the team leader was unanimously praised by all members of his team. However, due to the underrepresentation of senior scientists in his team, the team leader is alone to train and supervise students and post-docs.

Assessment of the unit's involvement in training through research

The group has housed 13 Master students (6 M2) and 5 PhD students (2 in process) since 2007. The committee has praised that most of the PhD students and post-docs obtained a high-impact first author publication for their work in the team. The members of this team are highly involved in L1 (Pharmacy), M1, M2, DIU and DU (Medicine) courses.



Assessment of the five-year plan and strategy

In the next years, the team leader wants to pursue his activity on the molecular and cellular characterization of hereditary breast cancers. He also wants to pursue the research project on the oxidative stress and DNA repair; mostly focused on ATM role in both processes. A program on uveal melanoma could lead to interesting developments.

The projects are adapted to the team task-force, they are highly translational due to interaction with the Curie Institute and the presence of diagnostic laboratories dedicated to breast cancer. The “niche” of hereditary breast cancer remains to be explored and the team has good projects.

In-unit collaborations can be easily developed (i.e. with Team 3 on DNA repair or oxidative stress, and with Team 2 platforms).

In this rapidly moving field, designing plans for 5 years would be inconsiderate. The committee trusts MH Stern to steer his lab in original scientific zones and to make innovative contributions to this field of research.

Conclusion

● Strengths and opportunities:

- Expertise in hereditary BC at the Curie institute and from internationally-renowned members of the team,
- Intelligent proposals and leadership,
- Vicinity of platforms (bioinformatics, NGS, pathology expertise, SIRIC's NGS),
- Well-defined cohorts of patients and controls (Enigma),
- Network (ICGC, French),
- In-unit collaboration with team 3,
- Clear translation strategy (new score, new techniques...),
- Curie success in funds raising (equipex, SIRIC...).

● Weaknesses and threats:

- BRCAness and non-BRCA1/2 BC are extremely competitive field. They will succeed by focusing on niches, as they have been cleverly doing so far, but fail if doing what everybody else is doing,
- Small team with two main areas : descriptive/genomic and functional. The latter may be harder to translate into forefront studies,
- Passage to NGS to manage,
- Additional permanent scientist would help developing the proposed project. A real strategy of CR/MCF recruitment should be proposed.

● Recommendations:

- The recruitment of a permanent researcher from the CNRS or the Inserm would improve the group efficiency,
- Consolidating functional analyses may help in the future.



5 • Conduct of the visit

Visit dates:

Start: Wednesday, January 15th 2013, at 1:30 PM

End: Thursday, January 16th 2013, at 6 PM

Specific premises visited: INSERM U830, Institut Curie, Paris

Conduct or programme of visit:

Wednesday, January 15th 2013

13:30	Welcome (closed-door) Visiting committee with the AERES Scientific advisor
13:45	AERES representative: the role and procedures of AERES
14:00	Director of the Unit (30' presentation, 30' discussion) : Presentation of the past activities and project
15:00	Coffee break
15:15	Team 1 - Mr Jacques CAMONIS (30' Talk + 30' discussion, including 5' only with the team leader)
16:15	Team 2 - Mr Olivier DELATTRE (40' Talk + 35' discussion, including 5' only with the team leader)
17:30	Debriefing on the team presentations

Thursday, January 16th 2013

8:30	Team 3- Ms Fatima MECHTA-GRIGORIOU (30' Talk + 30' discussion, including 5' only with the team leader)
9:30	Team 4 - Mr Marc-Henri STERN (30' Talk + 30' discussion, including 5' only with the team leader)
10:30	<i>Coffee break</i>
11:00-12:00	Parallel meetings with personnel: Discussions with engineers, technicians, administrative Discussions with staff scientists Discussions with students and post-docs
12:00	Lunch
14:00	Discussion with the representatives of the Institut Curie and Université Paris Descartes
14:45	Discussion with the head of the Unit (if necessary)
15:15	Private meeting of the visiting committee (in presence of the AERES scientific advisor)
18:00	End of the visit



6 • Statistics by field: SVE on 10/06/2013

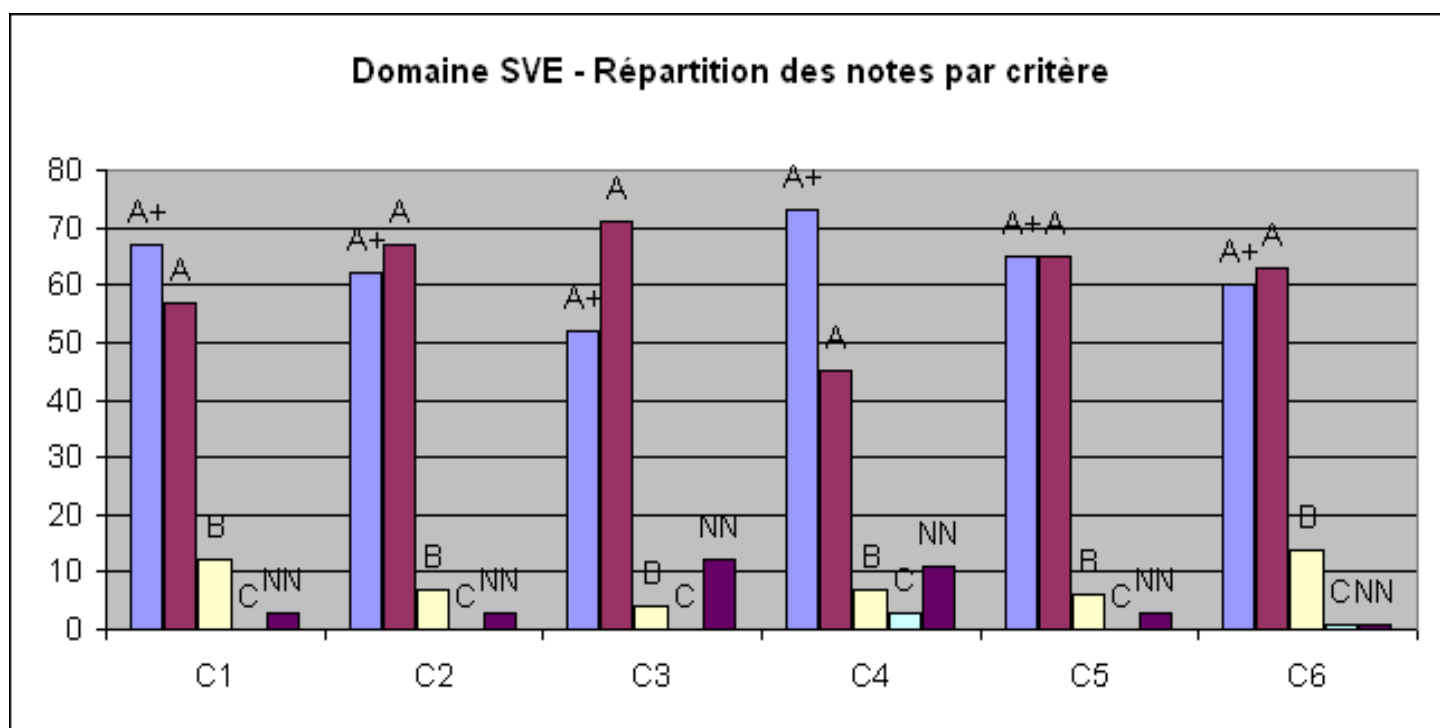
Grades

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	67	62	52	73	65	60
A	57	67	71	45	65	63
B	12	7	4	7	6	14
C	0	0	0	3	0	1
Non Noté	3	3	12	11	3	1

Percentages

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	48%	45%	37%	53%	47%	43%
A	41%	48%	51%	32%	47%	45%
B	9%	5%	3%	5%	4%	10%
C	0%	0%	0%	2%	0%	1%
Non Noté	2%	2%	9%	8%	2%	1%

Histogram





7 • Supervising bodies' general comments

A E R E S
Section des Unités
20, rue Vivienne
75002 PARIS

Paris, le 17 avril 2013

Concerne : Rapport : S2PUR140006114 - Génétique et Biologie des Cancers - 0753172R
Unité IC/CNRS UMR3244/UPMC : Directeur : Olivier Delattre

Chers Collègues,

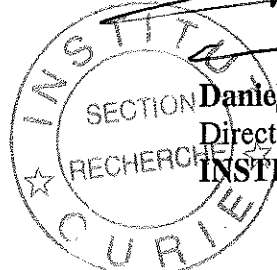
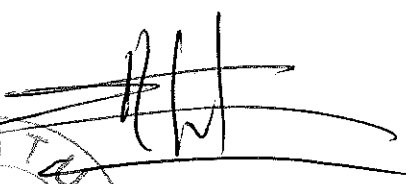
En tant qu'organisme hébergeur et déposant unique des rapports des unités de recherche du site de Paris de l'Institut Curie – Vague D, je vous informe avoir bien reçu en date du 2 Avril dernier, le rapport d'évaluation de l'AERES sur l'unité IC/CNRS INSERM U830.

J'ai lu ce document avec attention et vous informe qu'il ne suscite de ma part aucune remarque ni commentaire. Je tiens à saluer le travail réalisé par les experts.

Afin d'assurer le succès continu de cette unité, j'ai bien noté les recommandations du comité pour appuyer ce plan en tenant compte de l'évolution de cette unité et tous les efforts seront faits en coordination avec les tutelles : l'Institut Curie et l'INSERM et notre partenaire l'Université Paris Descartes (Paris 5) pour assurer les soutiens nécessaires.

Je tiens à exprimer tous mes remerciements aux membres du comité d'évaluation pour leurs commentaires et recommandations très pertinents qui sont basés sur un travail d'analyse approfondie. Je remercie également l'équipe de l'AERES qui a soutenu la mise en oeuvre de l'ensemble de cette évaluation.

Je vous prie d'accepter, Chers Collègues, mes plus cordiales salutations.



Daniel LOUVARD
Directeur de la Section de Recherche
INSTITUT CURIE