SNIC - Signalisation, noyaux et innovations en cancérologie

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on research units and interdisciplinary research units:

Signaling, Nuclei and Innovations in Oncology

Under the supervision of the following institutions and research bodies:

Université Paris-Sud

Centre National de la Recherche Scientifique - CNRS

November 2013

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

Department for the evaluation of research units

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

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

On behalf of the expert committee,

- Mr. Henri-Jacques DELECLUSE, chair of the committee

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

Evaluation report

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

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

Unit name:	Signaling, Nuclei and Innovations in Oncology
Unit acronym:	
Label requested:	UMR
Present no.:	UMR 8126
Name of Director (2013-2014):	Ms Joëlle WIELS
Name of Project Leader (2015-2019):	Ms Joëlle WIELS

Expert committee members

Chair:

Mr Henri-Jacques DELECLUSE, German Cancer Research Center (DKFZ), Heidelberg, Germany

Experts:

Mr Vincenzo CONSTANZO, Italian Foundation for Cancer Research Institute of Molecular Oncology (IFOM), Italy

Mr Paul FARRELL, Imperial College London, United Kingdom

Mr Hinrich GRONEMEYER, Institut de Génétique et de Biologie Moléculaire et Cellulairen (IGBMC), Strasbourg (representative of CoNRS)

Mr Christoph ROESLI, German Cancer Research Center (DKFZ), Heidelberg, Germany

Ms Tatjana STANKOVIC, University of Birmingham, United Kingdom

Mr André VERDEL, Université Joseph Fourier, Grenoble

Scientific delegate representing the AERES:

Mr Daniel OLIVE

Representatives of the unit's supervising institutions and bodies:

Mr Étienne AUGE, Université Paris-Sud

Mr François DAUTRY (representative of PhD Program Oncology Paris-Sud University, École Doctorale n°418)

Mr Alain EYCHÈNE (representative of CNRS)

1 • Introduction

History and geographical location of the unit

The UMR 8126 was created in 2010 on the basis of the unit 'Molecular interactions and Cancer' (UMR 8126 2006-2009). The new structure consisted of the staff present in the initial structure and of Ms Svetlana DOKUDOVSKAYA who joined the unit in 2010. The unit was reorganized into 3 teams, the first of which comprises four groups, to foster more scientific interactions between the investigators. The unit UMR 8126 currently comprises 13 researchers, 9 technicians or engineers (ITA), 5 post-doctoral fellows and 14 PhD students. Among the 14 staff scientists, 6 are "directeurs de recherche" (five employed by CNRS, one by Inserm), 3 are "chargés de recherche" (all at CNRS), one is "Maître de Conférence-Praticien Hospitalier" (MCU-PH) and 3 are "Emeritus". A young scientist has just been recruited by INSERM as "chargée de recherche". Among the 9 technicians and engineers, 6 were already working in the unit in 2008, a further 3 have been recruited by CNRS during the current contract.

The applicants now wish to simplify this structure of the unit in the next funding period by creating the following 6 autonomous teams:

- team 1 "Intracellular traffic, macromolecular complexes and cancer" (Ms Svetlana DOKUDOVSKAYA);

- team 2 "Proteomics and Epigenetics" (Mr Vasily OGRYZKO);

- team 3 "Nuclear organization and pathological models" (Mr Yegor VASSETZKY and Mr Marc LIPINSKI);

- team 4 "Oncogenesis and resistance to apoptosis in B cell lymphomas" (Ms Joëlle WIELS);

- team 5 "Genome maintenance and molecular microscopies" (Mr Éric LE CAM);

- team 6 "Tumor microenvironnement, exosomes and microRNAs in solid tumors" (Mr Pierre BUSSON).

The unit is hosted in the first and third floor of the Institut Gusatve Roussy (IGR) in Villejuif. The available space appears to be commensurate to the size of the unit.

Management team

The current director is Ms Joëlle WIELS, who wishes to be prolonged in her functions in case of renewal. Mr Marc LIPINSKI is acting as deputy director and also wishes to retain these functions in the future. Ms Joëlle WIELS and Mr Marc LIPINSKI respectively served as deputy director and director in the UMR 8126 between 2006 and 2009. This ensures continuity in the team management and stability within the research unit. A general assembly, to which all members of scientific, technical and administrative staff are invited, takes place every 3 months basis and addresses the general organization and micromanagement of the laboratory, as well as the needs for new pieces of equipment. Technical and administrative members of staff prepare these meetings during working hours before the general assembly. Team and group leaders meet once a month to discuss the scientific strategy. Resources from IGR and CNRS are shared among the groups. The management team has also introduced mechanisms of financial solidarity between the scientists to weather short-term difficulties, although the details of the procedure were not revealed during the evaluation. The unit has nominated two technicians and engineers as health and safety officers.

AERES nomenclature

SVE1_LS1 et LS6

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1 (0,10)
N2: Permanent researchers from Institutions and similar positions	9	10
N3: Other permanent staff (without research duties)	9 (8,50)	9 (8,50)
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	1	1
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	7 (6,20)	2
N6: Other contractual staff (without research duties)	2	
TOTAL N1 to N6	**29 (27,70)**	**23 (21,60)**

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	11	
Theses defended	17	
Postdoctoral students having spent at least 12 months in the unit*	12	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	11	10

2 • Overall assessment of the interdisciplinary unit

Strengths and opportunities related to the context

1) The overall scientific quality of the work is very good, with some examples of excellent work. PIs are recognized in their field of research for the originality and vision of their projects.

2) The philosophy of the management team is to create the working conditions that facilitate 'creation of knowledge', in reference to the mission of the CNRS. This includes the establishment of democratic structures, solidarity and collaboration between the groups driven by technical expertise on proteomics and microscopy, as well as common scientific interests.

3) The unit has demonstrated its ability to attract a good level of external funding, particularly in form of PhD stipends.

4) The experts committee has been impressed by the huge effort put in the teaching of graduate students.

5) The unit has developed extensive international collaborations, particularly with Russia, which represents a source of scientists and of technical expertise, and is expected to allow access to high throughput devices.

6) The unit has the ability to attract young researchers and to offer career perspectives as attested by the recent recruitment of Ms Svetlana DOKUDOVSKAYA as a independent group leader and of a young scientist as "chargée de recherche".

7) Members of the unit have access to high-quality core facilities on the IGR site.

8) The research unit benefits from the proximity of the IGR hospital and has been able to recruit clinicians who are or were members of the unit during the last five years.

Weaknesses and threats related to the context

1. There is some heterogeneity in the structure of the groups, with a relative scarcity of young researchers and post-doctoral scientists. This situation needs to be addressed as quickly as possible to aid continuity of the present structure in 5 years.

2. Although the experts committee appreciates that the research projects of the PIs are generally complex, the modest number of publications with a very high impact factor remains a limitation for the long-term development of the unit.

3. The relative lack of resources and expertise in Bioinformatics on site is a constraint on the full development of the proteomics platform and of other high-throughput technologies.

Recommendations

1. In the context of the generation change with both director and deputy director intending to retire after the next funding period, the experts committee feels that it is urgent to prepare for the future. In this context, the representative of the CNRS and the director of the Institut de Recherche Intégrée en Cancerologie of the Institut Gustave Roussy (IRCIV/IGR) informed the committee that three priorities have been defined (genetics and epigenetics, immune response and DNA repair) for the center. The research projects developed by the members of the UMR 8126 fit well within this strategy and can make important contributions to it.

2. It is important to increase the level of funding to maintain the equipment and in particular the microscopes to the highest levels of quality. Attempts to obtain funding from the european union should be made and help with the applications should be sought from the CNRS.

3. Ideally, the unit should try to recruit (a) bioinformatician(s) for large-scale data analysis. This could be combined to efforts at the IGR level to improve services in this crucial research area.

4. Priorities for certain topics in which the unit can achieve excellence and publications in journals with very high impact should be defined. This does not mean that only one topic should be selected but rather to focus efforts and make the best out the creativity and technical expertise available. Combining the expertise in biochemistry and in imaging technologies, eg in DNA repair, might represent a fruitful approach. In this context the unit may consider recruiting people with a strong interest in this area.

5. The proximity of the IGR hospital is an important asset for the unit and the clinical interactions with the IGR hospital should be maintained and if possible expanded. There is a need to foster exchanges between young clinicians and young researchers in form of formal and informal exchanges though e.g. student initiatives.

3 • Detailed assessments

Assessment of scientific quality and outputs

The scientists in the UMR 8126 tackle important questions about fundamental nuclear functions (DNA replication and repair, chromatin organization), many of which are directly or indirectly relevant to human diseases e.g. malignant lymphomas, micro/nano objects secreted by tumor cells and several models of virally-induced oncogenesis. The unit is also strongly involved in translational research with projects on inhibitors of anti-apoptotic proteins, histone deacetylase and galectin 9 and identification of biomarkers. Despite the apparent diversity in research themes, interactions between the groups are genuine. Some topics such as the study of chromatin structure, malignant lymphomas or EBV-associated diseases are shared by at least two groups. Most groups make intensive use of proteomics and more generally of the technologies developed by the investigators. The imaging platform is also very useful for many research projects within the unit. Altogether, the available technical expertise is impressive, although the experts committee feels that its potential has not been fully exploited yet. The unit has been very successful in attracting external grant funding, in particular in form of PhD stipends. The 6 units PIs have published 150 papers during the last funding period, many of them in good or very good specialist journals such as J Exp Med., PLoS Pathogens or Blood and a few of them in high ranking non-specialist journals such as Mol Cell, PNAS or Genome research. The unit PIs have also collaborated to studies reported in excellent clinical (Lancet Oncol, JCO journals).

Assessment of the unit's academic reputation and appeal

All team leaders are well known to their peers and their contributions to their respective fields is recognized through regular publications and communications in scientific meetings. Three group leaders have been granted a 'Prime d'excellence scientifique'. Many of the group leaders act as referees for scientific journals or as editors for books, some of them have organized scientific meetings and are members of French evaluation committees.

The international reputation of the deputy director led to the recruitment of three principal investigators from the ex-USSR. Furthermore, the unit now hosts a "Laboratoire international associé (LIA)" for 4 years (LIA LFR2O) funded by the CNRS and the Russian Academy of Sciences and co-headed by the deputy director. The majority of post-docs in the lab come from abroad.

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

Two patents have been filed and two were granted in the last five years. Three groups receive grants from Servier Laboratories. Others collaborate with biotech companies such as Cellvax biotech company in form of a Convention industrielle de formation par la recherche (CIFRE), BioChoros with the support of ARC and OSEO grants and Abbot Laboratories (USA).

A better dialogue between Science and Society is an important goal in the unit. PIs are involved in continuous education programs and Associations for patients with Facioscapulohumeral dystrophy or suffering from spastic paraparesis. The director was one of the founding members of Institut Emilie du Châtelet pour les études sur les femmes, le sexe et le genre. The deputy director has a long record in the promotion of a rich dialogue between scientists and civil society. He has created the Partenariats institutions-citoyens pour la recherche et l'innovation (Picri) as well as the "centre francilien de l'innovation" in his important role as the elected vice-président of the regional council of Île-de-France in charge of Higher education, Research and Innovation. Lately, he has been granted a Mission on Sciences and Citizens by the president of CNRS.

Assessment of the unit's organisation and life

A most striking feature of the unit is the apparent satisfaction of its members with the management of the unit. Meetings with technicians and engineers, students and postdocs, as well as with young researchers showed that they are well integrated into the structure of the laboratory and that their contribution is acknowledged. Lab members praised the director for the high degree of transparency in all decision-making processes that are largely based on democratic principles. One worry was the difficulty of getting access to sufficient funding to keep large pieces of equipment, in particular microscopes, to the highest standards. Similarly, funds for young investigators to attend international meetings are very limiting. A general assembly attended by all lab members is held every three

months to decide how to allocate resources and to deal with daily life matters in the lab. Team leaders meet once a month to discuss scientific policy issues and projects.

Lab members attend a mandatory weekly scientific meeting Master students, PhD fellows and post-docs organize journal clubs. The existence of a coffee room in the unit also favors internal discussions and exchanges between students.

The budgets granted every year by the CNRS and by Université Paris Sud and by Institut Gustave Roussy are mainly dedicated to consumables and tissue culture media that are used by all teams. In case one team runs into temporary financial trouble, ad hoc arrangements are decided between team leaders.

Three members of staff are officially in charge of maintaining health and safety regulations. A single technician, in charge of all administrative and financial matters, felt overwhelmed with work and was desperate for the unit to be able to recruit an additional post.

Assessment of the unit's involvement in training through research

Over the 2008-2013 period, 17 students have successfully defended their PhD thesis, 15 of whom are now post-docs in various labs in France or elsewhere. Each of these students published at least one publication as first author during their thesis. Another 14 PhD students are currently working in the lab and are enrolled in the PhD Program of Oncology administered by the Université Paris Sud. Discussions with the head the PhD Program of Oncology confirmed that the UMR 8126 has an excellent reputation. Eleven members of the unit can formally supervise students (HDR). Several PhD fellows in the laboratory have jointly participated in the creation in 2011 of the Association des jeunes chercheurs de l'Institut Gustave Roussy. The unit has also successfully supervised 20 MSc theses during the last 5 years.

The director and deputy director are heavily involved in the PhD Program in Oncology of Université Paris-Sud, the former as one of its founding members and current deputy director, the latter as a member in its scientific advisory board.

The deputy director also takes an active part in the organization of the Master of Oncology curriculum offered by the Université Paris Sud. One of the group leaders and another scientist are coordinators of specialized curricula within this Master.

Most PIs contribute to teaching in various Masters at the University Paris Sud (M2 Cancérologie and M2 Toxicologie humaine, évaluation des risques et vigilance), Université Pierre et Marie Curie (M2 Biologie moléculaire et cellulaire, spécialité Génétique), Universities Versailles Saint-Quentin-en-Yvelines (M2 recherche Biologie intégrative et moléculaire), Paris-Descartes (M2 Sciences du médicament, spécialité Pharmacochimie), and Paris-Est Créteil (M2 Biothérapies tissulaires, cellulaires er géniques). The unit is a regular training laboratory for various fellows preparing technician or engineer diplomas.

Assessment of the strategy and the five-year plan

The scientists in the unit have proposed a broad and ambitious research program that retains most of the previous research topics. However, following the retirement of the scientists in charge, research projects on neuroblastoma and some of the projects on malignant lymphomas will be discontinued. The director and the deputy director of the unit have announced their intention to retire at the end of the next funding period. The general flavor of the projects will remain identical which should guarantee continuity and the experts committee anticipates that the scientific output will globally remain at the same level. The application for renewal foresees the creation of 6 independent teams from the currently existing 3 teams. The question of the long-term orientation of the unit has to be raised. The committee did not currently identify a natural successor of the current director among the younger investigators. The next five years will be crucial for those scientists who will continue after 2018 to define a future research strategy, which should be aligned with the broad strategy of IRCRV/IGR. Overall the future projects are seen as well designed although the committee recommends some degree of prioritization to facilitate publication in journals with very high impact factors, which in turn would increase funding for large pieces of equipment and help attracting young investigators. The recruitment of two scientists as CR2 and CR1 are two important steps in the right direction but more efforts are necessary to keep and improve the ratio of young to experienced scientists within the unit. The proteomics core facility can increase the scope of its service projects, provided that adequate bioinformatics support can be secured. This core facility would greatly benefit all the groups on site.

4 • Team-by-team analysis

(Previous team 1 will be presented split into 4 teams)

Previous Team 1 Nuclear processes and apoptotic signalling

Name of team leader: Mr Marc LIPINSKI

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015[2]
N1: Permanent professors and similar positions	1	
N2: Permanent EPST or EPIC researchers and similar positions	5	
N3: Other permanent staff (without research duties)	4	
N4: Other professors (PREM, ECC, etc.)	1	
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	5	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**16**	

Team workforce	Number as at 01/01/2015 (For future team 1) Ms Svetlana DOKUDOVSKAYA	Number as at 01/01/2015 (For future team 2) Mr Vasily OGRYZKO	Number as at 01/01/2015 (For future team 3) Mr Marc LIPINSKI & Mr Yegor VASSETZKY	Number as at 01/01/2015 (For future team 4) Ms Joëlle WIELS
N1: Permanent professors and similar positions				
N2: Permanent EPST or EPIC researchers and similar positions	1	1	2	1
N3: Other permanent staff (without research duties)		3		1
N4: Other professors (PREM, ECC, etc.)				1
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1		
N6: Other contractual staff (without research duties)				
TOTAL N1 to N6	**2**	**5**	**2**	**3**

[2] Please see below for the details about the future teams

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015[3]
Doctoral students	8	
Theses defended	11	
Postdoctoral students having spent at least 12 months in the unit	9	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar Qualified research supervisors (with an HDR) or similar positions	8	6

Team workforce	Number as at 01/01/2015 **(For future team 1)** Ms Svetlana DOKUDOVSKAYA	Number as at 01/01/2015 **(For future team 2)** Mr Vasily OGRYZKO	Number as at 01/01/2015 **(For future team 3)** Mr Marc LIPINSKI & Mr Yegor VASSETZKY	Number as at 01/01/2015 **(For future team 4)** Ms Joëlle WIELS
Doctoral students				
Theses defended				
Postdoctoral students having spent at least 12 months in the unit				
Number of Research Supervisor Qualifications (HDR) taken				
Qualified research supervisors (with an HDR) or similar positions	1	1	2	2

[3] Team 1 will be restructured – Please see below

Team 1: Intracellular traffic, macromolecular complexes and cancer

Name of team leader: Ms Svetlana DOKUDOVSKAYA

• Detailed assessments

Assessment of scientific quality and outputs

This is a young research group created during the year 2010. The group is working on a newly discovered multiprotein complex (the SEA complex) in yeast and linked to cancer in mammals. The identification and initial characterization of the complex were made by the group leader and were described in two publications in 2011 (in Mol. Cell Proteomics and Autophagy). Two follow up publications are in preparation. Studies are conducted in parallel in yeast and human models, and address both structural and functional aspects of the complex. In light of the short history and small size of this group (3 people: the group leader, 1 post-doc and 1 PhD student) the scientific production appears satisfying.

Assessment of the unit's academic reputation and appeal

The group leader obtained the Prime d'Excellence of CNRS. In addition, the group leader has set up collaborations with three well-known international teams to study different structural aspects of yeast SEA complex. Members of the group were invited to give oral presentations although in a relatively small number of events (1 international and 2 national meetings, and 3 seminars). The group leader obtained grants to initiate the research program. However, the group will need to rapidly find other funding to pursue its research program.

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

The configuration and research topic of this group do not allow evaluation of this criterion.

Of note, one member of this group (a student) co-funded and managed an association of young scientists.

Assesment of the unit's organisation and life

The work initiated by this young group is in direct line with the initial plan, proposed by the group leader. Students and postdocs are satisfied by the team management (implicating regular meetings, frequent informal exchanges and well-defined research projects).

Assessment of the unit's involvement in training through research

The group leader trained 5 students (2 PhD, 1 Master 2 and 2 Master 1) and 2 post-docs. The group leader has obtained the "Habilitation à Diriger la Recherche" (HDR) in 2012.

Assessment of the five-year plan and strategy

In the next five-year period, the group leader plans to:

1. study the function of the SEA complex both in yeast and human;

2. determine and analyze the structure of yeast SEA complex;

3. characterize the function of one member of the SEA complex, Nprl2, in anticancer treatments and DNA repair.

The project is original and in the continuity of the findings made by this group since its creation. It proposes to combine studies of the same complex in two organisms and to study both structural and functional aspects of the complex. It also proposes to further address the role of one specific member of the complex in cancer-related topics. Overall, this is an ambitious project and the group leader will need to make priorities among the main objectives by first capitalizing on their recent findings related to the yeast SEA complex.

Conclusion

- **Strengths and opportunities:**

The group leader has initiated an original research program. Moreover, the results obtained confirmed the connection between this research program and cancer-related topics, with a potential for setting up collaborations with nearby research groups and/or clinicians. The group leader also established strong collaborations with well-known experts to address the structural aspects of the project.

- **Weaknesses and threats:**

Funding for the next 3 years needs to be secure rapidly.

The current composition of the team is undersized compared to the proposed research program and the know-how necessary to develop the human part of the project is rather limited.

International competition is developing.

- **Recommendations:**

Taking into consideration that despite a limited manpower of this group the conducted research project has a strong potential for important findings, the group leader needs to prioritize is different main aims to avoid a deleterious dispersion of the forces, as well as to publish and secure funding relatively rapidly.

Team 2: Proteomics and Epigenetics

Name of team leader: Mr Vasily OGRYZKO

• Detailed assessments

Assessment of scientific quality and outputs

The group has gained international recognition within the proteomics / nuclear research community with the development of two novel sets of methodologies for I) the in vivo study of protein-protein interactions (PUB-MS and PUB-NChIP) and II) the investigation of the surface state (i.e. the protein conformation) of selected proteins (proteome footprinting). Considering the limited manpower (4 people: 1 PhD student, 1 post-doc, 2 technicians), the group has produced sixteen scientific publications both in topic-related journals (e.g. Journal of Proteome Research, Proteomics and Genome Research) and in more general journals (e.g. PLOS ONE, Molecular Cell and PNAS). The experts committee has unanimously acknowledged the scientific quality of this team.

Assessment of the unit's academic reputation and appeal

The group is internationally recognized in the field of nuclear proteomics. The group head has been invited to national and international meetings and has given seminars in several (mainly estern) european countries. Furthermore, he has reviewed manuscripts and grants for international journals and funding agencies and participated in the application of one patent. Importantly, the group head and his engineer have an additional affiliation as staff of the proteomics platform (core unit) at the institute.

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

Beside the presentation of a lecture in the popular lecture series at the Interdisciplinary University of Paris, the group leader has participated in a patent application in collaboration with a scientist from the Institut Pasteur (title of the application: process of screening a molecule as a candidate drug for the treatment of bipolar disorder).

Assesment of the unit's organisation and life:

The group has not only trained several PhD and Master students but has also hosted five international interns from Kazakhstan and the Ukraine. Furthermore, the group participates in international collaborations with Poland and Kazakhstan.

Assessment of the unit's involvement in training through research

The group has housed 4 Master students, 4 PhD students and 1 post-doc since 2008.

Assessment of the five-year plan and strategy

In the next years, the group leader wants:

- to use the PUB-MS technique (which was developed in the lab) for the study of ubiquitinated and/or SUMOilated neighborhoods of target proteins;

- to apply the proximity biotinylation technique to analyze genome topology on single-cell level;

- and to serve as a proteomics platform for the whole institute.

Altogether the strong proteomic skills will favor their involvement in important projects both from this unit as well as strong local and international collaborations. These technical developments are clearly the major asset of this team that would ally both strong proteomic knowhow and their integration in novel scientifc projects.

Conclusion

- **Strengths:**

The team is internationally recognized for his skills in proteomics as evidenced by the quality of the publications.

Their objectives are clearly stated and they are fully integrated in the lab and the IGR.

- **Weaknesses:**

One of the major challenges is the limited number of trained scientists and engineers that could help developping their projects.

- **Recommandations:**

The group has to cover the span between its own research interests and the requirements of an institute platform/core facility. Having both limited instrument time and restricted manpower, this balance might be challenging, which is why the experts committee expressed some concerns about the adequation between the number of projects and the team task-force. Unquestionable, the unit "Signaling, Nuclei and Innovations in Oncology" requires sophisticated proteomics support and the group has developed a unique proteomic tool box for the investigation of protein-protein interactions in the nucleus. Thus, the committee feels that there is a clear need for the identification of techniques which can be offered in the frame of the institute platform (e.g. standard techniques and analyses realizable by a trained technician) and technical developments carried out by the research group for its own research and the research needs of the unit. To widen the range of proteomic techniques for the institute platform and considering the acquisition of the new instrument (Q-Exactive from Thermo) with its wide application area, the employment of a bioinformatican for proteomic data analysis might be favorable.

Team 3: Nuclear organization and pathological models

Name of team leader: Mr Yegor VASSETZKY and Mr Marc LIPINSKI

- Detailed assessments

Assessment of scientific quality and outputs

The group has a strong reputation in the field of nuclear organisation, with a particular emphasis on the pathogenesis of lymphomas and facio-scapulo-humeral dystrophy (FSHD). In the last quinquennium the group has been productive and published 29 manuscripts, with PIs as senior authors or co-authors. These include key manuscripts in high impact factor journals such as Genome Research (IF 14,37), JBC (IF 5,3) and Nuclear Acid Research (IF 8,05), as well as several manuscripts in Plos one (IF 3,7).

Assessment of the unit's academic reputation and appeal

One of the froup leaders is a world expert in regulation of transcription and chromatin organisation. The other group leader is a leading researcher in the field of pathogenesis and nuclear organization of the autosomal dominant disorder facioscapulohumeral dystrophy (FSHD). Mr Yegor VASSETZKY is also chair of the International scientific advisory Board of the Institute of Molecular Biology and Genetics (Kiev, Ukraine) and the editor of the scientific journal 'Biopolymers and Cell'. In the period of 2009-2013 he has been invited to give several lectures at international meetings.

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

One of the group leaders was a vice president of the Regional Council Ile-de-France in charge of higher education, research and scientific and technical innovation from 2004 to 2010. He is a member of several Boards such as Université Paris-Diderot, Etablissement public d'amenagement et d'urbanisme de la Région Île-de-France, President of the Agence regionale de l'environnement et des nouvelles energies. Mr Yegor VASSETZKY is a member of the board of directors of a biotech company (Affitech, Denmark) and pursues an active collaboration with associations of patients through AFM, FSHD, Europe.

Assesment of the unit's organisation and life:

The number of staff includes 2-4 PhD students and 2 postdoctoral fellows. The group is suffering from a shortage of permanent technical staff.

Assessment of the unit's involvement in training through research

Three students have successfully completed PhD programmes and four are currently working in the group. ML is a deputy director of École Doctorale de Cancerologie in Université Paris Sud and organizer of the Master 2 diploma of Cancerologie in Université Paris Sud. Mr Yegor VASSETZKY lectures within M2 of Cancerologie (Université Paris-Sud) and at Université de Versailles Saint-Quentin en Yvelines, Latvian University in Riga and Université Libanaise in Beyrouth.

Assessment of the five-year plan and strategy

The proposed studies have four different aspects and are part of two independent projects. The first project is related to the nuclear organisation in lymphomas and is focusing on chromosomal regions whose nuclear spacial proximity renders recombination and occurrence of translocations. The group is aiming to identify loci in the proximity of IgH region on the chromosome 14 during normal B cell differentiation that have potential to become partners in translocations. The group is also aiming to determine whether HIV infection leads to nuclear reorganisation with consequent proximity of IgH and c-myc locus, that may be responsible for high frequency of t(8;14) observed in HIV positive Burkitt lymphoma. The second project is related to the pathogenesis of FSHD with two specific aims:

a) to determine the consequences of observed SDF1/CXCR4 overexpression in FSHD muscle on cellular signalling;

b) to use iPSC from FSHD muscles as a model system where it can be tested whether defective nuclear matrix attachment and reduced number of D4Z4 repeats represent the main cause of FSHD phenotype.

Conclusion

- **Strengths**

The team leaders are both internationally recognized in the field of nuclear organization in diseases such as lymphomas and FSHD. They have made important contribution in transcription regulation.

Their project is original and fully in the scope of their long term perspective on nuclear organization.

- **Weaknesses**

The identification of two different projects within the team: nuclear organization in lymphomas and pathogenesis of FSHD is highly challenging.

- **Recommendations**

The group has been productive and generated a number of important publications related to nuclear organisation in lymphomas and FSHD. Addressing the role of viral infection in the spatial nuclear organization is likely to give clear answers, while identification of potential IgH partners during B cell differentiation is more open ended and the relevance of the findings for lymphomagenenesis uncertain. Similarly, addressing the role of SFD1/CXCR4 axis in FSHD muscles is also likely to be successfully accomplished. The outcome of the last aim, ie modelling FSHD defect in iPSC is less predictable and consequently the group have decided to focus on correction of the molecular defect in differentiated muscle cells. Although this aim is not cancer related, it has a clear translational angle and is worth developing as it could serve as a paradigm for the molecular targeting in future cancer-related projects.

Team 4: Oncogenesis and resistance to apoptosis in B cell lymphomas

Name of team leader: Ms Joëlle WIELS

• Detailed assessments

Assessment of scientific quality and outputs

The group has an international reputation in oncogenesis and apoptosis regulation in lymphoma cells. Publications from the group are good, including notable senior author papers 2009 Leukaemia (impact factor 8.3), 2010 Cell Signal (IF 4.2) and J Infect Dis (IF 5.8), 2011 Am J Pathol (IF 4.5) and Cell Death and Disease (IF 6.0). There are also substantial contributions to several high impact papers from a group member as coauthor, eg J. Clin Oncol (IF 18.0), Lancet Oncol (IF 21.8), Blood (IF 9.0).

Assessment of the unit's academic reputation and appeal

The group leader is an internationally recognised expert on oncogenesis in B lymphoma. She is particularly well known for research on mechanisms of apoptosis in lymphoma cells. Since 2010 the group has included two independent researchers. Altogether they have a very good track record in the fields of lymphoma and apoptosis mechanisms.

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

The group leader serves on the Scientific Commission of the Ligue Nationale Contre le Cancer and CNRS-APHP-CEA. She has also played a role in promotion of women in science through Institut Emilie du Chatelet. One of the staff scientists served as President of the scientific committee head of the Pôle de Biologie of Faculté de Médecine Paris Sud. She has also played an international role in promoting research and cancer treatment in low income countries, particularly in Africa.

Assesment of the unit's organisation and life

The teams is well organized with good interactions between scientist as well as an excellent training devoted to students.

Assessment of the unit's involvement in training through research

The group leader is a member in the scientific boards of the École Doctorale de cancérologie and of the Master Biologie Santé - spécialité Cancérologie de l'Université Paris-Sud. Since 2008, four students working in the group have obtained their M2, one has obtained her Doctorat de Pharmacie, four have successfully defended their PhD, and two PhD students are currently working in the group.

Assessment of the five-year plan and strategy

The plan has several components. Continued investigation of Gb3 and glycosphingolipid signalling in BL cells has been central to the group's research for several years now and will be continued. The group is clearly well placed to undertake that work. Fundamental and more translational studies directed towards identifying novel agents that might stimulate cell death in lymphomas are a logical way forward and the group has a strategic advantage in systems that they plan to investigate. Finally the clinical and translational studies involving characterisation of early lymphoid lesions in children after transplantation and investigation of CLL in Senegal are likely eventually to provide a clinical benefit.

Conclusion

- **Strengths:**

The group has maintained a very good level of research productivity.

The group leader makes a substantial leading international contribution.

- **Weaknesses:**

They need to foster the interactions between the apoptosis mechanisms in lymphomas and the studies in clinical samples from transplanted patients.

- **Recommandations:**

There is a coherent interest in apoptosis and lymphoma that binds the group together. It is expected that Professor Joëlle WIELS will retire at the end of the forthcoming 5 years period, together with two other scientists. The way to ensure research continuity will be to align research activity with the higher level research themes of the IGR, particularly genetics and epigenetics of cancer, immunology and DNA repair. Apoptosis research will lie within both immunology and DNA repair.

Team 5 Genome maintenance and molecular microscopies

Name of team leader: Mr Éric LE CAM

Workforce

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

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

• Detailed assessments

Assessment of scientific quality and outputs

The group has continued developing imaging technologies in its molecular microscopy facility. Using transmission electron microscopy and atomic force microscopy they have studied various aspects of DNA metabolism. In particular they have studied a specific helicase, Srs2, revealing its role in the regulation of homologous recombination in the yeast Saccharomyces cerevisiae. This work has been published in Molecular Cell and part is yet to be published. The team has also participated in the structural characterization of the filaments formed by the Cernunnos/XLF-LigIV human molecular complex, resulting in a publication in the Proceedings of the National Academy of Sciences. More recently authors observed the action of the Rad51 recombinase that resulted in the removal of nucleosomes from double stranded DNA during the extension of the nucleoprotein filament. This is an important

[4] In the future will be Team 5

observation never reported before. Due to their expertise, members of this team are involved in numerous scientific collaborations.

Considering the small task-force the group has demonstrated a very good level of scientific production with 32 papers published.

Assessment of the unit's academic reputation and appeal

The group is well recognized in the field of microscopy mediated analysis of DNA metabolism proteins. Group members have been participating to national and international meetings. The recruitment by Inserm, in 2013, of a young scientist as “chargée de recherche” has greatly boosted the capacity of working on DNA recombination proteins. The group leader participates to the scientific committee of the ARC and Inserm. He also teaches at Master level in various disciplines. Through these teaching engagements, the group leader promotes the laboratory, enhances its visibility and contributes to its attractiveness. The team also has long-term collaboration with the Centro Nacional de Biotecnología, in Madrid. This collaboration enhances its international visibility.

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

This issue was not applicable.

Assessment of the unit's organization and life

The team has an excellent organization with two young and enthousiastic researchs that confirm that this team is well organized and managed.

Assessment of the unit's involvement in training through research

They are involved in the training within Masters (UPMC) and workshops about electron microscopy.

Assessment of the five-year plan and strategy

In the next years, the group leader wants:

- to continue the studies concerning structural and functional characterization of DSBs repair machineries involved in NHEJ and to study telomere-Rap1 structure

- to develop techniques allowing the isolation and analysis of DNA structures associated with a specific DNA locus to study the structure of stalled replication forks. This project is of high importance for the entire field of DNA replication and genome stability.

- to develop new tools for molecular and cellular imaging analysis and to investigate at the molecular level replication and recombination events. This project will be important for the institute and collaborators interested in using these techniques.

Conclusion

- **Strengths:**

Excellent publication track with the most up to date techniques necessary to analyse DNA. The team leader is an internationally recognized expert in these methods. The young researchers associated to the project are talented.

- **Weaknesses:**

They need to focus their scopes of research and attract more students.

- **Recommandations:**

Although the projects proposed are in the field of expertise of the group, there are concerns about the feasibilty of these aims in the short term. These goals are quite ambitious and will require the development of techniques that do not exist at the moment and for which no preliminary evidence has been generated. There is the risk that the group might lose its edge on DNA recombination analysis in trying to elaborate these novel techniques,

especially following the recruitment of a DNA recombination expert. Thus, there is a clear need in the nearest future to identify the major scientific aims and to prioritize defined projects. It would be helpful to recruit PhD students, who will be perhaps more attracted by more defined and achievable scientific goals.

Team 6 Tumor microenvironnement, exosomes and microRNAs in solid tumors

Name of team leader: Mr Pierre BUSSON

Workforce

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

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The group is known for its activities in two areas of translational research, one organized by the group leader, which was initially directed towards the identification and exploitation of novel targets for therapy against EBV-positive nasopharyngeal carcinomas and focused in the past 3 years on ovarian carcinomas and the study of tumor-derived exosomes. Another part of the team led by another senior scientist studies microRNAs in neuroblastoma. In the reporting period (2008-2013) the team members published a total of 39 original publications (13 with team members as first or last author) and 3 review articles; the team cites as its 5 major publications 1 Blood 2009 (IF 9.3), 1 Semin Cancer Biol 2012 (IF 7.4), 1 Br J Cancer 2011 (IF 5.2), 1 Virol J 2013 (IF 2.1) and 1 Infect Agent Cancer 2012 (no IF). The team members have contributed to major publications (IF>10), such a 1 Lancet Oncol 2009

[5] In the future will be team 6

(IF 25.1), 1 J Clin Oncol 2010 (IF 18), or 1 J Exp Med 2009 (IF 14.1). Together this is a highly productive group, which should consider increasing the level of publications led by the team even if this would decrease the overall number of publications.

Assessment of the unit's academic reputation and appeal

The group is recognized in the respective fields and team members present regularly work at national and international meetings. In the reporting period the team leader has been invited to two international meetings (Tozeur, Tunis, 2008; Canton, China, 2011) and several national and European institutes for seminars.

The team leader is involved is several activities of academic reputation, including a stirring committee (Herpes virus and cancer network of INSERM 2008-2010), several scientific committees for international workshops, is designated overseas coordinator of the university grants committee of Hongkong and got a PES (CNRS) 2012-2016.

The group is well funded by ANR, INCa, Ligue, laboratoire Servier and others but no grant has (yet) been obtained that extends funding beyond 2014.

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

The team leader has been instrumental in formalizing a Translational Research hospital convention with the clinical teams of IGR (2011-14) and established collaboration with the Institut de Recherche Internationale Servier since 2011. In this context one patent has been filed; in addition the team has applied for another patent.

Assessment of the unit's organisation and life

The team is well organized.

Assessment of the unit's involvement in training through research

Eight theses have been completed in the reporting period, 2 are ongoing. Both the team leader and another senior scientist of the team coordinate curricula for M2 students.

Assessment of the strategy and the five-year plan

Based on its expertise the team will continue studies along three lines of research:

- project (1) continues the research of the immunosuppressive functions of tumor-borne gal9 and approaches to neutralize this effect. The idea is to generate more mABs with gal9-neutralising activity of selective monocyte and lymphocyte populations. For this project collaboration with teams of the Institut de Biologie de Lille (IBL) will provide important materials and expertise. The aim is to monitor if mAbs can be identified that systemically alter the effects of tumor-derived gal9 on distribution/survival od CD4+Th1 or Tregs. This project is definitely challenging but given the experience of the team it is worth pursuing.

- project (2) targets the promising and increasingly recognized potential of exosomes and other vehicles like “Lex-large extracellular chromatin fragments”. The team will characterize these particles with an emphasis on TRAF-interacting LMP1 (infection membrane protein 1)–containing particles from EBV infected cells. They have obtained interesting preliminary results about naïve and LMP1 containing exosomes/Lex concerning histone content and the DNA binding ability of LMP1 itself.

- project (3) has as rationale to enforce activation of the EBV lytic cycle to induce apoptosis of latent EBV-infected cells. In the presentation and discussion of the project the team leader explained that a decision to embark on this project has still to be taken.

Conclusion

- **Strengths:**

Excellent publication track. Very strong translational research in both the fields of immunosuppressive factors and EBV related pathologies. Very strong interactions with industry. The team leader is an internationally recognized expert in the field.

- **Weaknesses:**

They need to focus their scopes of research since among the three major projects presented the last one on the enforcement of EBV lytic cycle is novel and might be challenging.

- **Recommandations:**

The projects proposed are in fully in the field of expertise of the group. Specifically the galectin 9 project has to be continued due to their excellent knowhow in this field including novel mAb. However, they might consider within their project on exosomes that while the plans to identify specific cargo DNAs is well accepted, the team may think about increasing its ambition using direct amplification and massive parallel sequencing or even ChIP-seq. The field witnesses currently increasing efforts in the identification and characterization of circulating DNA, chromatin and tumor cells as non-invasive real-time surrogates for tumor tissue-based biomarkers, and the team is well positioned to move to a competitive edge in this field.

5 • Conduct of the visit

Visit dates:

Start: November 13th 2013, at 08.30 am

End: November 14th 2013, at 02.00 pm

Visit site:

Institution: UMR 8126 CNRS

Address : Institut Gustave Roussy - Pavillon de Recherche
94805 Villejuif

Conduct or programme of visit:

November 13th	
08.30 am	Welcome (closed door) Expert committee members with the AERES Scientific delegate (DS) (the role and procedures of AERES)
09.00 am	Director of the unit: presentation of the past activities and project
10.00 am	Coffee break
10.15 am	Parallel meetings with personnel: - discussions with engineers, technicians, administrative; - discussions with staff scientists; - discussions with students and post docs.
12.15 pm	Lunch
01.30 pm	Team 1 – Intracellular traffic, macromolecular complexes and cancer (Ms Svetlana DOKUDOVSKAYA)
02.00 pm	Team 2 – Proteomic and epigenetic (Mr Vasily OGRYZKO)
02.30 pm	Team 3 - Nuclear organization and pathological models (Mr Yegor VASSETZKY and Mr Marc LIPINSKI)
03.30 pm	Coffee break
03.45 pm	Team 4 – Oncogenesis and resistance to apoptosis in B cell lymphoma (Ms Joëlle WIELS)
04.30 pm	Team 5 – Genome maintenance, Molecular microscopies and bionanosciences (Mr Éric LE CAM)
05.30 pm	Team 6 – Tumor microenvironment, exosomes and microRNA in solid tumors (Mr Pierre BUSSON)
06.30 pm	Debriefing on the team presentations

November 14th	
09.00 am	Discussion with the representatives of the managing bodies
10.15 am	Coffee break
10.30 am	Discussion with the head of the unit (if necessary)
11.00 am	Private meeting of the experts committee (in presence of the DS)
01.00 pm	End of the visit
01.00 pm	Lunch

6 • Supervising bodies general comments

UNIVERSITÉ PARIS SUD

Comprendre le monde, construire l'avenir®

Le Président de l'Université Paris-Sud

à

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

Orsay, le 27 mars 2014

N/Réf. : 75/14/JB/LM/AL

Objet : Rapport d'évaluation d'unité de recherche
N° S2PUR150007940

Monsieur le Directeur,

Vous m'avez transmis le 10 mars dernier, le rapport d'évaluation de l'unité de recherche Signalisation, noyaux et innovations en cancérologie - n° S2PUR150007940 et je vous en remercie.

L'université se réjouit de l'appréciation portée par le Comité sur cette unité et prend bonne note de ses suggestions.

Vous trouverez en annexe les éléments de réponse de Madame Joëlle WIELS, Directrice de l'unité de recherche.

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

Jacques BITTOUN
Président

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Signalisation Noyaux Innovations en Cancérologie UMR 8126

Directrice
Joëlle Wiels

Directeur adjoint
Marc Lipinski

Villejuif le 19 mars 2014

Agence d'évaluation de la recherche
et de l'enseignement supérieur (AERES)
Membres du panel de notation

Madame, Monsieur, chers collègues,

Nous avons pris bonne connaissance du rapport établi par le comité de l'Aéres suite à la visite qu'il a effectuée les 14 et 15 novembre derniers afin d'évaluer notre unité de recherche. Nous souhaitons en premier lieu remercier les membres du comité d'évaluation à la fois pour la qualité de leur écoute et leurs questions très pertinentes le jour de la visite ainsi que pour leur rapport tout à fait précis et constructif. Nous n'avons pas relevé d'erreurs factuelles à rectifier dans ce projet de rapport.

Dans son évaluation, le comité a estimé que la qualité du travail réalisé était très bonne et incluait même des exemples d'excellents travaux. Il a apprécié la « philosophie » générale de l'équipe de direction, la capacité de l'unité à lever un bon niveau de financements sur projets, et les efforts considérables faits dans le domaine de la formation aux niveaux doctorat et master. Il s'est également félicité de l'ampleur prise par les collaborations développées au niveau international et de la capacité de l'unité à recruter de jeunes chercheurs, en particulier avec l'arrivée en 2010 d'une nouvelle responsable d'équipe et le recrutement par l'Inserm en 2013 d'une Chargée de recherche. Enfin, le comité a constaté l'excellence des plateformes accessibles et le potentiel d'interaction avec la clinique sur le site de l'Institut Gustave Roussy (IGR).

Quelques faiblesses, dont certaines que nous avions nous même identifiées, ont aussi été notées par le comité. Celles qui concernent le manque relatif de jeunes chercheurs à l'organigramme et l'absence d'expertise en bioinformatique méritent certainement d'être prises en considération et nous nous efforcerons d'agir en priorité pour corriger ces deux points même si le second relève aussi de la politique plus générale du développement de la recherche à l'IGR. Deux post-doctorants viennent d'ailleurs de rejoindre l'Unité dans les groupes de Svetlana Dokudovskaya et Vasily Ogryzko.

Pour ce qui concerne les recommandations émises par le comité, non seulement elles ne nous posent aucun problème mais elles rejoignent parfaitement les objectifs que nous nous sommes fixés et pour lesquels le soutien de nos tutelles et de notre hébergeur est absolument essentiel.

Nous voudrions en particulier souligner les points suivants.

– Nous avons déjà commencé à envisager l'avenir des équipes qui constituent l'UMR 8126 dans l'optique du départ en retraite, à la fin du prochain contrat, des actuels directrice et directeur adjoint. Nous apprécions que le comité ait noté que les thématiques de l'Unité s'intègrent bien dans les priorités définies par l'IGR et pourront en constituer d'incontestables atouts.

– Nous savons que maintenir un haut niveau de fonctionnalité et d'excellence des équipements disponibles dans l'unité nécessite des financements très importants. Nous sollicitons depuis plusieurs années le soutien des différentes tutelles (CNRS, Université Paris Sud, IGR) pour assurer la jouvence nécessaire des microscopes mais ces demandes restent malheureusement infructueuses. Des demandes auprès de la Communauté Européenne vont être faites. Pour ce qui concerne les contrats de maintenance des microscopes, seule une partie est prise en charge depuis 2012 par l'Université Paris Sud (programme MRM). Des demandes européennes vont être faites. Par contre, nous voulons noter l'excellent soutien apporté par l'IGR à la plateforme de protéomique dont Vasily Ogryzko est responsable. Dans un très proche avenir, nous espérons que nos deux tutelles et notre hébergeur uniront leurs efforts pour non seulement assurer la maintenance et des conditions optimales d'utilisation de la plateforme de microscopie moléculaire dont nous disposons aujourd'hui, mais aussi pour continuer de l'améliorer, en particulier avec l'acquisition d'un microscope à force atomique de nouvelle génération fortement souhaitée par l'équipe dirigée par Eric Le Cam.

– Pour ce qui concerne la pérennité des financements sur projets qui constitue une remarque récurrente du comité, nous tenons à souligner que tous les chefs d'équipes font des efforts considérables pour assurer leur fonctionnement quotidien. Il faut noter que depuis début 2014, Svetlana Dokudovskaya a obtenu un financement de la Ligue contre le cancer et que la lettre d'intention pour une demande de contrat à l'ANR coordonnée par Pierre Busson a été retenue.

– Nous sommes pleinement conscients de la nécessité de trouver très rapidement le moyen de recruter un(e) bioinformaticien(ne) qui développerait ses travaux dans l'Unité. Nous avons eu la chance d'avoir à l'effectif pendant deux ans une bioinformaticienne dans le cadre du programme européen des « Marie Curie Fellows ». Nous n'avons malheureusement pas pu la stabiliser à l'IGR, malgré notre désir et nos tentatives. Là encore, nous espérons qu'il sera possible de trouver dans un avenir proche, avec nos tutelles et notre hébergeur, des solutions de financement pour répondre à cette recommandation du comité.

– Nous avons aussi bien conscience qu'il serait souhaitable d'attirer de nouveaux chercheur-e-s afin de développer et/ou de pérenniser les projets scientifiques actuels ou à venir (notamment pour l'équipe de Joëlle Wiels dont les chercheuses actuelles partiront en retraite à la fin du contrat). Une candidature d'un jeune chercheur qui souhaite rejoindre l'équipe de Vasily Ogryzko est d'ailleurs en cours d'évaluation par l'Inserm. De plus, et bien que le contexte général n'y soit pas favorable, nous nous efforcerons comme nous l'avons fait dans les années récentes de renforcer notre potentiel en personnel technique.

– Définir des priorités thématiques au sein de l'Unité est une approche que nous envisageons afin de tirer le meilleur parti des compétences des personnels et de notre présence à l'IGR. En ce sens, le recrutement récent par l'Inserm d'une jeune chercheuse, spécialiste de la thématique de la « recombinaison homologue », dans le groupe d'Eric Le Cam s'inscrit tout à fait dans leurs objectifs thématiques maintenant ciblés plus clairement vers l'étude de la réparation, de la recombinaison de l'ADN et de la caractérisation des intermédiaires de réplication. Par ailleurs, pour ce qui concerne les craintes exprimées quant aux études menées chez l'humain par le groupe de Svetlana Dokudovskaya, il nous semble que l'environnement de l'Unité et plus largement de l'IGR où les compétences sont nombreuses pour les études chez l'humain lui permettra d'acquérir les savoir-faire nécessaires. Enfin, Vasily Ogryzko prendra en considération les recommandations émises par le comité et définira clairement l'ensemble des techniques offertes par la plateforme de protéomique.

– Enfin, nous sommes fermement déterminés à continuer de développer nos relations avec les secteurs cliniques de l'IGR, comme indiqué dans le document préparatoire au renouvellement de contrat avec l'Université Paris Sud et le CNRS.

Nous vous prions d'accepter, chers collègues, l'expression de nos plus cordiales salutations.

Joëlle Wiels, directrice

Marc Lipinski, directeur adjoint