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

Department for the evaluation of research units

AERES report on unit:

Centre de Recherche Jean-Pierre Aubert

JPARC

Under the supervision of the following institutions and research bodies:

Université de Lille 2 – Droit et Santé

Institut National de la Santé Et de la Recherche Médicale - INSERM

Centre Hospitalier Régional Universitaire de Lille

January 2014

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

Department for the evaluation of research units

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

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

On behalf of the expert committee,

– Mr. Erwan BÉZARD, 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 resultof the evaluation by the experts committee,the composition of which is specified below.

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

Unit name:	Centre de Recherche Jean-Pierre Aubert
Unit acronym:	JPARC
Label requested:	Centre INSERM
Present no.:	UMR 837
Name of Director (2013-2014):	Mr Pierre FORMSTECHER
Name of Project Leader (2015-2019):	Mr Luc BUÉE

Expert committee members

Chair:	Mr Erwan BEZARD, CNRS, Université de Bordeaux
Experts:	Ms Dominique BONNET, University College London, United Kingdom
	Mr Jean-Christophe CORVOL, ICM, INSERM, Paris (representative of CSS INSERM)
	Mr Patrick DALLEMAGNE, Université de Caen
	Mr Gilles FAVRE, Institut Claudius Regaud, Toulouse
	Mr Gunnar C. HANSSON, Gothenburg University, Sweden
	Mr François-Xavier MAQUART, Université de Reims (representative of CNU)
	Ms Maria Grazia SPILLANTINI, Cambridge University, United Kingdom
	Mr Giles YEO, Cambridge University, United Kingdom

Scientific delegate representing the AERES:

Mr Laurent GROC

Representatives of the unit's supervising institutions and bodies:

Mr Régis BORDET, Université Lille 2 – Droit et Santé

Ms Monique CAPRON, Université Lille 2 – Droit et Santé

Mr Frédéric GOTTRAND, Centre Hospitalier Régional Universitaire de Lille

Mr Etienne HIRSCH,INSERM

Mr Bernard SABLONNIÈRE (representative of doctoral school n°446 "Biologie, Santé")

1 • Introduction

History and geographical location of the unit

The Jean-Pierre Aubert Research Center (JPARC) was created on January 1st 2007. It resulted from the fusion of the four Inserm units present at the time at the Lille University Medical School, and led to the pooling of Inserm personnel and resources dedicated to studying cancer and the neurosciences. Joined by the current team 3 for the current contractual period, JPARC is now proposing to welcome a new team of medicinal chemistry. The unit, scattered in different buildings situated at walking distance from each other, is located on the Lille 2 campus, at the foot of the University Hospital Research Center, of which it is a flagship.

Management team

Mr Pierre FORMSTECHER has managed the JPARC since its beginning and in particular during the current 5 year contract period (2010-2014). He smoothly passes the torch to Mr Luc BUÉE, who acted as deputy unit director during the current contract.

AERES nomenclature:

SVE1-LS5 Neurobiology

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions (PR, PU-PH, MCF, MCU-PH)	40	46
N2: Permanent EPST or EPIC researchers and similar positions	16	15
N3: Other permanent staff (without research duties)	44	45
N4: Other professors (PREM, ECC, etc.)CCA, AHU	3	
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) PH+Post-doc	30	21
N6: Other contractual staff (without research duties)	20	7
TOTAL N1 to N6	**153**	**134**

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	37	
Theses defended	41	
Postdoctoral students having spent at least 12 months in the unit	12	
Number of Research Supervisor Qualifications (HDR) taken	10	
Qualified research supervisors (with an HDR) or similar positions	47	51

2 • Assessment of the unit

Strengths and opportunities related to the context

The unit had an excellent scientific production over the past years. The international visibility of key researchers is also excellent. They performed an impressive emphasis upon intellectual property management: 19 filed patents or patent applications, 2 spin-off companies and 1 drug entering Phase I. They launched successful programsof translational research in their field of expertise. The integration of clinicians within the unit and close relationship with university hospital is also excellent.

Weaknesses and threats related to the context

Publication profile could be improved by aiming at publishing in higher impact journals perhaps favoring larger andmore comprehensive studies instead of splitting data into several reports as it seems to occur in some cases. The national funding situationcould surely be improved, as well as the relative lack of international funding (the unit support comes mostly from French grants). At the international level, they are in a very competitive field for at least what concerns research on Alzheimer's and Parkinson's diseases.

Recommendations

Here are the recommendations that the committee would like to offer for the unit:

- setting up a lab life at the unit level;

- establishing mechanisms by which the different teams will learn to know each other: internal seminars, day of retreat for all team leaders at the center, etc;

- promote social and after-work interactions between PhD students and post-docs from the different teams to further improve the communication within the unit;

- increase the possibility for career progression for university employees.

3 • Detailed assessments

Assessment of scientific quality and outputs

JPARC as a unit has produced a large number of contributions (>580 peer-reviewed papers) with >300 with JPARC members signing a first and/or last authors and >270 in collaboration. The major contributions appeared in top journals while most production comes out in leading specialty journals. The appraised period has seen an attempt to publish in high profile journals, an effort that must be pursued while the “salami” publishing strategy (slicing into several papers stories that could be told in one single very high profile publication) should be avoided. Both the former and proposed directors are fully aware of such a need.

Assessment of the unit's academic reputation and appeal

JPARC is obviously well connected with the academic world as supported by the large number of published collaborations (>270), the numbers of grants received in collaboration, and the extensive network supporting the research efforts. The committee wishes to see more international students (PhD, post-doc) as well as more visiting professors or scientists. This is in contrast with the strong involvement in excellence grants such as SIRIC OncoLille, the Labex DISTALZ and the LIA Neurobese (which strikingly does not lead to a lot of exchanges between California and Nord-Pas de calais).

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

JPARC is a leading unit in Europe with regard to the interaction with the economic world. Not only JPARC holds a number of funded collaborations with industry but it also features the striking particularities of (I) issuing a large number of patents (19), (II) favoring the spin-offing by JPARC researchers (2 spin-off companies) and (III) having one proprietary molecule (protected by one of their patent) entering Phase I clinical trial. This is clearly an asset of JPARC that must be continued.

Assessment of the unit's organisation and life

Attention of director’s efforts should be directed towards the aim of creating a lab life, a sense of unity and belonging. Both the scattered organization in several (3 now, 5 tomorrow) buildings as well as the variety of research topics (neuroscience, oncology, medicinal chemistry) call for active policies favoring scientific exchanges and the cross-fertilization among research topics (the experts committee clearly sees the advantage of mixing oncology and neuroscience). Experience demonstrates that such communication among teams is achieved through students and post-docs. Regular internal seminars (scientific and technical) as well as social events should be organized for budding future visibility of JPARC/Campus through dissemination of scientists willing to send their own students in such environment.

Assessment of the unit's involvement in training through research

JPARC members are involved in teaching at university and in training through research at the expected level for a unit of that size on a campus like Lille. The meeting with the head of the main École Doctorale (446 Biologie Santé Lille, Nord, France) indicated that the unit is very active in the training of graduate and PhD students in the university. Moreover, the training effort of the unit is quite evident at the interface between fundamental and clinical research, since both scientific and medical students obtain excellent research training in the unit. The unit is obvisouly well-visible in the university for its training and formation capacity.

Assessment of the strategy and the five-year plan

Transition between the former and proposed director is exemplary with a continuity in envisionnning what the future of the unit should be.

The committee, however, felt that teams in general are very large (6 teams for >220 persons) and that the emergence of new independent teams should be supported. JPARC structure is currently at odds with international view of research organization in smaller teams led by a single team leader. While the committee ackowledges the history, it also encourages more junior researchers to take their responsibility and accept to face the challenge.

4 • Team-by-team analysis

Team 1: Alzheimer's & tauopathies

Name of team leader: Mr Luc BUÉE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	9	9
N2: Permanent EPST or EPIC researchers and similar positions	5	4
N3: Other permanent staff (without research duties)	4	4
N4: Other professors (PREM, ECC, etc.)	1	
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	5
N6: Other contractual staff (without research duties)	7	2
TOTAL N1 to N6	**27**	**24**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	10	
Theses defended	10	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	11	13

• Detailed assessments

Assessment of scientific quality and outputs

The group has contributed to the understanding of tau protein phosphorylation and splicing with the discovery of the abnormal tau splicing and tau protein pattern in myotonic dystrophy, topics that continue to be investigated with success. Another original aspect of the research in the group is the study of the interaction between the environment and development of tau dysfunction and related diseases. This includes the epigenetic studies. The output is good, many papers have been published by the group, and some in excellent journals (J. Neurosci., Neurology, Diabetes). The Alzheimer's field is very competitive and sometimes publishing in good but not excellent journals is the way to publish first, this is a pity because the work that the group is doing could be published in top

journals and this is what the group should aim for. This point is also recognised by the principal investigator in his report were he hopes that the arrival of new postdoc-fellows will allow to publish in top scientific journals.

Assessment of the unit's academic reputation and appeal

The group is at the forefront of international research on dementia in particular on research in tau protein pathology and Alzheimer's disease. Accordingly the principal investigator is often an invited speaker (including plenary lectures) at international conferences on neurodegenerative diseases and is awarded important prizes.

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

The interaction of the team with the environment, either social, economic or cultural is excellent. The team has helped to develop facilities for clinical diagnoses for Alzheimer's disease and tauopathies in the neighbouring hospital, has several patents, a spin off company and a drug going to phase one. They are involved in the public engagement inscience, with interaction with students, patients and general lay people.

Assessment of the unit's involvement in training through research

A team member is in charge of the doctoral studies and members of the group have trained and are training several students at different levels. Therefore the group is greatly involved in training through research. Besides this the team has been involved in European training consortia.

Assessment of the strategy and the five-year plan

The plan for the next 5 years is clearly described, it is strong and based on results previously obtained from the group but also develops new findings in the field such as spreading of tau protein. The original epigenetic work will be further developed. The group has several transgenic models that will be used for identification of toxic mechanisms that could become a target for therapies. The link with team 6 will become stronger when they become member of the center and it is likely that new molecules will be developed and tested in the available model. The future of the team is solid.

Conclusion

This is a strong team at the forefront of international research on Alzheimer's disease and tauopathies in particular. The future plan supports that the international visibility and competitiveness of the group will continue in the future.

- ***Strengths and opportunities:***

Large number of publication in specialty journals.

Historical focus maintained upon a booming field (anticipation).

Exciting high risk/high gain project on tau presence/translocation to nucleus.

Spin-off company with a compound entering phase I directly arising from team's work (basic & preclinical science).

International collaboration.

Large visibility as supported by the number of invitations, the Claude Pompidou Prize, etc.

- ***Weaknesses and threats:***

The team project is situated in a highly competitive field.

- ***Recommendations:***

Underselling the high-quality work of the team, acknowledged by the group leader, should be minimized in the future.

Supporting the budding off of junior teams.

Team 2: Development and plasticity of the postnatal brain

Name of team leader: Mr Vincent PRÉVOT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	7	6
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	7	3
N6: Other contractual staff (without research duties)	3	1
TOTAL N1 to N6	**22**	**15**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	5	
Theses defended	8	
Postdoctoral students having spent at least 12 months in the unit	5	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	8	7

Assessment of scientific quality and outputs

The team assembled by the group leader to study the 'Development and Plasticity of the Postnatal Brain' is a very strong one. The group leader and a researcher are internationally recognized investigatorsdoing beautiful work; a junior researcher is a rapidly rising star. They have been productive scientifically, as evidenced by their list of impressive publications. In particular, 4 Cell Metabolism, 1 PLoS Biology, 1 PLoS Genetics and 1 PNAS papers that have emerged from the teamcan be highlighted.

Assessment of the unit's academic reputation and appeal

A number of researchers in this team are *bona fide* world leaders in their respective subject areas, particularly in the specialties of tanycyte biology and hypothalamic development and plasticity. They are also well known and respected in the broader fields of fertility/reproduction and obesity respectively. Part of their strength is that they represent a very 'outward-looking' and cosmopolitan lab, with close interactions with the Saban Research Institute in

Los Angeles California, USA. This is consequently reflected in the attractiveness of the lab to many researchers from outside France, which is always a healthy situation for any research institute.

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

It is clear that fertility and obesity are critical topics that are ever present in the social, economic and cultural environment of today. The members of this team certainly play their part, actively interacting with the media and lay public, both in terms of disseminating their scientific findings, but also in engaging the lay public on broader scientific issues. Here, the teams links with the Saban and with EU consortia, ensures that this engagement is truly international.

Assessment of the unit's involvement in training through research

Members of this team have displayed a commitment to training of the next-generation of scientists. For example, the team members were key drivers in a FENS (Federation of European Neuroscience Societies) summer school and other European union wide training programmes. They have trained a number of masters, PhD students and post-docs.

Assessment of the strategy and the five-year plan

The strategy and five-year plan is well structured, with a nice mix of exciting projects ranging from low to high-risk prospects. The committee is somewhat surprised however, that the team did not focus a more on the topics in which they are undoubted worl-leaders. Specifically, tanycyte and hypothalamic development are only addressed in one of the objectives; and the actual biology of tanycytes, particularly their role as 'gate-keepers' in regulating the transport of peripheral signals and hormones into the hypothalamus, is not addressed at all.

Conclusion

This is a very strong team, within a very good unit, and their strategy is a good exemple of what is required to ensure international competitiveness.

- **Strengths and opportunities:**

World-leader team in the tanycyte and post-natal hypothalamic development fields.

Team is well known in the field of reproduction and obesity.

- **Weaknesses and threats:**

Puzzling lack of ANR (Agence National Recherche) funding.

- **Recommendations:**

Recruitment of an electrophysiologist.

Take advantage of the team's expertise and study the tanycyte biology.

Further increase interactions within the unit.

Team 3: Early stages of Parkinson's disease

Name of team leader: Mr Alain DESTÉE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	3
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	4
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**9**	**10**

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

- Detailed assessments

Assessment of scientific quality and outputs

The Team "early stages of Parkinson's disease" is a relatively young team created in 2010 with a main focus on the biology and symptomatology associated with early Parkinson's disease. During the last 4 years, the team has participated in the identification of a new gene involved in PD (EIF4G1) in collaboration with a laboratory in Canada, and participated to the genetic effort in Parkinson's disease (new mutations in known genes (SNCA) involved in Parkinson's disease). By using transcriptomic analyses, the team has identified the impairment of new molecular pathways in peripheral blood cells from Parkinson's disease patients. In addition, the team has implemented a new rotenone-base model of Parkinson's diseasein order to investigate the early phase of Parkinson's disease (unpublished yet). In parallel, the clinicians of the team have built well-characterized cohorts of Parkinson's disease patients, particularly at the early stage of the disease. Thanks to these efforts, the team has played an important role in international Consortia of genetics and clinical research in Parkinson's disease, although there are more limited scientific production as primary authors (e.g. Lancet Neurol publications).

Assessment of the unit's academic reputation and appeal

The team is well recognized at the national and international level in the genetics of Parkinson's disease with several international collaboration and invitations to international events. The reputation goes far beyond what could be expected from a team that size. The preclinical work, however, does not succeed in attracting the same attention or the same appeal. We recommend the team to look for international post-docs in both domains.

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

Involvement of the group leader in several national policy making councils, effort in publicizing science towards lay audience, patient organizations. Such involvement is clearly above what could be expected from a small team but the efforst are down to a single individual.

Assessment of the unit's involvement in training through research

The team is participating in the local Master and PhD programs, as well as the training of medical students for the clinicians. Since 2008, the team has hosted 6 Master 2 and 4 PhD students.

Assessment of the strategy and the five-year plan

The projectis in the continuity of previous objectives and findings. The project focuses on the investigation of the new molecular cascades that have been identified by transcriptomic analyses in peripheral blood cells. The project is relatively straightforward concerning the part aiming at deciphering the role of these pathways by using gene targeting approaches in animal models and cell models. The toxic model is probably interesting for exploring these pathways at a very early stage of the disease although the link between the peripheral markers and the pathological process in the brain remains to be clarified. Pharmacological approaches are also proposed, particularly with new potential neuroprotective compounds. Is the toxic model sufficiently reproducible for testing these compounds ?

The biomarker project is based on the cohorts that have been implemented by the clinicians and the expertise of the team in transcriptomic and RNAseq analyses. Is the RNA a suitable material for clinical use as a peripheral blood marker ? Is there any protein marker that could be used instead ?

Conclusion

In conclusion, a good team with a large collaboration network thanks to their cohort management and expertise in genomics. Attention to be paid onto (I) managerial transition and (II) relative weakness of the preclinical research output.

- ***Strengths and opportunities:***

Arrival of new team members (scientist, post-doc) stregthning the working capacity.

Well defined cohorts allowing to focus on early stages of the disease.

The Ghrelin project is an asset for the team.

- ***Weaknesses and threats:***

Team management at time of current PI retirement is unclear with a clear threat upon cohort management (or access to cohorts).

Is the toxic model aneasy reproducible and viable model for testing disease-modifying compounds ?

Funding of preclinical research.

Peripheral blood biomarker is highly competitive field: How to use RNA as clinical screen ?

- ***Recommendations:***

Careful analysis of the selected spreading model vis-à-vis the current available manpower for testing disease-modifying candidates. A better focus on transcriptomics and genomics may be recommended.

Team 4: Factors of persistence of leukemia cells

Name of team leader: Mr Bruno QUESNEL

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	5	7
N2: Permanent EPST or EPIC researchers and similar positions	3	4
N3: Other permanent staff (without research duties)	4	9
N4: Other professors (PREM, ECC, etc.)	1	
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	8	7
N6: Other contractual staff (without research duties)	4	1
TOTAL N1 to N6	**25**	**28**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	4	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	5	8

- ## Detailed assessments

Assessment of scientific quality and outputs

The team as a whole have produced a high number of publications (163 since 2008) mostly in specialised journals like Blood, Leukemia, Haematologica and a couple of high impact factor papers in New England Journal of Medicine, Nature Medicine, etc, either as primary or as collaborations. Most of these publications come from their work on the genetic analysis and screening of mutations and the association of these mutations with clinical outcome. This team is indeed recognised nationally for their work on this aspect and is really well-linked with clinical consortium and well-involved in the follow-up of clinical trials. The work on the aspect of cell dormancy is producing considerably less.

Assessment of the unit's academic reputation and appeal

The team is well recognized at the national level for their genetic analysis and screening of mutations in leukemia. The team is a member of the European Leukemia Net and its reputation in dormancy is also recognised by his invitation to international meetings.

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

The team has been helping the creation of a Biotech company, they have link with industrial company (SERVIER, ONcoVET), and have some visibility at the European level with an involvement in the European Leukemia Net.

Assessment of the unit's involvement in training through research

The team is participating in the local Master M2R Lille, as well as in the training of PhD students and masters. Since 2008, the team has hosted 18 Master 2 and 11 PhD students. The implication of the team in the overall graduate training is thus excellent, both in fundamental and clinical cursus. To note here the lack of post-doctoral fellows.

Assessment of the strategy and the five-year plan

The projectis in the continuity of previous objectives of the team especially on the aspect of genetic screening using both targeting mutations analysis and next generation sequencing technique. The recent to the team of a brilliant pharmacogenomic investigator nicely complements the study of genomic markers. The project will also bring the xenotransplantation model for the study of clonal evolution. The project on dormant cells will be extended with the use of new mouse models (both syngeneic, xenotransplantation model and possibly melanoma model). The insertion of 4 members of team 4 will bring a new expertise in tumor metabolism, cell death and drug targeting DNA notably which might be helpful to better define dormant cells.

Conclusion

The team is well-recognised for its works on genomic analysis, “minimal residual disease” evaluation after treatment and thus should continue to build-up upon its establsihed track-record. The addition of the xenotransplantation model both for the study of clonal evolution and pharmacogenomic is certainly going to strenghten this aspect of the work. The aspect of dormant cells is a really competitive field.

- ***Strengths and opportunities:***

A clear opportunity will be to build-up upon established track-record especially genomic study and minimal residual disease evaluation.

Another opportunity will be to take advantage of primary patients samples.

Development of new models for dormancy / residual malignant cells (like xenotransplantation, melanoma project).

Rising of pharmacogenomic with the hiring of an experienced researcher.

Genomic screening is an asset.

- ***Weaknesses and threats:***

Very competitive field with highly specific (re)definition of dormancy concept needed.

Unclear what is the effect of immortalisation of dormant cells.

- ***Recommendations:***

Taking advantage of the minimal residual disease and chemoresistance with the pharmacogenetic project, should help bring the themes of the team together and help reinforce collaborative studies between team members. It will be indeed helpful to delineate better the “dormancy concept” and see how this overlaps with minimal residual disease and chemoresistant cells. This will allow more interaction between team members.

Take advantage of the integration of new researchers with expertise on solid tumors and metabolism.

Take advantage of the establishment of the xenotransplant model to study “dormant cells” and look into the overlap with chemoresistance.

Considering cooperation with team 5 for stemness project.

Working onto inter-team scientific exchanges (especially with other oncology teams via SIRIC) should be encouraged.

Recruitement of more post-docs should also be encouraged.

Team 5: Mucins, Epithelial differentiation and Carcinogenesis

Name of team leader: Ms Isabelle VAN SEUNINGEN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	12	13
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	5	5
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	2
N6: Other contractual staff (without research duties)	2	
TOTAL N1 to N6	**24**	**22**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	11	
Theses defended	8	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	4	
Qualified research supervisors (with an HDR) or similar positions	14	13

- ## Detailed assessments

Assessment of scientific quality and outputs

The team has a long experience in the field of mucins, since it is a continuation of a group working on the structure and biology of mucins for over 40 years. It started out by the Aubert group that identified MUC5AC and MUC5B and the human orthologue of MUC4 (previously described in rat by Carraway et al.). The group has then decided to focus on the transmembrane mucins MUC1 and MUC4 in relation to cancer development. These are two different mucins belonging to two different groups of transmembrane mucins. The MUC1 mucin has been extensively studied in relation to cancer for many years. The MUC1 interaction with galectins and galectin 3 has been studied by several groups. The MUC4 mucin is unique in higher organisms as it is only one of its type (NODO-AMOP-VWD) in comparison to MUC1 (SEA-type) that is part of a larger family. Little is known of the MUC4 mucin except that it might bind ErbB2. Actually, the role of the transmembrane mucins is still an open question and they are probably important

for some of the altered properties of cancer cells and metastasis as they are important for cell interactions. Less is understood on how these molecules could be involved in tumor cell progression.

The team is very familiar with mucins, a difficult area to work with. There are few competent groups in the world in this area and, as the interest is increasing, there is an interesting opening for further development. The study of gene regulation and role of epigenetics is unique for the group and has given important knowledge. This team is the only known research group that is able to develop this area.The scientific production of the team is globally satisfactory. Its most recent focus on the study of the role of cell membrane-bound mucins in epithelial carcinogenesis was very productive. However, many of the papers of these last five years were produced in collaboration and are not related to the main and highly visible topics of the team (e.g. Ann Surg Oncol., Eur J Surg Oncol, Ann Surg).

Assessment of the unit's academic reputation and appeal

The group benefitsfrom international and national recognition in the field of mucin biology. It participates in several national networks. International recognition of its director is well demonstrated by her participation as invited speaker in specialized international meetings. Concerning attractivity, it should be noted that the number of post-docs who joined the group during the last five years was very limited and should be increased in the future. Globally, the team leader should recruit more skilled scientists and full time researchers to reinforce the group. The team has a great ability to raise funds. However, these allocations are essentially fromregional and national origin. No European grant was obtained during the last five years.

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

The group was strongly involved in the diffusion of scientific information by press articles and conferences. It also developped strong translational research with clinician teams. Its director must be cautious, however, concerning the risk of thematic dispersion induced by too many and too diffuse and collaborative projects.

Assessment of the unit's involvement in training through research

The team is very well involved in training through research since several of its members have been involved in the conception and coordination of several modulesand teaching units of the master degree (level master 1 and master 2). It also participates inthe animation of the doctoral school ED 446.

Assessment of the strategy and the five-year plan

The number of models under study seems excessive and the ten research programs mentioned in the project of the team (not including translational research projects) may be difficult to manage at the same time. The large number of projects induces a serious risk of thematic dispersion. The group is recommended to focus more on fewer projects, particularly interesting is the MUC4 mucin and its normal function, for example NIDO-AMOP-VWD domains, and focus less on MUC1 as there is more competition and especially too many incorrect publications to work against (more difficult to publish that something is wrong than to publish something new).

Conclusion

This team makes globally a very good job and beneficiatesfrom an international recognition in the field of mucin biology. However, its director must avoid a dispersion of thematic projects and focus on the areas of excellence in which the team is recognized. The group includes too few skilled full-time scientists and the recruitment of new full-time researchers and post-docs should be highly encouraged. Publications of the team should be more focused on its field of excellence. European grant applications should be deposited.

- ***Strengths and opportunities:***

Good productivity considering the number of researchers.

Great visibility in the mucin field.

Main project on mucins (especially MUC4) is unique, very interesting and original.

- ***Weaknesses and threats:***

A significant number of publications are actually outside the scope of the team.

Ten research projects for 1 researcher/2 maître de conferences/several clinicians: risky imbalance.

- ***Recommendations:***

While investing succesfuly upon translational research, the team should not loose focus upon its core expertise and research focus.

Change recruitment policy, favor hiring skilled Post-doc researchers with an aim to do more ground-breaking science.

Aim for fewer, but better publications.

Team 6: Onco and Neurochemistry

Name of team leader: Ms Patricia MELNYK

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	8	8
N2: Permanent EPST or EPIC researchers and similar positions		
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	2	2
TOTAL N1 to N6	**12**	**12**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	6	
Theses defended	10	
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	6	6

• Detailed assessments

Assessment of scientific quality and outputs

The scientific quality of the members of the team is strongly established. Their scientific production in terms of articles during the previous period (2008-13) is important with 66 published articles, some in excellent journals of the field (e.g. ACS Chem Biol, J Med Chem). Their integration in JPARC could however lead to an increase of the impact factor of their papers.

Assessment of the unit's academic reputation and appeal

The academic reputation of the members of the team is good and especially attested by the number of international congresses to which they were invited during the previous period. Their international reputation remains however to be improved. Their ability to obtain grants is excellent.

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

The industrial development strategy of the members of the team is excellent with 13 patents, the contribution to the marketing of a drug and the creation of a spin-off, at a level well beyong the national competition.

Assessment of the unit's involvement in training through research

The activity of the members of the team in training through research is very good and correlated to their number.

Assessment of the strategy and the five-year plan

The strategy of the future team will succeed if it becomes a true resarch team and not only a “service delivery platform”. Consequently it will have to limit the number of its projects and to give the priority to those which will concern validated targets concordantly studied with the other teams of JPARC. This medicinal team will have also to be a “prime mover” in this field.

Conclusion

The integration of a medicinal chemistry unit in a biology reaserch center is an exciting challenge with some risks but the results previously obtained by the members of the future team speak for the succes of the objective of the latter especially in its novel scientific environment. A chance should be given to this project.

- ***Strengths and opportunities:***

Patent publications and deliveries.

Successful past collaborations with JPARC teams.

Industrial partnerhsip.

Technological transfer strategy, among the rare example of succesfull transfer of academic medicinal chemistry to market/clinic.

Large number of post-docs.

Opportunity for improving publication profile within thre JPARC environment.

Strong local and institutional support.

- ***Weaknesses and threats:***

Different locations from the rest of the teams (5 min walk but still away…).

Lack of scientific focus (too many projects).

Succeed in integration of biology and biology researchers in the projects.

- ***Recommendations:***

Integration of biologists into the medicinal chemistry team.

Co-supervision of PhD students or post-docs on specific projects with the other teams ?

Management of distance by regular scientific meetings, journal clubs, etc..

5 • Conduct of the visit

Visit dates:	
Start:	20.01.2014, at 9.00 am
End:	21.01.2014, at 3.00 pm
Visit site:	Centre Jean Pierre Aubert
Institution:	Université Lille 2
Address:	Faculté de Médecine - Pôle Recherche Institut de Médecine Prédictive et Recherche Thérapeutique, 59045 Lille France
Specific premises visited:	Biserte and IRCL buildings

Conduct or programme of visit:

January 20th 2014

08.45-09.00 am	Arrival to laboratory
09.00-09.25 am	Committee discussion (closed door)
09.25-09.35 am	Presentation of AERES by the scientific delegate (DS) M. Laurent GROC Presentation of experts committee by the chair M. Erwan BEZARD
09.35-10.20 am	Unit presentation by Mr Pierre FORMSTECHER and Mr Luc BUÉE (Past/Future)
10.20-10.40 am	Coffee break
10.40-11.20 am	Team 1 - Mr Luc BUÉE
11.20-12.00 pm	Team 2 - Mr Vincent PRÉVOT
12.00-12.40 pm	Team 3 - Mr Alain DESTÉE/Ms Marie-Christine CHARTIER-HARLIN
12.40-01.30 pm	Lunch (on site) with all lab members (free discussions)
01.30-02.10 pm	Team 4 - Mr Bruno QUESNEL
02.10-02.50 pm	Team 5 - Ms Isabelle VAN SEUNINGEN
02.50-03.30 pm	Team 6 - Ms Patricia MELNYK
03.30-04.00 pm	Coffee break
04.00-05.30 pm	Parallel meetings: - meeting with students/postdocs - meeting with ITAs - meeting with researchers (without team leader and director)
05.30-05.45 pm	Meeting with the head of the École Doctorale (head: Mr Bernard SABLONNIÈRE)
06.00 pm	End of the day

January 21th 2014

08.45-09.00 am	Arrival to laboratory
09.00-09.35 am	Meeting with institutions (tutelles)
09.35-10.15 am	Interview with Mr Pierre FORMSTECHER et Mr Luc BUÉE (closed door)
10.15-03.00 pm	Closed door final meeting (lunch on site)
03.00 pm	End of the visit

Specific points to be mentioned:

The meeting with the funding/supporting institutions was particularly impressively attended by institution representatives from INSERM (national and local representatives), Université de Lille 2 (Research vice-president + deans of medecine and pharmacy), Centre Hospitalier Régional Universitoire (Research vice-president of the directoire), Université de Lille 1, Université d'Artois, Institut de Recherche sur le Cancer de Lille and the Nord-Pas-de-Calais region. Those representatives expressed their support and the importance of the unit for the local and national strategy. The experts committee was unanimous in stating this had not been seen before in previous committees.

6 • Supervising bodies general comments

Université Lille 2
Droit et Santé

Service de la Recherche, de la Valorisation
et de l'Information Scientifique (SeRVIS)
Affaire suivie par Christophe BOUTILLON
Directeur du SeRVIS
christophe.boutillon@univ-lille2.fr / 03.20.96.52.16

Le Président de l'Université

à

Monsieur le Professeur Pierre GLAUDES
Directeur de la Section des unités de recherche
Agence d'Evaluation de la Recherche et de l'Enseignement Supérieur (AERES)
20 rue Vivienne
75002 PARIS

Lille, le 24 mars 2014

V/Réf. : E2015-EV-0593560Z-S2PUR150007720-006354-RT

Objet : Observations de portée générale sur le rapport d'évaluation de l'unité *Centre de Recherche Jean-Pierre Aubert (JPARC)*

Monsieur le Directeur,

Considérant le rapport que vous m'avez récemment transmis, je vous remercie au nom de l'Université Lille 2 et en particulier du directeur et des membres de l'unité *Centre de Recherche Jean-Pierre Aubert,* pour la qualité de l'évaluation effectuée les 20 et 21 janvier 2014 par votre comité d'experts.

Les appréciations et recommandations formulées seront soigneusement prises en considération et discutées avec le directeur de l'unité dans le cadre de la structuration de notre recherche pour le prochain plan quinquennal (2015-2019).

Vous trouverez ci-dessous les observations de portée générale sur le rapport d'évaluation de l'AERES, émises par le Directeur de l'unité *Centre de Recherche Jean-Pierre Aubert.*

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

Pr. Xavier VANDENDRIESSCHE

UMR 837
Centre de recherche Jean-Pierre Aubert
Rue Polonovski, Lille, France
Luc Buée, Directeur-adjoint
Tél. : 33 (0) 3 20.29.88.50
luc.buee@inserm.fr

Comité dévaluation AERES
Vague E

Lundi 24 mars 2014

Dear Madam, dear Sir,

First of all, we would like to thank the AERES visiting committee for the time spent and the very helpful analysis of our research centre activity. We would like also to take this opportunity to emphasize two points: 1) the added-value of team 6 to the projects of the research centre and 2) on the involvement of the two Cancer teams (4 and 5) in the newly appointed Comprehensive Cancer Center "SIRIC ONCOLille". In fact, the two Cancer teams (4 and 5) are key founder teams of the newly appointed Comprehensive Cancer Center "SIRIC ONCOLille" by French National Cancer Agency (INCa). Professor Bruno Quesnel who leads the team 4 is the coordinator of the research program on "Tumor Dormancy" and Professor Christophe Mariette (Team 5) is the coordinator of the second research program of SIRIC ONCOLille on "Tumor Resistance".
This emphasizes the excellence of the translational research developed by our teams at the regional and national levels.

Regarding the team-by-team analysis, each director has only minor comments.

Team 1
We thank the expert committee members for their evaluation report.

Team 2
We thank the expert committee members for their evaluation report.

Team 3
We would like to underline that the managerial transition has already been prepared by Professor Destée during the first "five-year period" with Dr. Chartier-Harlin, Inserm research Director (DR2), acting as a deputy director of the current team and participating to all board of directors of the JPArc (see the program of the AERES visit). She animates the research group, is the PI of the CRB collection and acts as a scientific coordinator in all the clinical research programs with Professor Destée since 1993. From the clinical point of view, a transition with Dr. Mutez is also taking place in the Movement Disorder Clinic of the Hospital. So, there will be no problem

regarding cohort's management and access to patients' samples after Professor Destée's retirement.
We acknowledge the AERES members opinion according to which "the reputation of our group goes far beyond what could be expected from a group of that size". We are aware that "the preclinical work does not succeed attracting the same appeal." Indeed, our previous project was focused on the identification of the deleterious pathways from early to late stages of Parkinson's disease and, as a natural continuity their investigation in preclinical models has only been set up and developed during the last few months. The validation of these disturbed pathways in those models demonstrates the efficiency of our scientific strategy. Of note, besides the rotenone models mimicking the early stages of the disease, we use other reproducible models such as SNCA transgenic mice to test compounds with neuroprotective potential. In the future, these aspects will be developed thanks to the support of the university Lille 2 with the recruitment of a "maître de conferences" by the end of 2014 and the integration of Dr. O Viltart in 2015. We also received funding from the Region Nord-Pas de Calais for a senior researcher to develop such experiments. Regarding biomarkers, they all present limits; adjustments and large scale validations are necessary before a transfer in clinical routine. Our transcriptome candidates will be tested thanks to technological evolutions not only from RNA, but also proteins together with □□synuclein and with the collaboration of other groups.
The "involvement of the Pr Destée's team in the interaction with social, economic and cultural environment that is clearly above what could be expected from a small team, but the effort are down to a single individual". Other members of the team are also similarly involved at the international and national level (ex: Dr Chartier-Harlin chairwomen of SAB of LECMA, Dr Vanbesien-Mailliot, elected member of the neurosciences section of the National University Council (CNU 69)...).
Our group is also highly implicated in the training of PhD students and post-docs at the international level through the organization of workshops in collaboration with the European Graduate School of Neuroscience (EURON) scientific board, the Rotary International Educative programs for North of France. We are also part of ERASMUS exchange student program.

Team 4
We thank the expert committee members for their evaluation report.

Team 5
1- Epithelial cancers and resistance:
Next to the excellent evaluation of the research on mucins by this team, it should be emphasized that the team led by Dr Van Seuningen is a key founder team of the newly appointed Comprehensive Cancer Center "SIRIC ONCOLille" by French National Cancer Agency (INCa) with Pr Christophe Mariette, a member of Van Seuningen team, being the coordinator of the research program of SIRIC ONCOLille on "Tumor Resistance".
This strategic positioning should lead this team, in the coming years, to become a national reference in the field of solid tumor resistance to loco-regional treatments.
This also emphasizes the excellence of the translational research developed by this team both at the regional and national levels.

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Email : jparc@lille.inserm.fr

2- Recruitment policy:
Recruitment policy is ongoing and was successfull in 2012 with the recruitment of a CR1 Inserm full-time researcher to lead the research necessitating original transgenic models of cancer and the on-going presentation of another young researcher to Inserm and CNRS CR2 "concours" in 2014 to develop emerging research on the role of epigenetics and differentiation of stem cells in epithelial tumors. A third young researcher, presently post-doctoral fellow at NCI (Bethesda), will come back in 1-2 years to become Inserm/CNRS full-time researcher and develop, in relation with the research of the team on solid tumor resistance to loco-regional treatments, a research theme focusing on the tumor-stroma relationship.

Team 6
We thank the expert committee members for their evaluation report and their acknowledgements of the exciting challenge of our project based on successful past collaborations with the centre.

Luc BUEE

Le Président de l'Université
Xavier VANDENDRIESSCHE

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