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

Department for the evaluation of research units

AERES report on unit:

Saint-Antoine Research Centre

CDR-SA

Under the supervision of the following institutions and research bodies:

Université Paris 6 - Pierre et Marie Curie

Institut national de la santé et de la recherche médicale

December 2012

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

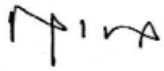
Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head



Pierre Glaudes

The president of AERES "signs[...], the evaluation reports, [...]countersigned for each evaluation department by the relevant head of department (Article 9, paragraph 3, of french decree n°2006-1334 dated 3 november 2006, revised).

Grading

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

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

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

Criterion 1 - C1: Scientific outputs and quality;
Criterion 2 - C2: Academic reputation and appeal;
Criterion 3 - C3: Interactions with the social, economic and cultural environment;
Criterion 4 - C4: Organisation and life of the institution (or of the team);
Criterion 5 - C5: Involvement in training through research;
Criterion 6 - C6: Strategy and five-year plan.

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

- Grading table of the unit: Saint-Antoine Research Centre, CDR-SA

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

- Grading table of the team: Progenitors and Endothelial cells during and after pregnancy

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

- Grading table of the team: Role of the transforming growth factor beta (TGF□) signaling pathway in tumor progression

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

- Grading table of the unit: Molecular lesions, initiation, and evolution of myeloid malignancies

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

- Grading table of the unit: Proliferation et differentiation of stem cells : application to cell therapy

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

- Grading table of the unit: Microsatellite instability and cancer: from biology to clinics

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

- Grading table of the unit: Cancer Biology and therapeutics

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

- Grading table of the unit: Graft-vs.-Host Reactions after Allogeneic stem Cell Transplantation

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

- Grading table of the unit: Biology and Treatment of Hepatobiliary Tumors

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

- Grading table of the unit: Immune system, Neuroinflammation and Neurodegenerative diseases (IN2)

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

- Grading table of the unit: Metabolism and age-related joint diseases

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

- Grading table of the unit: Cystic Fibrosis: Physiopathology and Phenogenomics

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

- Grading table of the unit: Genetic and acquired lipodystrophies

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

- Grading table of the unit: Neuroendocrine Mechanisms of Longevity and Age-related Disease

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

- Grading table of the unit: Metabolic and biliary, fibro-inflammatory diseases of the liver

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

- Grading table of the unit: IGF system, foetal and postnatal growth

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

Evaluation report

Unit name:	Saint-Antoine Research Centre
Unit acronym:	CDR-SA
Label requested:	UMR_S
Present no.:	938
Name of Director (2012-2013):	Ms Jacqueline CAPEAU
Name of Project Leader (2014-2018):	Mr Bruno FEVE

Expert committee members

Chair:	Mr André PELEGRIN, IRCM, Université Montpellier 1
Experts :	Mr Serge ADNOT, Université Paris Est Créteil Val de Marne
	Ms Jane APPERLEY, Imperial College London, UK
	Mr Robert BALLOTI, Université de Nice Sophia Antipolis
	Mr Laurent BARTHOLIN, Centre de Reherche en Cancérologie, Lyon-Est
	Mr Luc BUEE, Université Lille 2
	Mr John DE VOS, Université de Montpellier
	Ms Marta GIRALT, Université Barcelone, Spain
	Mr Wieland KIESS, University of Leipzig, Germany
	Mr Diether LAMBRECHTS, Katholik University of Leuven, Belgium
	Ms Isabelle LECLERCQ, Katholik University of Leuven, Belgium
	Ms Nathalie THERET, Université de Rennes 1
	Mr Iniaccio TORRES ALEMAN, Institut Cajal, Madrid, Spain
	Mr Philippe ROINGEARD, Université Francois Rabelais, Tours
	Mr Michel SAMSON, Université Rennes 1

Scientific delegate representing the AERES:

Mr Jean GIRARD

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

Mr Paul INDELICATO, Université Pierre et Marie Curie

Ms Anne ROCHAT, INSERM

Mr Pierre TIBERGHIEN, Etablisement Français du Sang

1 • Introduction

History and geographical location of the unit:

The Saint Antoine Research Center (CDR SA) was first created as an emergent CDR in January 2008 and as a full CDR including 9 research teams in January 2009. Since its creation, it is affiliated to academic Institutions, Inserm and University Pierre and Marie Curie (UPMC). The CDR is thus quite a new one and was thus evaluated as such. The research teams are hosted in 2 different buildings of the Saint Antoine Hospital Campus (Kourilsky and Faculté de Médecine).

Management team:

The project leader who will act as Director in January 2014 has been elected in December 2011. He will be assisted by an administrative director (general secretary) and different committes with dedicated missions.

AERES nomenclature:

SVE1_LS4

Unit workforce:

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	59	65	64
N2: Permanent researchers from Institutions and similar positions	28	25	25
N3: Other permanent staff (without research duties)	85	79	19
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	2	5	1
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	18	18	7
N6: Other contractual staff (without research duties)	19	23	5
TOTAL N1 to N6	**211**	**215**	**121**

Percentage of producers	***100 %***

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	43	
Theses defended	63	
Postdoctoral students having spent at least 12 months in the unit*	32	
Number of Research Supervisor Qualifications (HDR) taken	19	
Qualified research supervisors (with an HDR) or similar positions	77	74

2 • Assessment of the unit

It appears to the committee that the current director during the past 5 years (2008-2012) as well as the project leader during the project preparation made a huge effort to move from several independent units and teams to a fully integrated research center. The CDR direction team should be congratuled for that. However, there is room for improvement and this must be done during the next 5 years contract with Inserm and UPMC if the CDR wants to position itself in the very competitive Paris' research area.

Strengths and opportunities:

The CDR is fully integrated in the Saint Antoine Hospital allowing real links with the clinic and structural support from the hospital, in particular, for clinical research and biobanks.

The CDR is composed of several good and even very good research teams. Collaborations have been mentioned in almost all presentations suggesting a clear will of collaborations between the teams.

Space for new groups will be available in the next years thanks to renovation of the Kourilsky building.

Since its creation, the CDR set up a scientific advisory board to be helped to define its scientific strategy and to prepare AERES and Inserm evaluations.

High financial support from Inserm and UPMC and high capacity of the research teams to obtain contracts from academic bodies (ANR, ANRS, INCa, Ligue contre le Cancer, EFS, …) as well as from industrial partners.

Participation of several teams in several "Investissements d'avenir" structures (IHU ICAN, IdEx Sorbonne, LabEx FR-ex and Immunomics, Cohort RADICO, EquipEx Hepather).

Weaknesses and threats:

The fact that the CDR addresses several medico-scientific topics within a global frame of physiopathology can be seen as a strength since real collaborations between the different teams could favor new ideas and projects. However, due to the scientific environment in Paris, it could be analyzed as a threat since it will be difficult for the CDR Saint Antoine to hire very competitive research teams in specific scientific topics.

Up to now, no international team recruitment following a dedicaded call.

The level of mutualized budget which is too low does not allow the Direction team to carry a scientific strategy at the CDR level. The power due to the available money is too centered in the teams and not enough at the CDR level.

Two independent buildings whose occupancy is not yet optimised for a research center.

Future of the technical platforms following the evolution of the management structure, from "IFR" to "SFR" . This evolution is often thought to be correlated to a decrease of funding by the supervising institutions and bodies making more difficult the access to these platorms.

Recommendations:

Define, express and display a more precise common scientific topic ("translationnal research" cannot be the only common topic).

More mutualisation at the scientific and financial levels.

As far as possible, aggregate all the CDR activities in adjacent premises.

As soon as possible, hire new groups by the way of an international call and with the help of the CDR SAB.

Attention should be paid to use all the "Investissements d'avenir" supports to build a common scientific CDR project and not to allow them to function as a centrifugal strength.

A global CDR strategy should be conducted on bioinformatics which is a crucial platform for many teams projects.

Organize at the CDR level a weekly internal seminar in which every investigator, clinician and engineer will present his/her results and projects in order to facilitate collaborations between teams and develop a common CDR scientific culture.

Give more information to the PhD students and postdocs on the available facilities and persons to contact to be trained for a particular technique.

Invite international researchers at the CDR Monday meeting.

3 • Detailed assessments

Assessment of scientific quality and outputs:

The CDR gathers very productive research teams with publications in high impact factor journals in their scientific field and, in some cases, in generalist journals (Nature, Science, New Eng J Med, JNCI, Cell). Some of the results can be considered as real breakthrough in their domain. Without being exhaustive, some examples are (i) World premiere: first injection into human of red blood cells generated in culture (cRBC), demonstrating that these in vitro generated cells behave similarly to transfused native RBCs, thus establishing the proof of principle for transfusion medicine; (ii) Identification of a mutant of the chaperone protein HSP110 in colorectal cancer (CRC) which could constitute a prognostic biomarker in stage III CRC, sensitizing cancer cells to chemotherapy (published in Nature Medicine in 2011, patented and recognized as "scientific hallmark of the year" in the 2011 Inserm final report); (iii) Demonstration of the existence of a bile acid gallbladder shunt, a mechanism by which the gallbladder may protect the liver and provide improvements in the therapeutic use of ursodeoxycholic acid and in understanding its actions including towards innate immunity via the vitamin D receptor (several publications in Hepatology, J Hepatol and Gastroenterology).

In a future presentation of the CDR scientific production, attention should be paid to clearly present publications fully integrated in the teams in a way different from clinical publications related to the clinical activity of the teams. As raw data, the table on page 5 of the CDR report can give a skewed view of the production of the most experimental teams which have no clinical publications.

Assessment of the unit's academic reputation and appeal:

The academic reputation and appeal of the different research teams from the CDR is ranked high or very high. It should thus be considered as high for the CDR based on an average calculation. However, the committee agreed to considered that this cannot be said for the CDR by itself. This is certainly due to the fact that the CDR is quite new (created in 2009) and that its identity and "spirit" remain to be developed. This will be a real challenge for the coming years and this should be taken into account as a priority for the five-year plan.

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

Due to its very strong links with the clinic and the quality of its research teams, the CDR has a high impact on the social and economic environment. Several teams leaders are international opinion leaders in their scientific or medical field of expertise. Many patents have been filled and several were licenced. Contracts with industrial companies and pharmaceutical laboratories are numerous. During the evaluation period, 16 patents were published, 7 patents were filled, 6 patents were licenced and a biotech company was created (HumanHepCell).

Assessment of the unit's organisation and life:

Major progresses have been made since the CDR creation in 2009 : strategy of organisation of an administrative team for the whole CDR, new high level SPF animal facility, "Forum of the CDR" (2-days annual seminar), "Monday conferences" (weekly seminar for external speakers), web site, common store.

However, there is room for improvement and this must be done during the next 5 years contract with Inserm and UPMC if the CDR wants to position itself in the very competitive Paris' research area. The governance tools seem to be here (several committees with dedicated missions) and the future director appears to be appreciated by his colleagues since his election in November 2011. A reinforced CDR's organisation should help him to develop a scientific strategy at the CDR level. Currently, the level of mutualized budget (20% of the funding allocated by Inserm and UPMC corresponding to less than 5% of the global income) is too low and does not allow the Direction team to carry a scientific strategy at the CDR level. The power due to the available money is too centered in the teams and not enough at the CDR level.

Even if the separate meeting with engineers and technicians did not reveal major problems, it outlines a lack of general discussions at the CDR level and some discrepancies between the teams' rules regarding engineer/technician position/presence on scientific publications, and buildings' rules concerning health and safety. If

the strategy to organise an unique administrative team for the whole CDR is appreciated, it remains to be finalized and optimized by the CDR Direction.

Assessment of the unit's involvement in training through research:

Very high involvement in PhD training (63 theses were defended from 2007 to end of June in 2012). Involvement remains to be improved for post-doctoral fellows with a specific orientation towards foreign candidates.

Overall, students judge that they are well trained and supervised and that the CDR provides a good scientific animation (lab meeting in each team every week, CDR Monday meeting and CDR annual seminar at Fontainebleau during 2 days). Most students have the opportunity to present their work in international meetings. Students regret, however, that the Monday meeting guests are rarely international researchers. Students are highly satisfied by the access to the CDR facilities and the training to different techniques provided within these platforms. However, they noticed that it is not always easy to know what is exactly available in these platforms (the existence of two different web sites for the CDR and the IFR/SFR is somehow confusing) and the right person to contact to be trained.

Assessment of the five-year plan and strategy:

For the next 5 years, the main scientific topics have been reduced from 3 to 2 : “Oncology-Hematology” and “Metabolism-Inflammation” illustrating a will to display a clearer strategy.

Quite a high number of research teams modifications are planned. The rationale of each of these evolutions is discussed in the different teams reports but, at the CDR level, it can be analyzed as a positive sign for its evolution.

The architectural evolution will still need some years since it will be completed only in 2015. However, the funding is here and, as far as it could be understood by the committee, some new research teams could be hired in 2014. In the next months, the strategy to hire these new groups should be precised at the scientific level as well as the practical one (Which topics will be favoured ? Which support will be allowed to the selected teams ?).

4 • Team-by-team analysis

Team 1 : Progenitors and Endothelial cells during and after pregnancy

Name of team leader: Mr Selim ARACTINGI and Mr Emile DARAI

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	7	7	7
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.)	1	1	
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	10	10	7

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	3	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	5	5

• Detailed assessments

Assessment of scientific quality and outputs:

History: Mr Selim ARACTINGI group is currently part of the team of Mr Pierre AUCOUTURIER. However, the themes led by Mr Selim ARACTINGI are very different from other thematic in the team. Therefore, the activity of the Mr Selim ARACTINGI group constitutes a new team project for the 2014-2018 period.

Achievements. The main themes of the Unit during the last 4 years focused on the study of the role of fœtal stem cells in tissue repair and tumor development, in the mother. This scientific niche aims at understanding the involvement of fœtal microchimerism in human diseases and to determine whether these fœtal cells present in the mother have beneficial or deleterious effects.

As part of this project, the team showed that endothelial progenitor cells of embryonic origin were involved in wound healing of the mother and also in the development of melanoma and breast cancer.

The team also showed that T cell precursors of fœtal origin can be transferred to the mother and colonize and reconstitute a functional thymus in the case of a mother carrying a genetic defect affecting lymphocyte lineages.

Finally, they showed that pregnancy augment angiogenesis in melanomas, through circulating agents.

All these works resulted in 24 scientific articles arising directly from the projects of the team. Publications are in journals of good quality, (FASEB J, PLoS one, Am J.Pathol, Int J Cancer, PNAS).

Assessment of the unit's academic reputation and appeal:

The works done by the team allowed the team leader to acquire a national and international reputation, as evidenced by the invitations (especially in Europe) and participation in the board of the journal "Chimerism", the journal of the specialty.

However, the team has yet little attractiveness for scientists. This trend seems to be reversed with the arrival of a new researcher (candidate for INSERM recruitment), who should bring a technical stability, which may miss to the team.

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

Industrial contracts with Astella, Wyeth, Osler, Poxel and Urgo.

Assessment of the unit's organisation and life:

This small team appears well organized. The two team leaders have found a good equilibrium for a shared leadership.

Assessment of the unit's involvement in training through research:

4 theses defended, 3 HDR, currently 3 PhD students.

Assessment of the five-year plan and strategy:

Projects are in line with previous work. Three themes of research will be developed:

1-Characterization of fetal cells that are mobilized during maternal wound healing.

The team has a GFP mouse model, which allows identifying and isolating cells of fetal origin from maternal tissues. This approach will allow them:

- To investigate the pluripotency of GFP cells isolated from the mother;

- To characterize the expression profile of these cells by RNA seq. They have already obtained results with qPCR on the expression of cytokine receptors. They will study the effects of the ligands of the identified receptors on the migration/invasion in vitro and in vivo. They will evaluate the epigenetic status of the fetal cells (EPC, endothelial progenitor cells);

They also will assess the possibility of reversion of healing defects in mothers with genetic alterations (OB / OB, Sickle cell disease, beta globin mutation). They will study the role of ligands/receptors previously identified, and the role of fetal cells.

2-Role of pregnancy on angiogenesis in normal or pathological tissues.

There are here two distinct parts. A Dermatology and an Obstetrics/Gynecology axes that are probably associated with respective clinical activities of the two leaders of the team. These studies will be conducted using appropriate mouse models (BRAFV600E, Nevi, BRAFV600E, PTEN-/-, melanoma, MMTV-vHRAS, Breast cancer, induced endometriosis) and human tissue xenografts in RAG2-/- mice). They aim to confirm the role of pregnancy on angiogenesis and to study signaling pathways in endothelial cells responsible for the increased angiogenesis. They will also study the effects of pregnancy on tumor cells.

3-Identification of stem cells responsible for benign proliferations of melanocytic cells.

This project aims to verify the presence of stem cells in nevi and congenital nevi, to characterize the specific molecular markers and their functional specificity (angiogenesis and signaling pathways).

The team continues to develop highly original projects with innovative approaches that can address important issues for skin or obstetric/gynecology conditions. The results obtained during the last 4 years show the ability of the team to carry out these projects.

The association of the two leaders of the team seems logical and mutually beneficial. It must be ensured that the role of the associated leader is not just restricted to the provision of normal and pathological human samples.

To switch from "very good" to "excellent" this team need to recruit scientists with strong expertise in cellular and molecular biology, will be a major asset. This process is already underway with the new recruit who ranked first on the complementary list of the 2012 CR INSERM competitive recruitment.

The team will need recruiting additional scientists to secure the scientific and technical achievements of the team. The Research Center may wish to provide a clear support to the team by promoting the recruitment of such researchers. One of the main tasks of these scientists will be to develop advanced molecular biology techniques for the studies of the signaling, transcriptional regulation and epigenetic modifications and thus further improve the scientific output of the team.

Conclusion:

- Strengths and opportunities:

Original projects, in the specific niche of fetal microchimerism. The papers published during the last 4/5 years are of very good level for a small team and predict a succesful achivement of the present project (or strengthen the feasability).

- Weaknesses and threats:

No basic scientist permanent position.

- Recommendations:

To switch from "very good" to "excellent" this team needs to recruit scientists with strong expertise in cellular and molecular biology, will be a major asset. The Research Center may wish to provide a clear support to the team by promoting the recruitment of such researchers.

Team 2 :

Role of the transforming growth factor beta (TGFβ) signaling pathway in tumor progression

Name of team leader: Mr Azeddine ATFI

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	4	4	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.)			
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	7	7	4

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

• Detailed assessments

Assessment of scientific quality and outputs:

The group participates in the Oncology research projects at the Saint Antoine Research Centre. Based on fundamental approaches, the group focuses on the role of the ubiquitin ligase system in the regulation of TGF-beta signaling, a major pathway involved in tumor progression. The originality of the work is based on the specific interest in deciphering the protein interacting network of three ubiquitin ligases, Phrf1, Tiul1 and Arkadia, which modulate the TGF-beta pleiotropic functions. The group leader can claim a substantial contribution to his field of research based on the high quality and reputation. During the last 4 years, he co-authored several articles in prestigious journals such as EMBO J (2008), Molecular Cell (2009), Cancer Res (2010). He also co-authored a comprehensive review in Nature Cell Biol (2010). Three articles are submitted, under review or in revision.

Assessment of the team's academic reputation and appeal:

The most evident cue of the lab reputation is based on the team leader implication with US universities over the last few years. As recognition of this, he is now a professor and the director of the "Tumor Cell Biology Program" at University of Mississipi Medical Center (UMMC, Jackson, USA). To support his research activity, he obtained two NIH grants for projects with the Harvard School of Dental Medicine. Besides, he has a worldwide recognized experience in the field of TGF-beta signaling, more particularly in the regulation of this pathway by ubiquitin ligases. In addition to his publications, the team leader's expertise is illustrated by the recruitment of one post-doctoral fellow from a world leader lab in the field of TGF-beta signaling (Imperial College, UK). The position of this fellow is now secure as a permanent researcher. Another academic researcher, who also worked in a worldwide recognized laboratory in the field of TGF-beta (Institut Curie, Orsay) joined the group in 2009. The laboratory is thus attractive for researchers coming from very good laboratories in the field of TGF-beta signaling.

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

The area of research of the lab is "academic/fundamental" research. Yet, the team leader is keen to establish close interactions with extra-academic partners. For instance, a several-year interaction between the group and the company Hybrigenics has led to important new discoveries concerning the TGF-beta signaling network, including PCTA, a new TGIF antagonist and ADAM12 a regulator of the type II TGF-beta receptor. This important connection has in fact led to joint publications in J Cell Biol (2007) and EMBO J. (2008).

Assessment of the team's organization and life:

The team is organized into 3 groups, each under the supervision of a permanent scientist and devoted to the study of one of the following ubiquitin ligases: Phrf1, Tiul1 and Arkadia.

The projects developed in the three groups appear to be scientifically pertinent, complementary, and well defined. Project leaders have the required expertize and the autonomy to conduct their projects. This team is dynamic and motivated. Permanent technical staffs are supervised collectively. Post-doctoral fellows and PhD students are directly supervised by their group leader.

The team leader is currently on permanent leave (in agreement with CNRS/INSERM) at the University of Mississippi where he is a professor and a director of the "Tumor Cell Biology Program". When he is absent, he directs and manages the team using phone and web resources. Scientific lab meetings are organized every week. These meetings allow discussing the projects and defining/refining research direction. In a context of a rigorous scientific organization and a fluent communication, the responsibilities that the team leader assumes in the US represent a strength for the team in terms of scientific exchanges, collaboration opportunities, network building, fund raising, transfer of technologies and acquisition of new expertise. For instance, many mouse models will be developed in the University of Mississippi, whereas most of the molecular aspects of the projects will be develop at Saint Antoine's.

It is important to note that the team leader clearly encourages and supports the researchers of his team to progress in their career in a combined effort to strengthen and to make the team durable and efficient. For instance, the team leader's group is co-headed by another scientist to guarantee an optimal management this subgroup. A postdoctoral fellow joined the lab in 2008 and was recruited as a CR2 at INSERM in 2009. The team leader is really supportive in the promotion of other scientists.

The team benefits from an administrative assistant. No detailed information was presented concerning how the staff is integrated within the Saint Antoine Centre administration and in US in the report. However the team leader clarified this point during the oral presentation and complementary discussions. Notably, he benefits from the Mississipi's university facilities including technical help and he also manages students and post-docs.

Assessment of the team's involvement in training through research:

The team leader's group trains Master's and PhD students as well as post-docs. The quality of research contributes to the very good training of PhD students. Two Master's students received competitive PhD fellowship from Research Ministry and Ligue Contre le Cancer.

The quality of supervision results from both the daily follow up by permanent researchers at Saint Antoine and from the "long distance" follow up by the group leader working in the US.

The report neither mentions specific activities in training/coordinating programs by the group's three junior academic researchers, nor does it indicate an implication in other educational projects.

Assessment of the five-year plan and strategy:

The scientific objectives of the team are centered on three ubiquitin ligases: Phrf1, TiulA and Arkadia. The group leaders have expertise in these proteins as attested by their past publications. The five-year plan and strategy is the natural continuation of previous works initiated in the team. The main goal of the proposal is to decipher the mechanism of action of Phrf1, Tiul1, and Arkadia related to tumor progression. Phrf1, Tiul1 and Arkadia are ubiquitin ligases that modulate TGF-beta signaling. TGF-beta plays a crucial role during tumor progression. One objective is to explore the effect of these three ubiquitin ligases in modulating TGF-beta activity in vitro and in vivo. The team has identified substrates for these three enzymes (Tgif for Phrf1, Smad7 for Tiul1 and SnoN/Ski for Arkadia). They will explore the functional significance of these interactions in vivo, in breast cancer since the team has genetic evidence in humans and experimental data for a role of these molecules and/or their partners in this type of tumor. More specifically, the team will also explore the role of TGIF in melanoma pathogenesis based on their preliminary observations in knockout mice and presented during the oral presentation. Notably, this will be achieved by generating different mouse models presenting impaired functions for the molecules cited above (xenografts into immune-deficient mice, conditional knockout mice, transgenic mice predisposed to breast tumorigenesis and genetically engineered mammary stem cells transplanted into a cleared mammary fat pad). Finally, and since E3-ubiquitin ligases usually are specific of several substrates, the team will screen for new Phrf1, Tiul1, and Arkadia substrates. The screening method is well-designed, original and is expected to generate pertinent data. Altogether, the global approach is of high interest because it addresses the functional relevance of three ubiquitin-ligases (and their substrates) during tumor progression. More specifically, this project should bring crucial information to better understand the ambiguous role of TGF-beta, which behaves either as a tumor suppressor or a tumor promoter. The proposed work could also lead to the characterization of unsuspected functions of the interacting network of ubiquitin ligases (during tumor progression but also during other biological processes).

Conclusion:

- Strengths and opportunities:

Ambitious projects relying on strong published and unpublished data (taking into account the ongoing projects and numerous data from papers cited as being under revision, the evaluation of the general feasibility is very positive).

The scientific quality of the publications and of the group leader is high.

The team has a worldwide recognized expertise in the competitive field of TGF-beta signaling.

The team is committed to develop mouse models to study the in vivo biological relevance of the results obtained in vitro.

Collaborations with foreign institutes will promote international recognition and facilitate the development of new exchanges.

The structural organization of the team and the research center fully supports the technical requirements for development of the project.

The strong motivation, and the energy developed by the team leader and the permanent researchers.

- Weaknesses and threats:

The team leader needs to be careful to any potential competiveness between the 2 sites of his research activities located overseas which can be considered as intra-team competiveness.

Many different mouse models (transplanted models, genetically engineered models, …).

No expertise in melanoma development.

The lack of visibility of the junior investigators (animation, publications, participation to international meetings, …).

The absence of structured translational projects with clinicians within the CDR to support the claimed objectives toward therapeutic issues.

- Recommendations:

Maintain a communication of high quality and facilitate student and researchers exchange/visit between the sites of the team.

As discussed during the visit, a deputy director should be nominated in the team to ensure the daily management when the team leader is abroad.

Researchers with a permanent position should apply for their own sources of funding and should obtain a HDR.

A strong expertise in modeling cancer in mice is a requisite for the success of the project. Expertise in melanoma development is also recommended. The US funding obtained by the team leader should permit the recruitment of a senior postdoc to fulfill this (these) mission(s).

Team 3 : Molecular lesions, initiation, and evolution of myeloid malignancies

Name of team leader: Mr François DELHOMMEAU

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	X	6	6
N2: Permanent EPST or EPIC researchers and similar positions	X		
N3: Other permanent staff (without research duties)	X	2	1
N4: Other professors (PREM, ECC, etc.)	X		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	X		
N6: Other contractual staff (without research duties)	X	5	1
TOTAL N1 to N6	X	13	8

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	X	
Theses defended	X	
Postdoctoral students having spent at least 12 months in the unit	X	
Number of Research Supervisor Qualifications (HDR) taken	X	
Qualified research supervisors (with an HDR) or similar positions	X	4

• Detailed assessments

Assessment of scientific quality and outputs:

The project of this new team which will gather saveral scientists/physicians, engineers and technicians from former Inserm units (872, 928 and 1009) aims at understanding some molecular events that may be essential during the development of myeloid malignancies.

The team members published 118 papers (2007 – 2012) in international journals.

The sub-group 1 published 21 papers, including 4 as first or last author in original research publications in the research subject (Blood x3 & NEJM x1). The sub-group 2 published 25 papers, including 7 as first or last author in original research publication in the research subject (Blood x1, BMC Cancer x2, Haematologica x1). The sub-group 3 published 72 papers, including 5 as first or last author in original research publications in the research subject (Blood x1, Leukemia x1, Haematologica x1).

This is an excellent output in the field of genetic mutations of hematologic malignancies, though it lacks focus. But as this team is new and is just setting up together, this lack of focus is not surprising.

Assessment of the team's academic reputation and appeal:

NA, as the team has just being created.

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

The team has 2 patents, members are experts in various governemental or charitable organizations.

Assessment of the team's organization and life:

The team's aim and functioning must be strongly improved. In the presentation and the paperwork, the integration of the two clinical groups in the project is overlooked. The project presented is the group leader's project and lacks the commitment of the other members of the team. It is obvious that the three sub-groups have a common focus and have many opportunities to cooperate and share their tools, workflows and expertise. But this has to be exposed more clearly and formalized by common projects and regular meetings of the team.

For this new team, with an ambitious project and a team-leader that will be involved part-time in hospital activities, a strong support from the CDR is necessary. This may be achieved in a first step by allocating to the team technical staff and/or support to obtain PhD students.

Assessment of the team's involvement in training through research:

NA, as the team has just being created.

Assessment of the five-year plan and strategy:

This new team has original results and program. The research project will benefit from the access to patients and patient samples, as several members of the team are clinicians in either childhood or adult myeloid malignancies, or will work in the Haematology laboratory of the St Antoine Hospital. By focusing on conceptual aspects such as the temporal occurrence of mutations in myeloid neoplasms, the team is taking a reasonable risk in a very competitive field.

However, as said above, a better integration of the research themes of the clinicians in the team's project is mandatory for the sake of scientific coherence and synergy within the team. For this young, starting team, a strong commitment of the Research Center, for space, equipment, but also technical staff and PhD students is essential. In addition, on-site collaborations must be increased in number and strengthened. The team should also aim to recruit full-time researchers. To this end, the team must reinforce its international visibility through collaborations, meetings and networks. Finally, giving the central topic of the team, i.e. NGS analysis in search of new mutations driving myeloid neoplasms, the absence of bioinformatic expertise on site is a serious concern. This concern is shared for the research projects of other teams of the CDR.

Conclusion:

- Strengths and opportunities:

- a promising young leader;

- access to patients and patient samples;

- an original project.

- Weaknesses and threats:

- lack of management, lack of implication of all the team members in the central project of the team;

- the sequencing and sequence data analysis expertises are not on-site;

- given the good track record of the team, it is surprising that it has not attracted funding for more researchers (PhD students or post-doc).

- Recommendations:

- a better integration of the research themes of the clinicians in the team's project;

- a strong support of the CDR for the start of this new team;

- increase International visibility.

Team 4 : Proliferation et differentiation of stem cells : application to cell therapy

Name of team leader: Mr Luc DOUAY

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	7	5	5
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	18	17	8
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)	3	1	
TOTAL N1 to N6	32	26	14

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	7	4

• Detailed assessments

Assessment of scientific quality and outputs:

Overall, the team is publishing regularly and at high level, including leader journals in oncology and hematology. Publications are well cited. Regarding the in vitro blood cell generation, there has been two world "premiere". One is the first in human transfusion of in vitro human ES-derived red blood cells. The second is the demonstration that the haemoglobin switch towards adult hemoglogin, that is still a roadblock to the in vitro generation of red blood cells from pluripotent stem cells, can be resolved in vivo as shown by the production of human adult hemoglobin after the injection of human ES-derived erythroid progenitors into immunodeficient mice. It is noted that the three sub-groups composing the team are heterogeneous in their respective output.

Assessment of the team's academic reputation and appeal:

All three subgroup leaders have earned international influence and are regularly invited in International congresses, including leading international events (e.g. Gordon Research Conferences on Red Cells in 2013). The in vitro generated red blood cells subgroup has particularly increased its visibility in this regards. Participation of the team in international projects like the US Army call for proposal "Blood Pharming" based on their own published work.

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

The team has international expertise that has brought several major international sources of funding. This expertise and two recent patents strengthen the move of the team to develop large-scale generation of functional and universal RBCs generated from iPS cells for clinical application. This major translational research project is supported by important funding such as the ISI/OSEO consortium "StemRed" and is done in collaboration with the "Etablissement Français du Sang".

Assessment of the team's organisation and life:

The two main themes of the team, i.e. cell engineering and hematologic stem cell graft registry, although functioning at a satisfactory level given the scientific output, appear more as the juxtaposition of two strong groups than as a unified team. There does not appear to be a formal common organisation.

There is a lack of full time researcher on the subject of red blood cell production, and this may impact on the scientific solidity of this part of the team, especially during the actual rapid growth in size on the people of the team and the number of sub-projects.

Assessment of the team's involvement in training through research:

In the past five years, the team has trained 6 master students (M2), 2 engineer students and 5 PhD students.

Assessment of the five-year plan and strategy:

The project presented is in line with the work carried out during the last 5 years. There are three work packages: red blood cell production, mesenchymal stem cells and epidemiological analysis of blood stem cell grafts.

The red blood cell production is a very attractive translational project aiming at a first clinical trial for polyimmunized or rare blood group patients. The feasibility of this risky project is backed by the expertise, the support of the EFS and large funding. However, as pointed above, the lack of permanent researcher could be a weakness. Indeed, and this is underlined by the team itself, there are several roadblocks that must be resolved in this project. The research avenues proposed to overcome these technical hurdles include propositions such as immortalizing erythroid progenitors (without loosing their differentiation capacity and without compromising their in vitro survival), in vitro globin switch, etc … that are basic science issues. Unless the team receives the expertise of research groups working on erythroid differentiation and globin gene expression, either by collaboration or by recruiting a full-time researcher with experience in this field, the solving of these issues could be delayed.

The mesenchymal stem cell project may need a support as this field is very competitive.

Conclusion:

- Strengths and opportunities:

- a very good track record;

- an International registry advantageously used for retrospective analyses;

- an outstanding translational project with a unique expertise in the field;

- collaboration with the EFS, with private companies.

- Weaknesses and threats:

- the deliverables of the red blood cell production project need to solve several basic scientific locks;

- the registry subgroup will be threatened by the coming departure of its leader.

- Recommendations:

- collaborations with groups involved in the transcriptional regulation of red cell differentiation and recruitment of a full time researcher;

- a reinforcement of the group focusing on mesenchymal stem cell to increase the production of this group with unquestionable expertise;

- a collaboration with the group “Graft-versus host reactions after allogeneic stem cell transplantation” could be envisioned to secure the future of this recognized expertise of the Saint-Antoine Research Center.

Team 5 : Microsatellite instability and cancer: from biology to clinics

Name of team leader: Mr Alex DUVAL

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	3	6	6
N2: Permanent EPST or EPIC researchers and similar positions	4	2	2
N3: Other permanent staff (without research duties)	6	6	1
N4: Other professors (PREM, ECC, etc.)	1		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	2	1
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	15	16	10

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	4	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the team	3	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	4	7

• Detailed assessments

Assessment of scientific quality and outputs:

The scientific output of the Mr Alex DUVAL Laboratory has been excellent in the last few years. Although the laboratory is still relatively new (created in 2006), quite a number of high impact papers have been published in recent years (JCO, Nature Medicine, JNCI, Gut, etc.). This is quite impressive.

Over the last years, the Mr Alex DUVAL Laboratory has used several innovative approaches to study the Mismatch repair (MMR)-deficient tumors. For instance, they collected a significant number of lymphoblast cells from CMMR-D patients, which is a quite rare disorder, and then developed a new diagnostic test that is now being used in France and the rest of Europe. Another example is their approach to identify frame shift mutations in the HSP110 gene, the concept of MGMT field effects to deactivate MMR genes as well as the study on microsatellite instability (MSI) in intestinal neoplasms from inflammatory bowel disease (IBD) patients. Each of these projects is built on unique and innovative approaches within the research area, allowing this group to perform research far beyond the state-of-the-art.

The Laboratory is to be complimented for the excellent "translational research" that it performs. Published papers include (1) some more fundamentally-oriented work, such as their paper in Nature Medicine describing the HSP110 frame shift deletion, (2) some translational biomarker-oriented research such as the work on the prognostic gene signature, and finally, (3) some more clinically-oriented work (e.g., the project on intestinal neoplasms in IBD patients). In each of these, the Laboratory has published high impact publications and as such, the expert committee considered that this Laboratory actually serves as a role model for the entire Center.

Assessment of the team's academic reputation and appeal:

There is a very clear focus of the Laboratory on investigating mismatch repair deficient (MMR) tumors (mainly in colorectal cancer). As a result the Laboratory is quite renowned for its expertise in this research area. The academic reputation of the group is thus excellent.

The contacts with industry (Promega and Qiagen), the recognition of the team by the French National Ligue against Cancer, the invitation to national and international congresses, as well as the Prime d'Excellence Scientifique (PES) attributed to Mr Alex DUVAL clearly prove that the Duval Laboratory has an excellent reputation, within France but also in the rest of the world.

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

In their report, the authors have put great emphasis on the economic value of their achievements. They describe how their findings have led to several patent applications. One of their patents (HSP110) was considered patent of the year by INSERM and has meanwhile been licensed to QIAGEN. Another patent developed to screen constitutional MMR-deficiency is currently used to diagnose this condition. There are also several contacts with industrial partners, such as Pfizer and PROMEGA. Overall, this convincingly shows that the research team has a lot of potential to create additional economic value for France.

Improved diagnosis of genetic disorders, such as constitutional MMR-deficiency is very important for patients and their families, and has an important social impact on their future lives.

Assesment of the team's organisation and life:

This is a medium-sized research group that is built around the team leader. There are biweekly meetings in the group to discuss results and ongoing experiments. There is quite a good balance in the number of full-time and part-time researchers, PhD students, post-docs and master students (no inverted pyramid situation). It looks as if the Laboratory is managed very well.

Assessment of the team's involvement in training through research:

There is a very important teaching component associated with the research from the team, as several of the MDs in the Saint-Antoine Hospital will do a PhD in the team. This interaction is very important and represents an important investment from the team to secure future interactions with the Hospital. Vice versa, the oncologists get important hands-on experience in performing translational research, which is an important asset for their future career in the era of personalized medicine.

So far the Laboratory has failed to attract international post-docs. Mobility (outside of the Paris region, as well as international) is largely absent. The number of PhD students (5 PhD students; 180 months) in the last 5 years can still increase. Overall, the involvement in training is very good, but there is room for some improvement.

Assessment of the five-year plan and strategy:

The 5-year proposal is ambitious and challenging, but will continue to build on experiments and projects initiated in the last 5 years. It clearly has the potential to become published in high-impact journals.

The proposal involves phenotyping a number of transgenic mouse lines, which were generated in the last few years. Additionally, it will continue to capitalize on the local biobank that has been established, e.g., by characterizing MMR-deficient tumors with recent omics technologies (RNA-seq and exome-seq).

Conclusion:

- Strengths and opportunities:

Excellent publication records so far should facilitate securing sufficient additional funding opportunities, including funding from European agencies. Initial contacts with industry are in place. These should facilitate industrial grants and other revenues in the future.

The interaction with the Saint-Antoine Hospital represents a very important strength of the team. The fact that the team is located in the same building as the hospital offers excellent biobanking opportunities to the team. In the last 5 years, an impressive biobank has already been established, which should allow the Laboratory to participate in national and international projects and play a key role in its research field.

- Weaknesses and threats:

The Laboratory is planning to embark on a number of challenging projects. For instance, the group is generating several transgenic mouse lines (e.g., HSP110, Mgmt and Msh2 KO trangenic mice) and plans to phenotype tumors arising in these mice. Additionally, it is mentioned that they plan to perform a number of next-generation sequencing experiments (genome-wide expression profiling and exome-sequencing of MMR-deficient tumors). Although these are very interesting and excellent projects, the Laboratory needs to realize that it will be quite challenging to perform such diverse projects, each involving different types of experiments and infrastructure needs. For instance, next-generation sequencing will involve having access to a high-throughput sequencer, novel bio-informatics (calling of indels in repetitive DNA sequences, which are mainly affected in these tumors), etc. Similar challenges exist for mouse phenotyping (imaging, histology, etc.) if the team members wish to continue publishing in high-impact factors. The Laboratory will have to capitalize on outstanding collaborations and might consider attracting people with the appropriate expertise.

- Recommendations:

The main recommendation is related to project prioritization, which should be done in order to ensure efficiency of the research.

Team 6 : Cancer Biology and therapeutics

Name of team leader: Ms Annette LARSEN and Mr Aimery DE GRAMONT

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	5	4	4
N2: Permanent EPST or EPIC researchers and similar positions	4	3	3
N3: Other permanent staff (without research duties)	6	5	3
N4: Other professors (PREM, ECC, etc.)	1		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2		
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	18	12	10

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	4	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the team	5	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions		

• Detailed assessments

Assessment of scientific quality and outputs:

The group directed by Ms Annette LARSEN and Mr Aimery de GRAMONT participates in the Oncology research projects at the Saint Antoine Research Centre. The dual leadership optimizes the group's expertise both in fundamental and preclinical programs (A. LARSEN) and clinical trials (A. De GRAMONT). The global objective is the development of novel anticancer strategies based on a better understanding of the molecular mechanisms involved in the functionality of anticancer agents against tumor invasion and metastasis (EMT). An original approach consists in the evaluation of drug sensitivity during tumor progression, in order to adapt the best treatment at the best time.

The program is well supported by pharmaceutical companies, including PharmaMar for the development of marine-derived anticancer agents and Roche for the combinatorial studies of anti-angiogenic agents.

There is a very high production of fundamental and clinical papers in cancer-related fields (93 from 2007 to 2012 with average IF = 7.8). About half of these publications can be attributed to team itself (first/last authors or numerous authors from the team), the others are issued from collaborations or from clinical collaborative groups. Some of the publications issues from the team itself are published in high impact journals like J Clin Oncol or Nat Rev Clin Oncol. Note that two papers were selected for the cover page in PNAS (2007) and Clin Cancer Res (2011).

Assessment of the team's academic reputation and appeal:

The two leaders are involved as coordinators for scientific networks: Inter-Cancéropôle (2007-2009), CAPES-COFECUB Brazil (2007-2011 and 2013-2014), EORTC (European organization for Research and Treatment of Cancer (2007-2011)); GERCOR (multidisciplinary group in oncology). One of the team leaders was selected for presenting the MIT 2012 Wogan lecture and is a member of the editorial board of Mol. Cancer Therapeutics.

High attractiveness: from 2007 to 2012, the group has hosted 5 graduate students from Brazil and one from Canada, for a total of 7 PhD students and 13 Master II.

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

The projects of the group involve industrial partners and 12 grants/contracts have been obtained since 2007 from international companies.

The team leader is widely involved with funding Associations and expert committees: ARC, Translational Research Advisory Committee and the Pharmacology and Molecular Mechanisms group of EORTC, Cancéropôle Ile-de-France.

Assessment of the team's organisation and life:

Lab's meetings are organized. No intervention of the Co-PI during presentation and discussion of the team project suggested to the visiting committee that the team had only one team leader.

Assessment of the team's involvement in training through research:

Several members of the group are teachers, thereby contributing to the training of students. One team member coordinates Master's 1 training programs and another one is implicated in the area of digestive oncology for the European School of Oncology and is responsible for digestive oncology at the UPMC Medical School.

Academic researchers: one team member belongs to the board of directors of the UPMC doctoral school and is involved in the M2 program in Oncology. Another team member is involved in tutoring courses at the UPMC Medical School.

Assessment of the five-year plan and strategy:

The next five-year plan is anchored in the precedent one, with two major axes to be developed.

The first one is based on the development of novel anticancer agents and their use in combinations. Novel anticancer agents are marine-derived ecteinascidins, whose mechanism of action has been elucidated by the group. The challenge now is to analyze the DNA-damage response of the cells to theses agents. A second part of this program is based on the study of the effects of combinations of angiogenesis inhibitors: bevacizumab (Avastin), erlonitib and tivantinib. Based on an in vivo screening approach (CRC xenograft model mice) of models resistant and sensitive to bevacizumab and nintedanib, the cell response will be characterized according to the pathways involved. Additional drug combinations will be tested in the available models.

This first axis of the project is strictly delineated, supervised by two academic researchers and supported by pharmaceutical companies, which provide financial resources. Starting from ongoing studies and acquired proof of concept, the strategy provides opportunities to extend this promising research area according to available observations.

The second axis involves the characterization of the molecular and functional aspects of cancer invasion and its link to drug sensitivity. It deals with three specific questions:

i) the influence of genotoxic stress on the invasive phenotype in CRC. Six drug-selected CRC cell lines have already been established to explore the effect of genotoxic stress on the EMT. The group will now analyze the sensitivity of the EMT phenotype to the drugs;

ii) the role of WISP-1/CCN4 and WISP-2/CCN5 in breast cancer, previously demonstrated by the team, will be evaluated in human samples (expression, deregulation) and its influence will be evaluated in vivo;

iii) colon cancer and the stemness of EMT. Linked to the precedent point, the deficient WISP2/CCN5 cells will serve to analyze their capability of inducing breast cancer phenotypes.

This second axis is admittedly more complex. The WISP subject adequately complements questions addressed in the first axis. WIPS/CCN regulators may be powerful targets for combined therapeutic strategies. The implication of two full-time senior Research Assistants (IRs) in this axis reinforces the possibility of success.

Conclusion:

- Strengths and opportunities:

There is a real continuum between fundamental, preclinical and clinical research. The group and its leaders enjoy international recognition and have tight connections with the pharmaceutical industry. Involvement in Master's and PhD student training is good.

- Weaknesses and threats:

The weakness and threats mentioned in this report simply describe all the areas lacking in adequate support (funding, students, interest, visibility) and stemming from the group's environment. However two academic researchers from the group are poorly involved in publication activities and one is even completely absent from the detailed research programs described in the report.

- Recommendations:

Boost collaborations within the group.

Team 7 : Graft-vs.-Host Reactions after Allogeneic stem Cell Transplantation

Name of team leader: Mr Mohamad MOHTY

Workforce

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

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

• Detailed assessments

Assessment of scientific quality and outputs:

As this team is new to Saint-Antoine these comments relate to the achievements of Prof Mohamad MOHTY in his previous position in Nantes. The fact that this team was positively evaluated last year by AERES, in the Centre de Recherche en Cancerologie Nantes-Angers is noted.

The focus of the group is the pathophysiology of graft versus host disease with particular emphasis on the role of immune mediators in human transplantation. In his previous positions in both Nantes and Marseille Prof Mohamad MOHTY played a prominent role in the development of internationally competitive allogeneic stem cell transplant programmes, not only gaining credibility as a clinical transplanter but also in the ability to develop transplant networks and acquire clinical outcome data and biological material as the basis for academic output. His success is indicated by first, final and collaborative authorship of an impressive collection of high quality publications inluding J Clin Oncol, Blood and Leukemia publications. His ability for productive collaborative working is shown in the large number of manuscipts emanating from regional, national and international transplant groups. This ability to work in a collegiate manner will be particularly important in the proposed research where some of the work (eg. Identifying biomarkers predictive of GvHD) will require very large numbers of patient samples.

At the present time the body of work addressing the proposed project is relatively small which is understandable, given that this was not his focus in Nantes. His move to Saint-Antoine and the reorganisation of transplant provision in Paris will provide him with the transplant numbers to make this work feasible.

Assessment of the unit's academic reputation and appeal:

The team leader's reputation in the field of transplantation is very good and he already holds an elected office in the European Group for Blood and Marrow Transplantation (EBMT). It is highly likely that his contribution will be recognised in his election as the next President of the EBMT.

The team leader is new to this unit but the unit itself is one of the oldest and most prominent transplant units in Europe. The previous team leader has an enviable reputation in the field, particularly in the area of autologous transplantation, and will benefit from the presence on-site of one of the main EBMT offices in Europe, responsible for the collection and analysis of outcome data of all transplants performed by EBMT members. This office is particularly strong in statistical survival analysis and has always attracted international visiting researchers. The combination of a large and internationally competitive clinical programme and this pre-existing resource has the potential of securing this unit's reputation as one of the premier transplant groups in Europe.

The previous team leader was an elected officer of EBMT for many years culminating in his Presidency of the annual meeting in 2011 (where incidentally Prof Mohty was the scientific secretary). He received many invitations to lecture at international meetings and is perceived as a leading authority in the management of haematological malignancies, in particular by autologous transplantation.

With respect to the present team leader's personal profile he is internationally regarded as a leader in the field of transplantation and is regularly invited to give lectures and plenary presentations at the world's leading haematology meetings including the American Society of Hemaology (ASH), the EBMT, the European Hematology Association (EHA) and the USA Tandem BMT meetings. His reputation as an able administrator locally, nationally and internationally is growing and well deserved, and it is highly likely that he will make considerable contributions to the organisation of international networks and the development of this technology, in the coming years.

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

As mentioned above, the juxtaposition of a high quality clinical unit and the EBMT data collection and analysis office provides an excellent platform for further development.

Assesment of the unit's organisation and life:

This is not assessable at the present time as the team is new to Saint-Antoine. However, the team is relatively small at the present time and will need to be enhanced to achieve the desired goals.

Assessment of the unit's involvement in training through research:

This is not assessable at the present time as the team is new to Saint-Antoine.

Assessment of the five-year plan and strategy:

The research goals are carefully and clearly elaborated. They focus on the role of immune mediators of graft versus host disease (GvHD) and are wide ranging. The team leader has previous experience in the role of dendritic cells and will continue the development of this field. One of the scientists has made an important contribution in the recognition of the role of invariant NKT cells (iNKT) and will continue in this area. In addition they plan also to study the role of cytokines in the induction of GvHD and to identify biomarkers as predictive of GvHD through protein profiling. The project is coherent and pertinent but they exist in a highly competitive field. Their advantage is that they work within a very active transplant unit and the team leader is likely to increase the allogeneic transplant activity to create an environment which will generate the necessary amount of clinical data and biological samples for their work. Their disadvantage is that they are a very small team at present and the team leader will be very involved in the forthcoming months in building the unit. From the description provided, it is not clear who will do the proteomics, whether this facility is present on site and whether there is adequate bioinformatic capacity. At the present time the team does not envisage animal models and this is an area that they might wish to consider as these provide a somewhat 'cleaner' model of a complex process which is usually complicated in humans by the co-existence of infection and immunosuppressive treatment.

Conclusion:

- Strengths and opportunities:

- large active transplant unit with the potential to increase the numbers of allogeneic transplants;

- clinically active and highly respected group leader;

- excellent and established clinical transplant networks that might provide additional material;

- previous immunological expertise;

- ability to attract national and international researchers.

- Weaknesses and threats:

- new and small group, also trying to maintain and grow clinical unit;

- lack of dedicated scientist;

- highly competitive field, particularly from better resourced US groups;

- no tradition of training clinical fellows in laboratory research.

- Recommendations:

- investment in at least one dedicated scientist and consideration of the use of animal models;

- development of a clinical fellow programme offering clinical experience followed by dedicated laboratory project;

- considerable pre-clinical discussion with proteomics and bioinformatics team as to the necessary samples and analysis before embarking on a potential 'me too' biomarker discovery project.

Team 8 : Biology and Treatment of Hepatobiliary Tumors

Name of team leader: Ms Françoise PRAZ and Mr Olivier ROSMORDUC

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	(5)	7	7
N2: Permanent EPST or EPIC researchers and similar positions	(4)	3	3
N3: Other permanent staff (without research duties)	(3)	3	1
N4: Other professors (PREM, ECC, etc.)	(0)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	(1)	2	1
N6: Other contractual staff (without research duties)	(0)		
TOTAL N1 to N6	(13)	15	12

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	(3)	
Theses defended	(2)	
Postdoctoral students having spent at least 12 months in the team	(0)	
Number of Research Supervisor Qualifications (HDR) taken	(2)	
Qualified research supervisors (with an HDR) or similar positions	(7)	9

• Detailed assessments

Assessment of scientific quality and outputs:

Good global scientific production with 42 publications directly related to the team research out of the 145 published ones in the reference period (17 publications are in the top 10 of their journal). Honorable level of publication in medium/high ranked journals (J Hepatol, Am J Pathol, Cancer Res, …), national and international visibility, especially for the clinical and translational aspect of the work of the team.

Assessment of the team's academic reputation and appeal:

The clinical team has a clear academic reputation: Active participation in organisation of international conferences, Active members of national scientific societies and national organisations (INSERM), coordination of the center of expertise in digestive oncology, active roles in the life of the university.

The co-PI is particularly active (and is a driving force) for federation of efforts of industry, pharmaceutical and academic partners, and clinicians to move forward with treatment of hepatocellular carcinoma (HCC) (OSEO initiative, DHU INCaDi, …). Several other scientists also have a good international visibility. The visibility of the other researchers is more limited to the french scene or to very specialized audiences. Team members are able to attract funding from various sources but recruitment of M2/PhD students and international post-docs is limited.

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

Very good and multi-levels: Investigators/coordinators of clinical trials and national clinical studies (PHPC, Phase III ANRS study), Members/experts for ministerial agencies and for pharmaceutical industry, federation of efforts of clinician, scientist and pharmaceutical industry to progress in the care for patients with liver cancer, Members/initiators of several networks (RICH, GERCOR, PRODIGE, …).

Participation to the life of the international scientific community: active members of national scientific societies, publications, members of editorial boards, reviewers, ….

Assesment of the team's organisation and life:

The groups of this team have theoretical complementary expertises from fundamental cell biology, pathophysiology and pre-clinical studies in animal models to clinical studies and trials. This complementarity could be used to create synergies and for fuelling translational bi-directional approaches. However, demonstration of a strong team management to create real synergy able to make significant advance in the field is currently lacking. There is a need for clear definition of the objectives of each group, for clear identification of points of convergence and synergy, for implementation of priorities and for making crucial decisions in terms of investment in the development of models and concepts necessary to make novel discovery and have a significant impact in the field.

Attention should be paid, as this emerging team is building up, for good integration of those different scientists and for the establishment of an environment favorable to exchanges, reciprocal self-criticisms to reach a level of collaboration that will allow for real synergy and reciprocal fuelling of the projects. New lab space is foreseen in order to relocate all the team members together and this will help reinforcing interactions, communications and hopefully synergy between projects.

At the organisation levels, it seems that the group is in need of technical structures and support in particular for maintenance of conventional animal housing enabling their animal experimental work. Effort for recruiting researchers at the post-doctoral levels but also in clinician involved in research is desirable.

Assessment of the team's involvement in training through research:

5 PhD and 12 M2 students have been trained since 2007 (for 8 scientists holding a HDR). Attractiveness for M2, PhD students and post-docs could be improved. Clear strategies and politics to increase the flow of students and the recruitment of students, physicians and post-doc scientists to the labs are lacking. Some team members are clearly involved in teaching and training in various programs, clinicians actively participate to training of juniors.

Assessment of the five-year plan and strategy:

There is a unity of theme in the proposed research program, with potential complementarity between the specific projects. Importantly, translational approaches are present in all parts of the projects. In addition, the clinical team has the population's recruitment and the tissue banking process implemented; it is used to the routine of clinical trials and has priviledged contacts with the industry but also with other investigators. Although willingness, potential and tools are apparently present to make this bi-directional translation, the general impression is a collection of individual projects and how those will converge to reach a common goal is not clearly apparent.

Conclusion:

- Strengths and opportunities:

- coherence: Unity of theme, complementary approaches with a potential for convergence, which is however not clearly apparent;

- translational aspects in all parts of the project;

- direct acces to human material and patients for testing, retrospective and prospective evaluations and for trials;

- privileged contacts and partnerships with industry and prominent position of the team as investigators;

- pro-activity in seeking federation of efforts from scientific, industrials, clinical and decisional organs to move forward for the care of patients with liver tumors;

- variety of funding sources.

- Weaknesses and threats:

International visibility of the research groups/team needs to be enhanced, both for the translational and more fundamental work. This will also help for recruitment of PhD and post-doctoral researchers and funding.

The field of HCC is difficult as this tumor is regarded as the complication of cirrhosis and up to date, except for prevention, therapeutic interventions are disappointing. Moreover, the search for new treatment is taken over by large industry. Therefore, the efforts of a small tranlational team should be towards creativity, innovation rather than exploring avenues already marked out by industry. In the projects, little emphasis is given to the relationship between the tumor and the non-tumor environment, although this appears now as critical and little is proposed to develop and implement experimental tools to specifically address such questions. While the clinical aspects as well as the basic molecular aspects are well developped, there is a relative gap in between (in vivo (pre-clinical) approaches on animal models).

Insufficient leadership and coordination appear as a weakness and a potential threat for productivity, international visibility and for making significant advance in the field.

- Recommendations:

It is understood that this team will now include groups of various origins. Attention should be paid, particularly at the beginning, for good integration of those different scientists and for the establishment of an environment favorable to exchanges, reciprocal self-criticisms to reach a level of collaboration that will allow for real synergy and reciprocal fuelling of the projects.

Need to attract young scientists and in particular post-docs (but also clinicians with a strong tropism for research).

Need for re-enforcing the leadership, for clear definition of the objectives and common goals; and from that to make appropriate decision in terms of development and priorities in order to be in a position for making significant contribution to this very competitive field.

Team 9 : Immune system, Neuroinflammation and Neurodegenerative diseases (IN2)

Name of team leader: Mr Pierre AUCOUTURIER

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	1
N2: Permanent EPST or EPIC researchers and similar positions		1	1
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.)	3	1	1
N6: Other contractual staff (without research duties)	1	1	
TOTAL N1 to N6	8	7	3

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the team	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	2

• Detailed assessments

Assessment of scientific quality and outputs:

This team is well recognized in the field of Prion disorders with participation to European consortia. These last five years have been characterized by a smart move toward a new scientific orientation on another neurodegenerative disorder: Alzheimer's disease. The team has produced 11 publications on both topics: Prion disorders and Alzheimer's disease. The highest impact factor with PLoS Pathog is above 9 and the lower 3. Many publications in J Immunol (~7). It should be noticed that the team leader has also a good publication record on his clinical activity in nephrology and immunity (IF range between 3-15).

Assessment of the team's academic reputation and appeal:

Even if the team is well recognized in the field of Prion disorders, the team has to gain recognition in the Alzheimer's field. Consequences of this lack of recognition are the difficulty to raise external funds for developing experimental models needed for the project. However, it should be noted that recent fundings have been obtained.

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

Different researchers participated to a general review (in French) in Medecine/Sciences and a radio show. They are also involved in translational research with a clinical research project on immune biomarkers (PHRC Imabio3). Due to the research topic, a better economic interaction may be expected.

Assesment of the team's organisation and life:

It is a small team with a team leader (PU-PH), a CR1 Inserm scientist, one engineer, one technician and two PhD students. Two research directors, involved in the former project, left or will be leaving the team. Within the research centre, this team is pretty isolated on the research project. There is only one clear association with the team "Neuroendocrine mechanisms of longevity and age-related diseases". The team should expand its collaborations since the team leader has already some links with other teams at the clinical level. The team is also aware of its "not ideal" location but did not succeed in its search of a new one. This team has the support of the CDR director for staying in the research centre.

Assessment of the team's involvement in training through research:

The team has trained 5 PhD students and 3 post-doctoral fellows. Two PhD students are currently enrolled and in regard to the size of the team, it is a clear involvement in research training.

Assessment of the five-year plan and strategy:

The five-year plan and strategy are clearly defined with a project on the adaptative immune system in Alzheimer's disease. There are three main aims: 1) role and therapeutic potential of regulatory T cells, 2) understanding of effector CD4+ T cell responses in the pathophysiology and immunotherapy of Alzheimer's disease using existing and new animal models, 3) identification and assessment of early immune biomarkers in AD. There is no doubt on the capacity of the investigators to fulfill the project but the environment may not be the best one for this kind of projects. The willingness of the executive board to include and support this team in the research center will be essential for the success of these investigators. A small team like this one will need additional support in this environment.

Conclusion:

- Strengths and opportunities:

The team has already a good expertive in neuroimmunology in Prion disorders and wants to translate its know-how toward Alzheimer's disease. It already demonstrated its capacity to develop animal model using TCR-transgenic mice (PLoS Pathog. 2011 Sep;7(9):e1002216).

The recent recruitment of a young CR1 Inserm investigator.

The obtention of fundings (PHRC and France Alzheimer association) indicate the relevance of the project.

- Weaknesses and threats:

Alzheimer's disease is a very competitive field and the team did not show its capacity to be included in the AD networks. Even if the project is well balanced, the team approach on immunotherapy is not commonly accepted and may raise further concerns and criticisms. The project has its assets and should be performed but it needs support from other AD teams in such a competitive topic. Thus, this isolated team has to join AD networks/consortia.

Similarly, it is a small team which is not fully included in the framework of the research centre.

In the research centre, all team leaders have a translational research between their clinical/biological and research activities. In the present project, the team leader has a good/excellent clinical research (nephrology/immunology) but not directly related to AD and thus may be disadvantaged compared to other teams.

- Recommendations:

The research centre must fully support this team if it wants to keep it competitive. The team has to find national and international collaborations on Alzheimer's disease to succeed in its project.

Team 10 : Metabolism and age-related joint diseases

Name of team leader: Mr Francis BERENBAUM

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	X	4	4
N2: Permanent EPST or EPIC researchers and similar positions	X		
N3: Other permanent staff (without research duties)	X	2	
N4: Other professors (PREM, ECC, etc.)	X		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	X		
N6: Other contractual staff (without research duties)	X	1	1
TOTAL N1 to N6	X	7	5

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

• Detailed assessments

Assessment of scientific quality and outputs:

During the last years this team has contributed to demonstrate the inflammatoty theory of osteoarthritis. More especially they underlined the role of several mediators as PGE 2, the NAMPT/visfatine and IL-1 B in OA. They also emphasized the interaction between cartilage, bone and synovium in OA.

This team has a good scientific production in agreement with its size. Excluding collaborative publications, they published 2 to 6 papers per year related to the research topics of the team. Most of them are published in the best journals of the speciality (Arthritis Rheum, Ann Rheum Dis). One can also notice a publication in Journal of Immunology, JBC and Nature Protocol.

Numerous reviews testify also of the scientific quality and level. The team is very active in oral presentations.

Assessment of the team's academic reputation and appeal:

This team, thanks to its director, has an excellent reputation. Indeed the team leader is a well recognized and international leader in his field. He is regularly invited to international meetings on rheumatology and osteoarthritis. He is the former president of the International Osteoarthritis Research Society (OARSI) from 2008 to 2009. He belongs to the executive committee of the ITMO (Institut Thématique Multi Organisme) named “circulation, metabolism, nutrition for AVISAN (Alliance pour les sciences de la vie). He is elected member of the “Conseil National des Universités”.

He is involved in the Labex program as member of the executive committee. He is also involved in the hospital University Department (DHU). In France, he can be considered as one of the leader in research on rheumatology.

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

The team achieved to establish an industrial partnership with the french medical company Pierre Fabre about chondroitine sulfate and subchondral bone. Another industrial partnership has been concluded for 2013-2015 with the french medical company Servier about strontium ranelate and chondrocyte signaling.

The team leads several actions in media toward general public and patients.

Assesment of the team's organisation and life:

The team which is relatively small in size does not seem to have any problems in its organisation and life. The 3 assistant professors are well involved in the scientific projects.

Assessment of the team's involvement in training through research:

The team is involved in several actions of training. The team leader set up and manages with an assistant professor a teaching unit of the master program “Integrative biology and physiology”.

No doctoral student is mentionned in the report and no thesis defended. Nevertheless right now the team leader is the only one to have an HDR. HDR is foreseen for the 3 assistant professors in the following months.

Assessment of the five-year plan and strategy:

This is one of the new teams of the CDR. Indeed the whole team with its leader will move from Jussieu to Saint Antoine in the following months. It is a great opportunity for this team because it will find an excellent scientific environment. New interactions will raise with several teams of the CDR as exposed in the report and confirmed by the oral presentation. It also will benefit of the CDR platforms and animal facilities. The link with the department of rheumatology (on the same site) will be easier and stronger.

The general theme remains focused on pathophysiology of OA nevertheless with some evolutions as for example the link between sub chondral bone and cartilage. The project is composed of 4 WP. The first aims to find new soluble mediators secreted by activated bone cells acting on chondrocytes. More especially the team will focus on the 14-3-3 protein. The second WP will study the link between hypertrophic chondrocytes and development of vascular channels in the tide mark. Considering the link between the adipokines and the OA the WP 3 will be devoted to the potential role of the metabolic syndrom in OA in obese people through glucose metabolism using relevant models. Logically the last WP is devoted to clinical and preclinial validation supporting by a murine OA model, a human bank of cartilage and a cohort of patients with hand OA. Each WP is under the resposability of an assistant professor. The different WP are not isolated but will develop relationships between them.

On the whole the scientific project is consistent despite the size of the team.

Conclusion:

● Strengths and opportunities:

- scientific environment of the CDR;

- true Interactions with other teams of the CDR;

- scientific abilities in the field;

- international recognition of the team leader;

- promising young researchers;

- excellent and original scientific project about the the pathophysiology of a world-wide disease without curative treatment.

● Weaknesses and threats:

- small size of the team related to the project;

- only 1,5 full time technical staff;

- right now only one HDR in the team;

- no doctoral student.

● Recommendations:

- to recruit doctoral students;

- to recruit full time researchers;

- to obtain HDR for the young researchers.

Team 11 : Cystic Fibrosis: Physiopathology and Phenogenomics

Name of team leader: Ms Harriet CORVOL

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	3	2	1
N2: Permanent EPST or EPIC researchers and similar positions	2	2	2
N3: Other permanent staff (without research duties)	4	7	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)	8	4	
TOTAL N1 to N6	17	15	4

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the team	1	
Number of Research Supervisor Qualifications (HDR) taken	4	
Qualified research supervisors (with an HDR) or similar positions	6	5

• Detailed assessments

Assessment of scientific quality and outputs:

This team is a young new emerging team resulting from a split from a former group headed by A. CLEMENT. This new team is now focusing on cystic fibrosis and therefore represents one of the few teams specifically involved in this area of research in France.

During the last few years, 63 articles have been published by the people implicated in the new team. The new team headed by Ms Harriet CORVOL includes two young researchers and one associate professor. Even if several of these publications came from collaborations, the production of this team is promising with recent papers published in Nat Genet, Hum Mutat, Hum Mol Genet, Am J Pathol, ...

An important point which is very promising for the future is that, during these last years, the team leader developed a national cystic fibrosis gene modifier program, with 3700 inclusions to date and preliminary GWAS performed in 1350 CF patients. The research program is partly based on a phenomic/genomic analysis of this study population in collaboration with other groups from Europ and USA, and with a program on functional genetics, to be performed by the young researchers who joined the team leader.

Assessment of the team's academic reputation and appeal:

The team leader is leading a national and international program on gene modifiers in cystic fibrosis, and is a partner in several other international programs (Nat Genet, 2012, studies performed by a US-France partnership). She coordinates national projects on this topic and is one of the leaders of the European consortium on Cystic Fibrosis. At present, the team is small but its project is based on a strong phenotypic database and on a genomic, phenomic/genomic program which is promising for the next future.

The team is already well known nationally and internationally, and the team leader is invited to participate in most european or international events on cystic fibrosis.

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

Cystic fibrosis has major social and economic impacts and many events are organized along the year on the scientific, medical and social aspects of this disease. The team participates actively in these events and contributed to articles in large public journals. The translational research conducted by the team is supported by a strong interaction between the hospital pulmonology department and the research lab since several members of the team are physicians and share their activities between basic and clinical research.

As mentioned earlier, the team succeeded during the last few years in building up a national phenotypic database on CF, and in creating the European CF Modifier Gene Consortium. Ms Harriet CORVOL is invited in international and national conferences and appears as one of a research leader in the field.

Assesment of the team's organisation and life:

The team is an emerging team and its size is still small. One of the researcher was recently recruited by the INSERM as a CR1. The group appears very homogeneous while focusing on a single thematic area but it will certainly help the success of the project to recruit additional researchers or postdocs. Also, the development and maintenance of the database will need the recruitment or close partnership with computer and database experts.

Assessment of the team's involvement in training through research:

At present, 3 PhD students and one post-doc are part of the team. Also, members of the group contribute actively to the training of MD and young pediatricians interested in CF pathophysiology and care. Members of the team contribute actively to the teaching programs of respiratory M1 and M2.

Assessment of the five-year plan and strategy:

The project is mainly based on the phenotypic database built up during the previous years with an ambitious genomic and phenomic/genomic program supported by a collection of biological samples from many patients with CF. The team leader appears very dynamic, as do the young and active researchers belonging to the group. These conditions provide a good basis and we can expect this new team to generate good research in the next future.

Conclusion:

- Strengths and opportunities:

- young emerging and dynamic team with an ambitious program supported by a strong established database;

- translationl research with good interactions between physicians and researchers involved in the pathophysiology and care of patienst with CF.

- Weaknesses and threats:

- small size of the team, no computer and database experts inside the team;

- functional genomics program not yet clearly defined.

- Recommendations:

The team is engaged in a wide genomic research project, the drawback is that at the start, they did not yet identify a clear research program. The team will benefit identifying clear research directions to improve its strength in terms of research achievements, publications, and attractiveness.

The development and maintenance of the database will need the recruitment or close partnership with computer and database experts.

Team 12 : Genetic and acquired lipodystrophies

Name of team leader: Mr Bruno FEVE

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	8	10	10
N2: Permanent EPST or EPIC researchers and similar positions	2	4	4
N3: Other permanent staff (without research duties)	12	11	2
N4: Other professors (PREM, ECC, etc.)		1	
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		1	
N6: Other contractual staff (without research duties)	2	2	1
TOTAL N1 to N6	24	29	17

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	6	
Theses defended	8	
Postdoctoral students having spent at least 12 months in the team	4	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	9	12

• Detailed assessments

Assessment of scientific quality and outputs:

The research group led by Ms Jacqueline CAPEAU (new PI Dr. Bruno FÈVE) meets high standards of scientific quality. It is a highly productive and successful team working in the area of adipose tissue pathophysiology, lipodystrophies and related metabolic and cardiovascular alterations. There are several characteristics to be remarked: large group with an excellent long-standing trajectory, successful translational approach from basic science to clinical research and high quality of publication report. Recruitment of the present team leader occurred two years ago. It appears that he has already established several basic and clinical projects on glucocorticoid-induced lipodystrophies, which are complementary to the traditional on-going research themes of the group: genetic and acquired lipodystrophies.

Outputs of the team during last five years, both in number and quality, have reached high international standards, including major breakthroughs in the field. This can be exemplified by some of their most outstanding papers published in prestigious generalist scientific journals such as The New England Journal of Medicine (2), together with more than fifty articles in journals with an impact factor in the top 10% of the area. Furthermore, they have also contributed a large number of reviews (with peer-review; quite a few of them by invitation) in top-ranking scientific journals such as Nature Rev Endocrinol, Trends Mol Med, Trends Endocrinol Metab. As an overall assessment, the team has been -and is still- a leading international reference in the field of adipose tissue pathophysiology.

Assessment of the team's academic reputation and appeal:

The background of the team in its research area is excellent. The group has been an internationally recognized reference for research on lipodystrophies since many years. They have highly contributed to new insights in the area, such as by identifying new genes responsible for some familiar lipodystrophies and characterizing cellular and molecular basis for the deleterious effects of antiretroviral drugs on HIV-infected patients. Its past team leader, Ms Jacqueline CAPEAU, is an internationally recognized expert on acquired lipodystrophy and associated metabolic syndrome in HIV-infected patients. The present PI and the rest of senior scientists of the team also have international reputation as depicted by their contributions to international and national meetings and committees. The team participates and also leads several granted international research projects and programs. Moreover, the team has long-term collaborations with recognized laboratories, both national and international, and also with other CDR teams.

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

The team is involved in the development of new treatments for lipodystrophies and identification of risk factors, and participates in clinical trials and in projects funded by ANRS. The team has been funded by several pharmaceutical companies. Senior members of the team also contribute to clinical formation of practitioners and patients' advice. The team contributes and/or is responsible of unique Biobanks from different types of lipodystrophy. The recent development of a Biomarkers plataform will contribute to an accurate and rapid assessment of metabolic, cardiovascular and hepatic disturbances in individual patients and cohorts.

Assesment of the team's organisation and life:

The composition of the group is remarkable as it gathers researchers in the mentioned distinct research aspects, from researchers experienced in clinical aspects and analysis of patients to other researches with solid expertise in molecular and cellular in vitro approaches.

They have defined three main research projects and the respective roles of senior scientists. They have also distributed the large staff of researchers between those subgroups. Considering the large size of the team, this internal structure constitutes a great initiative.

Assessment of the team's involvement in training through research:

The involvement of the team in student formation is very good, not only by the high number of master and doctoral students trained but also for their participation in related teaching duties. Several members of the research group are teachers in the faculties of medicine and sciences of the UPMC, and participate in master and PhD programs. Members of the group also actively participate in summer schools, doctoral schools and national training of young physicians. Remarkably, all PhD students were funded by national or international agencies.

Assessment of the five-year plan and strategy:

The future research proposed by the team is coherent with its excellent background on lipodystrophies and their cellular and molecular basis. Moreover, the proposal, organized in three main subjects (i.e., genetic lipodystrophies, acquired HIV-related lipodystrophies and glucocorticoid-induced lipodystrophies), fully covers the main scientific areas to be studied. Combination of the analysis of clinical disturbances in patients together with more basic research approaches (at molecular, cellular, biochemical, omics levels) is remarkable and will contribute not only to descriptive results but also to identify molecular mechanisms underlying pathological alterations. This will further enable major breakthroughs in the field. The renowned quality of the scientific staff together with the scientific excellence of the proposed project will likely maintain or even improve the already leading international position of this team.

Conclusion:

- Strengths and opportunities:

Main strengths: excellent translational team with a large critical mass, long term collaborations with other recognized national or international laboratories, active collaborations within the CDR.

- Weaknesses and threats:

The proposed research program is broad and quite ambitious. Although this can be viewed as a threat, it may also provide the advantage of having the opportunity to further develop those research approaches being most promising. However, this prioritization will require a well defined leadership and deep coordination between the three project leaders and the rest of the staff.

- Recommendations:

This is an excellent team with a solid international reputation that deserves sustained support. The team should take the opportunity to fully unite the group and prioritize interests and efforts. Regarding the organization and managing of the research group, recruitment of some new postdocs would be interesting. The dynamics of the group could also be enriched with more students from abroad. The team leader should focus on the cohesion of the whole group of researchers. Follow-up of the development of the inflammatory and metabolic biomarkers platform for complete metabolic investigations and treatment of the patients affected by genetic or acquired lipodystropies should be prioritized. Maintenance of scientific collaborations, participation in health programs and networks, and if possible, increased interaction with pharmaceutical companies is recommended.

Team 13 : Neuroendocrine Mechanisms of Longevity and Age-related Disease

Name of team leader: Mr Martin HOLZENBERGER

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	2	2	2
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	1	1
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	6	6	3

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	3	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the team	1	
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 :

Mr Martin HOLZENBERGER authored a paper in Nature when forming part of the Le Bouc´s lab in the same institute that represented a turning point in the field of the genetics of aging in vertebrates. This paper has been cited over 800 times. Based on the relevance of this finding the PI has continued along this line of research and during the last years has built a reputation in the field. He has engaged in very good collaborations resulting in high quality publications. The in-house work of the group is following a more conventional path in terms of topics and publications but have produced, within the evaluated period, a very solid paper in the field of aging and IGFs (PLOs Biol, Endocrinology, PLoS One). More recently, in later years its output has somewhat decreased together with the number of high impact publications but this is probably a trough in the production of the group as its methodological approach usually requires years to produce results.

Assessment of the team's academic reputation and appeal:

The reputation of this group is based on its steering role in showing that the IGF system may be an important genetic regulator of aging in vertebrates. Based on the generation of very good mouse models the group maintains active collaborations with several strong international teams. They also document important collaborations with local groups. The PI has been invited to deliver lectures in different institutions and meetings. The group has participated in european consortiums and organized a yearly meeting at a national level. The amount of foreign students recruited by the group is very modest while the two recently incorporated junior researchers come from very good institutions.

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

The group has obtained support from non-scientific corporations and participated in TV programs related to their work. Otherwise, they do not appear to be very active at this level, no production of patents or contracts with industry are shown.

Assesment of the team's organisation and life:

This first appraisal is based on the information provided by the team. Based on it, the group is organized in a conventional, effective manner to carry out their duties. Exchange of ideas, regular follow-up meetings, etc ... form the basis of this internal daily life.

Assessment of the team's involvement in training through research:

The group is actively involved in forming students and PhD students in a regular basis. They are affiliated to two universities for teaching purposes. They appear to have a good activity in this regard for a research lab of their size.

Assessment of the five-year plan and strategy:

The research plan for the next years represents a continuation of the line of work followed by the group since its inception and therefore is not particularly original for them. As the PI has a long experience in the design of research projects all possible risks are well accounted for. Part of the development of the project is not specified as it relies on results that will be obtained along its course, but this is justified because it is partly an observational, exploratory design. The project, divided in 3 parts corresponding to each of the group senior investigators is consistent and well interconnected among the 3 leaders. Based on previous experience the work plan is entirely feasible and will reasonably be developed along the alloted time frame.

Conclusion:

- Strengths and opportunities:

The team built its prestige mostly on a high profile paper in Nature several years ago that shifted the field of aging into a new momentum. The group is now profiting of its prestige and has produced several very good papers in the field. The incorporation of 2 experienced researchers will improve the skills and resources of the team. The group has a strong background on international, highly productive collaborations with top research teams. In-house collaboration also appears profitable. Opportunities rely fundamentally in the very active field of work of the group. Research into aging processes is one of the most busy research topics nowadays and funding opportunities in age-related pathologies abound. However this is a double-edge sword.

- Weaknesses and threats:

The competition in the field of work of the group (aging and endocrine homeostasis) is becoming more and more intense. The main technical approach used in the past by the group, (that heavily rely on directed transgenesis), is now becoming common in most labs so the relative edge of the team will be lost in the near future. The group plans to keep using the same methods for the next five-year plan, while new methodological approaches are not envisaged.

- Recommendations:

Overall performance of the group is correct so no major recommendations are issued. An increase in publication output of the group (no collaborations) will be desirable. It is also advisable to explore new technological venues to maintain their competitiviness by recruiting new personnel specialized in new techniques.

Team 14 : Metabolic and biliary, fibro-inflammatory diseases of the liver

Name of team leader: Ms Chantal HOUSSET

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	14	9	9
N2: Permanent EPST or EPIC researchers and similar positions	4	2	2
N3: Other permanent staff (without research duties)	17	12	3
N4: Other professors (PREM, ECC, etc.)		1	1
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	3	2
N6: Other contractual staff (without research duties)	1	1	
TOTAL N1 to N6	40	28	17

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	11	
Theses defended	8	
Postdoctoral students having spent at least 12 months in the team	6	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	15	10

• Detailed assessments

Assessment of scientific quality and outputs:

The research, which covers basic, translational and clinical issues is partitioned over 5 themes.

1. ABCB4 gene variants and disease. Following-up on the discovery that ABCB4 gene mutations cause low-phospholipid associated cholestasis, the research focused on the cellular and molecular mechanisms of gene defects and led to the development of useful in vitro models and to the development of a novel therapeutic approach of the disease. This is described in publications in top level specialist journals in the field of Hepatology (Gastroenterology, Hepatology, Journal of Hepatology) and high ranking journals of biochemistry/cell biology (eg. Journal of Biological Chemistry).

2. Metabolism of bile acids in disease. Using mouse models of disease, the team provided the first experimental proof that enterohepatic circulation is perturbed in cystic fibrosis, leading to gallbladder shunt of bile acids. This novel concept is published in the world leading specialist journal Gastroenterology. Also, investigation of the pathophysiology of Primary Biliary cirrhosis, at the molecular and translational level, led to improved definition of predictive factors and to improved treatment of the disease with drug associations involving UDCA. Again this was described in several papers, published, amongst others, in the top level Hepatology journals (Gastroenterology, Hepatology, Journal of Hepatology).

3. Cellular mechanisms in liver fibrosis. The work led to the innovative conclusion that not only stellate cells, but also portal myofibroblasts are critical in development of fibrosis. Further, work on hepatitis C, NASH, NAFLD led to the development of important experimental models, and to clinical treatment strategies. This led to primary research papers and reviews in top Hepatology journals and to a patent application.

4. EGF-R and IGF1-R in wound healing and hepatocellular cancer. The topics are more diversed in this theme and led to several publication in excellent specialist journals in the cancer field (Clinical Cancer Research, Cancer Research, Oncogene). Of note, the interesting concept of the mechanisms of EGFR activation stimulated by the intracellular redistribution of a scaffold protein.

5. Diagnosis of liver fibrosis. In this theme, the team evaluated the prognostic and diagnostic potential of a algorithm (FibroTest) as a biomarker of fibrosis, and searched for improvements. The work led to publications in excellent hepatology journals.

The overall scientific production of the team is excellent, and continuous throughout the years. The research has brought significant advance in understanding the pathophysiology of biliary disease. It has built further on earlier findings (disease associated with mutations in ABCB4 gene), and has brought new and innovative concepts to light (cholecystopathic shunt of bile acids). The team has also opened new venues in understanding the cellular mechanisms of liver fibrosis (role of portal myofibroblasts), and has very efficiently translated basic science findings into clinical applications.

The key results are published in top-level journals in the field of gastro-enterology and hepatology, ensuring efficient dissemination of the data. It is too early to evaluate citation rates of recently published papers; however, invitations to the main American and European meetings (American Association for the Study of Liver Disease, European Association for the Study of the Liver) enhance the visibility of the work of the team.

The team contains 6 subteams and there are several publications demonstrating collaborations among the subteams, ensuring the coherence of the team as a whole.

Assessment of the team's academic reputation and appeal:

The academic reputation of the team as a whole is excellent at the national and international level as assessed by:

- publication of papers which were advertised by the editorial board by means of specific editorial comments;

- publication of invited editorials;

- publication of reviews in high-ranking hepatology journals;

- invitation to high-ranking international meetings;

- organisation of national and international meetings and training courses;

- coordination of national and European research networks;

- coordination of the national reference center on Inflammatory Biliary Diseases.

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

- Clinical network. The effective translational perspective of the research is a major strength of the team and this is supported by basic science. The team benefits from its participation to a wide national and international clinical network, in which the team plays coordinating roles (e.g. national reference center for Inflammatory Biliary Diseases; FP7 FLIP network on Fatty Liver disease).

- Design of therapy. The research of the team led to new therapeutic approaches and improved prognosis of biliary disease, further underlining the societal value of the research.

- Economy. Four patents were filed, including two with license. The work also led to the creation of a start-up (HumanHepCell), which is the second company created by the team (Biopredictive was created in 2002).

- Social commitment. The participation of team members to patient associations underscores its commitment to social values.

Assesment of the team's organisation and life:

Several publications of the team are authored by members of the various subteams, indicating that all team members share a common vision of the research which is partitioned over basic, translational and clinical themes around a common and coherent theme of biliary pathophysiology. The output proves the efficiency of the management. However, there is no clear description of the decision-making process in the team, which is unexpected given the high number of senior scientists and clinicians in the team.

Assessment of the team's involvement in training through research:

The involvement of the team in training through research is two-fold. First, at the local level, the team has trained 34 Master students, 1 MD-PhD, 24 PhD students and 6 post-docs. Three scientists obtained the HDR.

Second, at the international level, the organization by team members of workshops via international scientific societies underscores the commitment of the team to train people in an international perspective. Also, co-tutorship of a PhD thesis with the University of Montréal is a further indication of the team's competence in the field.

Assessment of the five-year plan and strategy:

The team will build further on its strengths, namely the translational research rooted in basic science and the wide clinical network.

1. Genetic defects in the ABCB4 gene. The proposed work is in line of successfull previous work on the function of ABCB4. New focus will be on (i) understanding molecular mechanisms (intracellular trafficking - use of new mouse models, and (ii) on developing therapeutic approaches. In the latter context, collaborations with the Physics Department of UPMC will widen the scope of the research towards design of therapeutic agents based on 3D structure analysis.

2. Bile pathophysiology. The proposed work will extend earlier work on CFTR deficiency. The involvement of the genetic background, intestinal microbiota will constitute the new focus. Also, the cholecystohepatic shunt of bile acids discovered in rodent models will be investigated in patients. In the same context, the role of nuclear receptors in lipid and bile acid homeostasis will be investigated in relation with intestinal microbiota and immunity.

3. Cellular mechanisms of liver fibrosis. Building further on the recently identified role of portal myofibroblasts in fibrosis, the work aims at further defining the role of this cell population. New transgenic mouse models will be investigated.

4. Therapeutic targeting of fibrosis.

The five year plan builds on the strengths of the previous research program period, and consists in extending this work towards improvements in understanding pathophysiology, in treating disease and establishing prognosis. The work was and remains coherent; the transfer to an emergent team of the EGF-R-related projects on wound healing and hepatocellular cancer, will allow for a welcome refocussing of the group on biliary pathophysiology. The proposed experiments are appropriate to answer the scientific questions and resort to up-to-date technology. The proposed work is feasible: funding, expertise, personnel, mouse models and equipment are all available.

Basic and applied research are intimately linked in the team, the translational perspective is well-developed thanks to the strong involvement of senior scientists in clinically-related activities.

Conclusion:

- Strengths and opportunities:

- very strong translational perspective of the work, with high potential for significant impact in basic science, development of improved therapies and efficient socio-economical output;

- strong and focused publication output in the field of hepatology;

- strong national and international networking.

- Weaknesses and threats:

- retirement of staff members : young people will need to be recruited (candidates are identified);

- as stated by the team leader herself, success will critically depend on efficient logistics;

- insufficient recruitment of foreign PhDs and Post-docs despite high international visibility of the team.

- Recommendations:

More international post-docs and PhD's should be recruited. This is a common problem at Saint Antoine, where the numbers of foreign young scientists is low and where most foreign PhDs and post-docs have actually obtained a master degree in France. The international recruitment policy should be discussed and harmonized with other team leaders at CDR Saint Antoine.

Team 15 : IGF system, foetal and postnatal growth

Name of team leader: Mr Yves LE BOUC and Ms Irène NETCHINE

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	4	4	4
N2: Permanent EPST or EPIC researchers and similar positions	4	1	1
N3: Other permanent staff (without research duties)	8	7	
N4: Other professors (PREM, ECC, etc.)	1	1	
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	4	1
N6: Other contractual staff (without research duties)	2	1	
TOTAL N1 to N6	22	18	6

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	3	
Theses defended	8	
Postdoctoral students having spent at least 12 months in the team	3	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	8	4

• Detailed assessments

Assessment of scientific quality and outputs:

The group has contributed to the international scientific community and to the scientific knowledge in a very substantial way: two key papers, one in J Clinical Endocrinology and Metabolism in 2007 and one in Nature Genetics in 2005 that were of particular value. In addition, the group continues to publish regularly in the leading journals of the field (J Clin Endocrinol Metabolism, Human Mol Genet, Human Mutat). They have shown for the first time that patients with Russel Silver syndrome (RSS) and Beckwith Wiedemann syndrome (BWS) all suffer from a variety of similar basic genetic and epigenetic defects. Indeed, the two entities, RSS and BWS, are mirror pictures of each other. In addition, the group has shown that patients carrying particular genetic or epigenetic markers will carry a high risk to develop tumours whereas other patients carrying yet other genetic or epigenetic markers do not. The group has also assembled a large cohort of patients with RSS and BWS and care for these patients and their families in a laudable and unique way. The group has been able to combine clinical knowledge and skills with true basic research efforts. Their publications represent pieces of translational research on the highest level and of the highest internationally competitive standard.

Assessment of the team's academic reputation and appeal:

The group has received international awards, such as the JCEM clinical publication prize and an EU graduate school award. The team leader has also received the very prestigious ESPE research award of the European Society of Pediatric Endocrinolgy, the latter being the leading international learned society in the field. The two lead researchers have attracted doctoral students and postdocs from France and from abroad continuously over the years. This development appears to even have increased recently demonstrating an increasing high international reputation of the group. Both team leaders are heading European research units (of the ESPE, European Society of Pediatric Endocrinolgy) or committees which organize and support such international research efforts.

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

This group was the only one amongst the teams reviewed that emphasized specifically ethical aspects of their work ! It is trusted that they devote their time to research in order to help their patients and their families ! This fact has to be specifically acknowledged and was anonymously observed by all outside reviewers during the site visit and as well as during reading through the reports. Their research directly adds to clinical care as the development of tumours can be forseseen and necessary examinations can be planned accordingly. – The group also interacts both in a general way and in specific clinical trials with the pharmaceutical industry. While doing so, they add to the advancement of patient care and influence industry in a positive way. They do not automatically give in to mere financial interest of the drug companies. The group has already filed a small number of patents and has set out to do so in regards to epigenetic risk testing in the future.

Assessment of the team's organisation and life:

The team leader is going to retire in the foreseeable future. It has become clear that the group has already started to proceed towards a transition of leadership from him to the co-PI. This appears to have been accomplished in a very agreeable, collegial and friendly way. The team is well organized and the structure of some key researchers and an appropriate number of junior staff working together is well developped.

Assessment of the team's involvement in training through research:

Teaching seems to play an important role in the life of the team. The group has even obtained EU funding for graduate and postgraduate efforts. The key researchers devote their time actively to training and all reviewers were convinced that they are quietly but succesfully pursuing the idea of teaching through research.

Assessment of the five-year plan and strategy:

Both in their written report and in their joint presentation, a clear study plan was described. The study plan is well focussed and based upon recent findings by themselves or other leading researchers from France and abroad. The projects follow clear hypotheses. The study plan is well described and the goals seem to be achievable within the scope of their group and the center. International and national collaborations as well as group work within the Centre are mentioned and will add to the overall success. It is to be expected that the research will lead to major discoveries and important publications will be written. The research plan is very competitive both in France and internationally. Findings will provide major contributions not only in pediatric endocrinology but also in basic genetics, epigenetics and cell biology. Ethical considerations will provide support for other groups in the centre who will expand their clinical work and consider ethical issues as well once this group´s example will have been fully recognized by all.

Conclusion:

This team is to be congratulated for their continuous excellence in basic science and clinical care. They should also be applauded for having put forward a careful and achievable as yet competitive research plan for the future. Their efforts should be supported without restrictions and wholeheartedly. They truly deserve every support that can be given to the centre and by the centre in the future.

- Strengths and opportunities:

The team is advancing well both in terms of research output, clinical care, ethical advancement and education. The team has been very succesful and is proceeding well. Future challenges such as transition of leadership are being addressed and young researchers are attracted.

- Weaknesses and threats:

There are no major weaknesses or threats for the team as such. An overall threat however could be a reduction in research funding and research efforts in the basic sciences around Europe. The team depends upon recognition both by hospital administration and politicians.

- Recommendations:

No specific one.

5 • Conduct of the visit

Visit dates:

Start: Thursday, 13 December 2012, at 8:30

End: Friday, 14 December 2012, at 17:00

Visit site(s): Hôpital Saint-Antoine – Bâtiment Kourilsky

Institution: INSERM

Address : 184, rue du Faubourg Saint-Antoine, 75012 Paris

Second site: Faculté de Médecine Pierre et Marie Curie – Site Saint-Antoine

Institution: UPMC

Address : 27, rue Chaligny, 75012 Paris

Specific premises visited:

No time was devoted to specific premises visits. All scientific presentations and discussions were performed in the seminar room in the Kourilsky building.

Conduct of visit:

The visit was well organized and the Committee appreciated the organization and hosting. Even if the program was very busy, all the committee members participated to all the scientific presentations and discussions. The committee was splitted in 3 sub-committees only for the meetings with the scientists, the engineers and technicians, and the PhD students and post-doctoral fellows.

Thursday, December 13

8:00 to 8:30 a.m.:	Welcome of the Committee
8:30 to 9:00 a.m.:	Restricted meeting of the Committee
9:00 to 10:00 a.m.:	Overview of the CDR past activity and project: J CAPEAU and B FÈVE
	(40 min presentation and 20 min discussion)
10:00 to 10:20 a.m.:	Coffee break
10:20 a.m. to 1:00 p.m.:	Presentation of team projects

(Oncology-Hematology pole: 4 teams; 40 min/team: 20 min presentation and 20 min discussion)	
- Team Mr Alex DUVAL:	Microsatellite instability and cancer
- Team Ms Annette LARSEN & Mr Aimery DE GRAMONT:	Cancer biology and therapeutics
- Team Ms Françoise PRAZ & Mr Olivier ROSMORDUC:	Biology and treatment of hepato-biliary tumors
- Team Mr Selim ARACTINGI & Ms Emile DARAI:	Progenitors and endothelial cells during and after pregnancy

1:00 to 2:00 p.m.: Lunch buffet

2:00 p.m. to 4:40 p.m.: Presentation of team projects

(Oncology-Hematology pole: 4 teams; 40 min/team: 20 min presentation and 20 min discussion)	
- Team Mr Azeddine ATFI:	Cell signaling and carcinogenesis
- Team Mr Luc DOUAY:	Proliferation and differentiation of stem cells: application to cell therapy
- Team Mr François DELHOMMEAU:	Molecular lesions, initiation, and evolution of myeloid malignancies
- Team Mr Mohamad MOHTY:	Graft versus host reactions after allogeneic cell transplantation

4:40 p.m. to 5:00 p.m.: Coffee break

5:00 p.m. to 7:00 p.m.: Presentation of team projects

(Metabolism-Inflammation pole: 3 teams; 40 min/team: 20 min presentation and 20 min discussion)	
- Team Mr Martin HOLZENBERGER:	*Neuroendocrine mechanisms of longevity and age-related diseases*
- Team Mr Pierre AUCOUTURIER:	*Adaptive immunity, neuroinflammation, and neurodegenerative disorders*
- Team Mr Francis BERENBAUM:	*Age-related joint diseases and metabolism*

7:15 p.m. to 8:45 p.m.: First restricted meeting of the committee AERES

Friday, December 14

8:30 to 11:10 a.m.: Presentation of team projects

(Metabolism-Inflammation pole: 4 teams; 40 min/team: 20 min presentation and 20 min discussion)	
- Team Ms Chantal HOUSSET:	*Metabolic and biliary, fibro-inflammatory diseases of the liver*
- Team Ms Harriet CORVOL:	*Cystic fibrosis phenomics and genomics*
- Team Mr Yves LE BOUC & Ms Irene NETCHINE:	*IGF system and fetal and postnatal growth*
- Team Mr Bruno FÈVE:	*Genetic and acquired lipodystrophies*

11:10 to 11:40 a.m.: Coffee break

11:40 a.m. to 12:40 p.m.: Meeting with the scientists, engineers, and doc. and post-doc. staffs

12:40 a.m. to 1:15 p.m.: Lunch buffet, and informal discussions with the representatives of INSERM, University, and Hospital present at the lunch

1:15 p.m. to 2:15 p.m.: Second restricted meeting of the committee AERES

2:15-2:45 p.m.: Meeting with the representatives of INSERM, University, and Hospital

2:45 p.m. to 5:00 p.m.: Final restricted meeting of the committee AERES

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

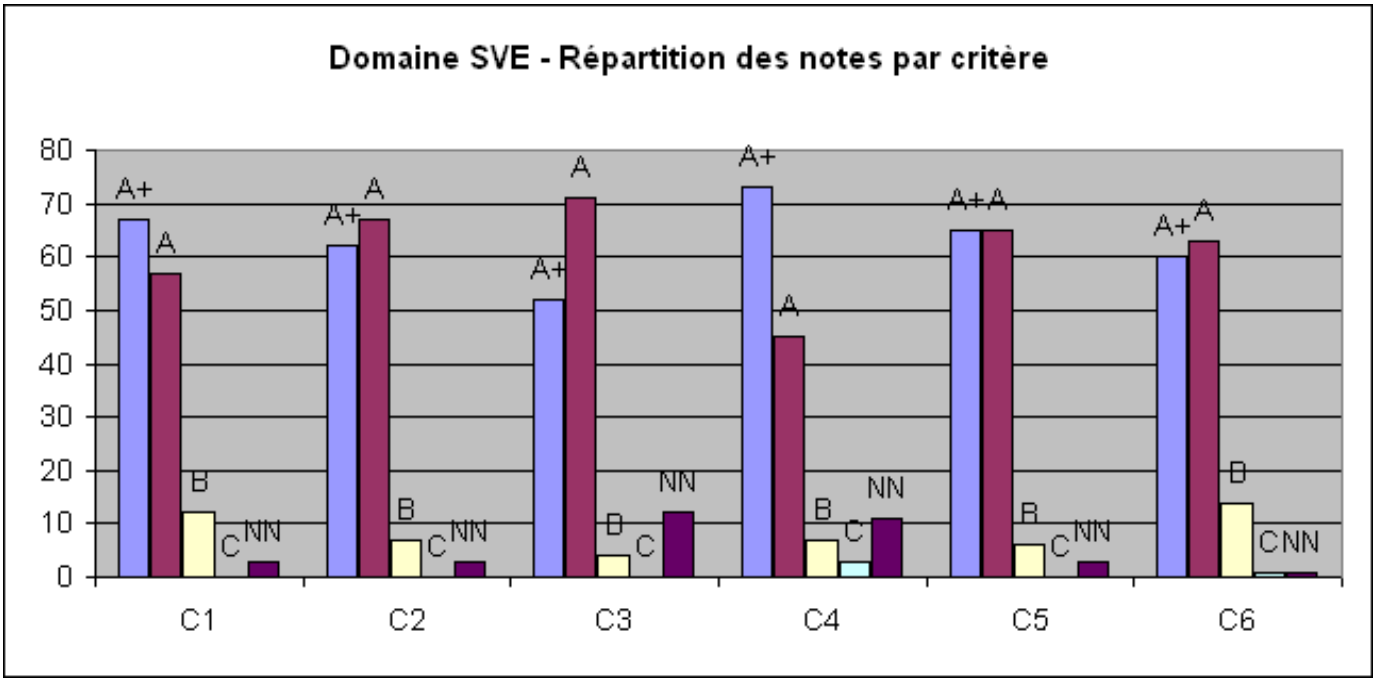
Grades

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

Percentages

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

Histogram



7 • Supervising bodies' general comments

Paris le 10 04 2013

Le Président
Didier Houssin
Agence d'évaluation de la recherche
et de l'enseignement supérieur
20 rue Vivienne - 75002 PARIS

M. le Président,

Nous avons pris connaissance avec le plus grand intérêt de votre rapport concernant le projet du Centre de Recherche Saint Antoine, porté par M. Feve. Nous tenons à remercier l'AERES et le comité pour l'efficacité et la qualité du travail d'analyse qui a été conduit.

Ce rapport a été transmis au directeur du laboratoire qui nous a fait part en retour de ses commentaires que vous trouverez ci-joint. Nous espérons que ces informations vous permettront de bien finaliser l'évaluation du laboratoire.

Restant à votre disposition pour de plus amples informations, je vous prie de croire, M. le Président, à l'expression de mes salutations respectueuses.

Le Vice -Président Recherche et Innovation

Paul Indelicato

Vice-présidence Recherche et Innovation
Tél. 01 44 27 20 09
www.upmc.fr

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THE SAINT-ANTOINE RESEARCH CENTRE

CdR Saint-Antoine

Current Director: Jacqueline Capeau

Proposed Future Director: Bruno Fève

General comments on the AERES report

1 • General comments for the Research Centre

We thank the AERES committee for its attentive and very careful evaluation or the "Centre de Recherche" (CDR) Saint-Antoine. We have appreciated the very positive comments on the strong integration of our unit in the Saint-Antoine Hospital, on the scientific quality of our teams, and on the collaborations between teams. The high financial support from academic institutions and industrial partners has also been underlined. The participation of several of our teams in a large panel of "Investissements d'avenir" is also mentioned as a very positive aspect.

Weaknesses and threats have been identified, with related specific recommendations. These issues have been discussed with all team leaders. We provide here below specific answers and concrete proposals.

General comments

- We have now programmed a dedicated international call for recruitment of two new teams. We have decided that this call will favor themes at the interface between the two poles of our CDR, "Oncology-Hematology" and "Metabolism-Inflammation" to strengthen the potential interactions within the CDR, and to provide new and complementary expertises in order to improve our competitiveness. We have selected two themes: "Metabolism and tumoral microenvironment" and "Chronic inflammation and immune activation" to improve the visibility of the CDR at the interface between cancer and metabolism. As for recently hosted teams, the CDR will financially support the installation of the new groups on the site. Nonetheless, we seek to ensure and pursue support to the teams already present within the CDR.

- This call is directly linked to our capacity to welcome new teams. We will take advantage of the renovation of the "Kourislky" building funded by INSERM and planed for 19 months from November 2013, to fully optimize the occupancy of these surfaces. Renovated laboratories will be dedicated to our teams currently present in this building, but also to welcome the team of F Berenbaum and the recruited new teams. The call will be submitted next September.

- The report recommended improving the level of financial mutualization. Thus, we propose to increase by 50% the percentage of the mutualized budget (from 20 to 30 % of the total budget allocated by INSERM and University Paris 6). More specifically this will participate to the development of existing or new common platforms in the CDR.

- The report has pointed that many teams will have significant needs in high throughput sequencing, and that the bioinformatics analysis of the generated data could represent a crucial and limiting step and propose to conduct a global strategy on bioinformatics. We agree that the development of a platform dedicated to bioinformatics will represent a major challenge for the CDR. Otherwise, the UPMC high throughput sequencing platform P3S plans to markedly increase the bioinformatics staff, and the CDR teams have a natural access to this platform. Therefore, we propose to recruit in priority during the next years a research engineer and an assistant-engineer in bioinformatics to provide a direct support to the CDR staff, complementary to the support provided by the P3S platform. They will also represent the privileged interface between our teams and the external structures involved in omics and sequencing analyses.

Specific comments on the CDR

- Administrative CDR activities will be further gathered in adjacent premises during the renovation of the "Kourilsky" building.

- We have already at the CDR level seminars in which investigators and clinicians present their results. We have certainly to increase their number. In addition, they also have the opportunity to present these data during the "annual day" of the CDR for PhD students and post-docs, and also during the annual Forum of the CDR in Fontainebleau.

- Information for PhD students and post-docs on our local available facilities is indicated on our Web site, and its accessibility will improved soon, by integrating links with our own CDR facilities and the current IFR/SFR platforms.

- We have already international researchers invited to give conferences in the CDR. In general, they give a talk when present in Paris for scientific collaborations and these conferences are generally planned as "exceptional" seminars, in addition to the CDR Monday meeting.

2 • Team-by-team answers and comments

"Oncology-Hematology" Pole

Team 1 :	Proliferation et differentiation of stem cells : application to cell therapy
Name of team leader:	Mr Selim ARACTINGI and Mr Emile DARAI

The members of the team have read with interest the comments done by the committee and acknowledge for constructive remarks. We fully agree that there is an urgent effort to recruit a full time scientist in addition to the persons already present. We have a candidate that has been ranked 1st in the complementary list of the CR1 Inserm competition last year. We hope that this year, this person could be recruited on a permanent position.

Team 2 :	Role of the transforming growth factor beta (TGF-β) signaling pathway in tumor progression
Name of team leader:	Mr Azeddine ATFI

None

Team 3 :	Molecular lesions, initiation, and evolution of myeloid malignancies
Name of team leader:	Mr François DELHOMMEAU

None

Team 4 :	Proliferation et differentiation of stem cells : application to cell therapy
Name of team leader:	Mr Luc DOUAY

QS1 - the deliverables of the red blood cell production project need to solve several basic scientific locks. Collaborations with groups involved in the transcriptional regulation of red cell differentiation and recruitment of a full time researcher;

Answer: The team is now full partner in the Labex "GReX" gathering all the French teams involved in erythropoiesis. The team is WP leader and is settling a tight collaboration with the group of Olivier Hermine for study of the transcriptional regulation of red cell differentiation.

A call for proposal of a full time researcher will be made.

QS2 - the registry subgroup will be threatened by the coming departure of its leader.

Answer: Regarding the international transplant registry, the present leader who has recently relocated and extended the facilities, will remain active until October 2015 and may even pursue later his expertise. Also, the team has additional leaders such as Mohamad Mohty chair of the Acute Leukemia Working Party, Laurent Garderet secretary of the Myeloma subcommittee as part of the chronic leukemia working party of the EBMT and Myriam Labopin as the head of statistics for Europe. The EBMT structure in Paris attracts many researchers and physicians from all over Europe. We feel confident that it will continue to thrive.

QS3 - a reinforcement of the group focusing on mesenchymal stem cell to increase the production of this group with unquestionable expertise.

Answer: This group does act in close collaboration with the RBC group, particularly in designing and performing all the animal experiments. One of its post-doc will apply in January 2014 for Inserm CR1 examination.

Collaboration with the GVH team of M.Mothy is scheduled through J.Voswinkel for clinical protocols.

Team 5 :	Microsatellite instability and cancer: from biology to clinics
Name of team leader:	Mr Alex DUVAL

We are grateful to the AERES committee for its scientific expertise. We feel that the evaluation of our research team is very positive. However, we would like to make a few comments to clarify some points that were raised by the committee as possible weaknesses and threats of our research project.

Of course, we are aware that performing such an ambitious project on MSI tumours will be challenging, but we strongly believe that it is feasible for several reasons:

(i) Next-generation sequencing will be performed outside the lab within devoted platforms that belong to the French national league against cancer (LNCC). Importantly, this project is already funded by this association, and bioinformatical approaches will be developed by dedicated scientists from the 'Tumour Identity Card' structure (belonging to LNCC) with an excellent training in the field. Laetitia Marisa (Research Engineer) belongs to this structure and is mainly devoted to our project;

(ii) Mouse phenotyping is already well organized within and outside the team. Pathologists attached to the team (*e.g.* Magali Svrcek, Jean-François Flejou) perform the histological examination of tumour specimens on a daily basis. They are assisted in this task by technicians from a dedicated platform of the SFR.

Finally, we agree that particular efforts should be made during the next few years to attract PhD and Post-Doc students from abroad to develop our projects. This will be done by further developing our collaborations with groups and labs working on MSI tumours in Europe, Australia and Asia.

Team 6 :	Cancer biology and therapeutics
Name of team leader:	Mrs Annette K. LARSEN and Mr Aimery de GRAMONT

We very much appreciate the detailed AERES report of our major accomplishments as summarized below:

1) A true continuum between fundamental, translation and clinical research

2) A strong production of quality research with high visibility

3) The solid international recognition of the team and the attractiveness of the lab (recruitment from Europe, Africa, North America, South America and Asia)

4) Excellent association with the pharmaceutical industry facilitating the implementation of our findings

5) Important contribution to teaching activities at our university including creation and coordination of new courses

Weaknesses and threats

One CR is not included in the research project because she has left for retirement early 2012.

The other CR has been working on an important collaborative project which is not yet accepted for publication. She is currently actively involved in an internal collaborative project on the function of WISP1/2 in the colon.

Recommendation

We completely agree with the recommendation and are actively boosting collaboration within the group. We already start seeing the result of this with 2 recent collaborative articles between established group members and the senior researchers (DR2) who joined the team a year ago.

Team 7 :	Graft-vs.-Host Reactions after Allogeneic stem Cell Transplantation
Name of team leader:	Mr Mohamad MOHTY

Weaknesses and threats

- Lack of dedicated scientist:
This team has already confirmed during the presentation that it will aim to recruit a dedicated scientist expert in the proposed topic. The discussions are currently quite advanced.

- Highly competitive field, particularly from better resourced US groups:
The group leader would like to emphasize that despite the competition from a single US group, there is currently no other French or European group addressing this topic. Thus, this is a clear window of opportunity for a European effort in the field.

- No tradition of training clinical fellows in laboratory research.:
The group leader has already trained 3 clinical fellows in laboratory research (PhD) in the last 4 years (A. Clavert, E. Brissot, F. Malard)

Recommendations

- Investment in at least one dedicated scientist and consideration of the use of animal models:
Please see above for recruitment of scientist; the use of animal models is currently under consideration through a collaboration with Inserm Unit 1098 at Besancon. This is a highlighted by a recent common publication (Couturier et al., Leukemia. 2013 Feb 12. doi: 10.1038/leu.2013.39. [Epub ahead of print])

- Development of a clinical fellow programme offering clinical experience followed by dedicated laboratory project:
This is currently under development; a university diploma ("Diplome d'Université") entirely dedicated to allogeneic stem cell transplantation has just been approved (March 2013) by the UPMC, and will serve as basis for setting a translational research training program that will start by September 2013.

- Considerable pre-clinical discussion with proteomics and bioinformatics team as to the necessary samples and analysis before embarking on a potential 'me too' biomarker discovery project.:
The team has already established a close collaboration with Dr Y. Foucher from the University of Nantes, team EA 4275; this team is internationally recognized in the field of bioinformatics and validation of biomarkers. An application for a common grant was made in February 2013 as part of the INSERM "'Systems biology 2013" call.

Team 8 :	Biology and Treatment of Hepatobiliary Tumors
Name of team leader:	Mrs Françoise PRAZ and Mr Olivier ROSMORDUC

The Saint-Antoine hospital has an important activity in medical and surgical managements of patients with liver cancer, which justifies establishing a team of basic and translational research dedicated to the study of these tumors (hepatocellular carcinoma and cholangiocarcinoma). This team will bring together complementary expertise previously scattered in 3 teams of the CdR and 1 team from the University whose research topics were less specialized, and less favorable to the visibility of the team members. This team will allow a better integration of the researchers and the clinicians in an environment favorable to conduct innovative projects in this highly competitive field, and ultimately attract young researchers.

The strategy chosen by the whole team to develop fundamental projects with great potential translational applications requires a governance adapted to these objectives, capable of interacting with both the industry and the academic structures. Very logically, the whole team wished a mixed governance with well defined and complementary missions: clinical and translational projects (OR), relations with the industry (OR), relations with the Faculty of Medicine (OR), the UPMC-UFR of Biology and the INSERM (FP), welcome and training of Master and PhD students (FP), funding and human resources management (FP), grant applications (FP, OR). The scientific policy and objectives, discussed in a collegial manner with the team, are placed under the joint liability (FP, OR).

Our expertise in translational research has led to significant advances in the understanding of the molecular mechanisms of liver carcinogenesis (cross-talk between RTKs, role of tumor environment and EMT, resistance to targeted therapies, cell cycle alterations...), establishing a rational for multicenter clinical trials (eg SEARCH). This expertise recently allowed us to coordinate translational research projects funded by OSEO and INCa and recruit two new post-doctoral researchers.

"Metabolism-Inflammation" Pole

Team 9 :	Immune system, Neuroinflammation and Neurodegenerative diseases (IN2)
Name of team leader:	Mr Pierre AUCOUTURIER

We would like to focus our answers on the following points:

Work force

Since december 2012, two more scientists have decided to join the team:

- Catherine Johanet, MCU-PH, St-Antoine hospital (Dpt of biological immunology)
- Marie Duchamp, AHU, St-Antoine hospital (Dpt of biological immunology)

The team will include 3 PhD students on January 2014.

Guillaume Dorothée will defend his HDR in 2013.

We will apply again for a MCU position at UFR927 this year.

Scientific interactions and visibility within the AD community/networks

In addition to IMABIO3, further national collaborative projects have been initiated (ANR/DGOS call "PRTS", in progress) with teams that are well-recognized in AD field (Luc Buée, Florence Pasquier, Sonia Alamowitch, Hugues Chabriat).

Guillaume Dorothée just initiated collaborations with international teams in the field of neuroimmunology in AD (Tony Wyss-Coray, USA; Alon Monsonego, Israel).

Of note, the recent acceptation for publication in Biological Psychiatry (IF>8), of a commentary/viewpoint article illustrates the improving visibility of the team in the scientific and medical field of AD.

In the same line, Guillaume Dorothée has been invited to give a presentation at the next *Journées Internationales de la Société Française de Neurologie* (Paris, October 2013). Part of his work has also just been selected for an oral presentation at the next *Alzheimer's Association International Conference* (AAIC 2013, Boston, July 2013).

Translational research

A part of the team leader's hospital duties will now be dedicated to developing serological studies, with a special focus on atypical forms of AD and cerebral amyloid angiopathy (ANR/DGOS project to be submitted in April 2013). As mentioned above, 2 additional persons are joining the team and will be involved in translational programs.

Team 10 :	Metabolism and age-related joint diseases
Name of team leader:	Mr Francis BERENBAUM

We would like to warmly thank the experts for the time they took for writing their report on our team.

Concerning the lack of HDR in our group, since our presentation, Dr Houard (MCU) has obtained his HDR last month, Dr Jérémie Sellam (MCU-PH) is now waiting for his HDR defence in the next 2 months and Dr Claire Jacques (MCU) is willing to defend her HDR in the next 3 years. So, the team is going to have 3 HDR in the next weeks and eventually 4 in the next years.

Finally, we do hope that our integration into the CdR will help us to give us the visibility needed for attracting full-time researchers during the next 5 years.

We hope that the experts for their final report will take this additional information into account.

Team 11 :	Cystic Fibrosis: Physiopathology and Phenogenomics
Name of team leader:	Mrs Harriet CORVOL

Recommendation n°1: The team is engaged in a wide genomic research project, the drawback is that at the start, they did not yet identify a clear research program. The team will benefit identifying clear research directions to improve its strength in terms of research achievements, publications, and attractiveness.
Answer: The team research program will, of course, be driven by the genome wide results. However, main program's directions have been identified:
(1) We will identify loci associated with several CF phenotypes' severity.
(2) The functional consequences of the variants will then be studied *in vitro* and *in vivo*.
(3) In parallel, we will determine unknown cellular mode of actions of therapies and new promising molecules in CF.

Recommendation n°2: The development and maintenance of the database will need the recruitment or close partnership with computer and database experts.
Answer: The recruitment of dedicated staff with expertise in database management and computer development will be one of our priorities, as the maintenance of the longitudinal phenotypic data collection is crucial.

Team 12 :	Genetic and acquired lipodystrophies
Name of team leader:	Mr Bruno FEVE

We thank the AERES committee for his very positive evaluation. We only want to make a few comments on the recommendations:

- It is suggested that some new postdocs should be recruited: two postdocs arrived in our group in December 2012 and March 2013, granted for 18-24 months to work on the pathophysiology of genetic lipodystrophies.
- It is also mentioned that the dynamics of our group should be enriched by more students from abroad. In fact, our report did not indicate that two foreign students have obtained their PhD during the last five years (Korean and Mexican), and this effort will be pursued.
- The development of both a metabolic biomarkers platform ad a clinical platform to explore and treat patients with genetic or acquired lipodystrophies has been clearly identified as a priority of our common project

Team 13 :	Neuroendocrine Mechanisms of Longevity and Age-related Disease
Name of team leader:	Mr Martin HOLZENBERGER

We agree with the expert assessment of our team performance and would like to comment on two points.

1. Concerning «Academic reputation and appeal», last sentence, it should be stressed that at the time of evaluation in 2012/2013 we had more foreign than French PhD students, and together, researchers and students in the lab represented six nationalities : British, Chinese, French, German, Moroccan and US American. Still, we agree that continued effort to increase international recruitment is necessary to ensure and demonstrate competitiveness and open-mindedness.

2. With respect to «5-year-plan and strategy», first sentence and «weaknesses», last sentence, we will increase our sensitivity to novel approaches and new methods to continue developing our research strategy. We would like to

emphasize that we focused for years on conditional mutagenesis *in vivo* and that our transgenic mouse models are today at the cutting edge of research, in particular the tamoxifen-induced knockouts that we efficiently combined with latest transgenic mouse mutants. Combining gene knockout with advanced mouse models of human disease including Alzheimer pathology represents a major step towards translational research and a significant shift of interest towards the field of age-related diseases and the role of somatotropic hormones in endocrine regulation of aging. We thus established numerous state-of-the-art phenotypic tests in the lab that allow us to perform comprehensive analysis in pathophysiology, in particular integrating behavioral, cognitive studies with immunohistochemical and molecular approaches. Naturally, we will carry on adding new approaches as our projects progress, all this to ensure that the group continues its longstanding contribution to scientific discovery.

Team 14 :	Metabolic and biliary, fibro-inflammatory diseases of the liver
Name of team leader:	Mrs Chantal HOUSSET

The recommendation for our team is more international recruitment, which we acknowledge.

So far, as detailed in our report, the team has recruited 7 foreign PhD students (out of a total of 23) including from Brazil, Chile, Lybia, Romania, Ukraine and Venezuela.

Currently we are in the process of recruiting a post-doc from Stockholm, Sweden, a graduate student from Philadelphia, US and a senior visiting scientist from Graz, Austria. On the basis of our international networks and of collaborative programs with other CDR teams, we are determined and in the position to reinforce this policy.

Team 15 :	IGF system, foetal and postnatal growth
Name of team leader:	Mr Yves LE BOUC and Mrs Irène NETCHINE

None