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

Department for the evaluation of research units

AERES report on unit:

Biological Adaptation and Ageing

B2A

Under the supervision of the following institutions and research bodies:

Université Paris 6 - Pierre et Marie Curie

Centre National de la Recherche Scientifique

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

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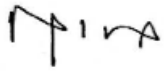
Department Head



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, when necessary, its in-house teams) received the following grades:

- Grading table of the unit: Biological Adaptation and Ageing (B2A)

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

- Grading table of the team: Photobiology

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

- Grading table of the team: Integrative Cellular Aging and Inflammation

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

- Grading table of the team: Eukaryote Translation

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

- Grading table of the team: Neuronal Cell Biology and Pathology

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

- Grading table of the team: Degenerative Processes in Neurons and Networks

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

- Grading table of the team: Brain Development, Repair and Aging

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

- Grading table of the team: Cellular Integration of Neuromodulatory Processes

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

- Grading table of the team: Phenotypic Control of Vascular Smooth Muscle Cells

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

- Grading table of the team: Genetics and Physiopathology of Muscle Tissues

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

Evaluation report

Unit name:	Biological Adaptation and Ageing (B2A) research unit
Unit acronym:	B2A
Label requested:	UMR
Present no.:	
Name of Director (2012-2013):	Mr Jean MARIANI, Mr Bertrand FRIGUET
Name of Project Leader (2014-2018):	Mr Bertrand FRIGUET

Expert Committee members

Chair:

Mr André NIEOULLON, Aix-Marseille University, Marseille

Experts:

Mr Ernest ARENAS, Stem Cell Neurobiology, Sweden

Ms Orna ELROY-STEIN, Tel Aviv University, Israel

Mr Laurent FAGNI, CNRS (representative of the CoNRS)

Mr Jon HUGHES, University of Giessen, Germany

Mr Frank LEZOUALC'H, INSERM, Toulouse (representative of the CSS Inserm)

Ms Anne NEGRE-SALVAYRE, CNRS, Toulouse

Mr Florence PINET, INSERM, Lille

Mr Ferdinando ROSSI, University of Turin, Italy

Ms Florence SOLARI, INSERM, Lyon

Mr Denis VIVIEN, University of Caen Basse-Normandie, Caen (representative of the CNU)

Scientific delegate representing the AERES:

Mr Dominique JOB

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

Ms Dominique DAEGELEN, INSERM

Mr Paul INDELICATO, Pierre & Marie Curie University, Paris

Mr Vincent MOULY, Pierre & Marie Curie University, Paris

Mr Bernard POULAIN, CNRS, representing the INSB (Institute of Biological Sciences)

1 • Introduction

The visit was conducted on December 11th-12th, 2012 at Campus Jussieu (Pierre & Marie Curie Univeristy, Paris, France, Building B, Room 501). The documents sent before the visit provided the Committee with an overview of the organization of the project, which involves the restructuring of 4 previous research units to yield the proposed Biological Adaptation and Aging (B2A) research unit. The report clearly showed the positionning of the 9 teams within the future unit in research aimed at a better understanding of adaptive processes related to aging. Various biological systems (including neuron, muscle and cardio-vascular systems in humans/mammals as well as other animal and plant species) will be used as experimental models to further access the cellular and molecular mechanisms of processes. The oral presentations and subsequent discussions first by the proposed director and then by each team leader on the first day of the visit helped to clarify various aspects of the project and to understand the involvement of each team in the new federative project (Institute of Biology Paris-Seine).

History and geographical location of the unit

The Biological Adaptation and Aging unit gathers together 9 teams previously belonging to 4 separate units at the Faculty of Sciences campus at the Pierre & Marie Curie University (UPMC): UMR7102 (CNRS-UPMC), UR4 (UPMC), UR5 (UPMC) and FRE3402, plus one team coming from the UMR-s 894 (INSERM-University Paris Descartes). The new unit will become a part of a new Research Federation, namely the Institute of Biology Paris-Seine on the Jussieu Campus (research Federation with 5 UMR and associated platforms). Although the research of each team deals with specific aspects of cell biology a major interest of the new unit will be a multidisciplinary approach of aging, providing a unifying goal. This B2A unit can thus be declined into 3 main axes :

1) Cell and molecular biological approaches to mechanisms of adaptation and aging (teams 1, 2 and 3);

2) Analysis of cellular and molecular processes involved in dysfunction related to aging with a special interest in repair and rescue mechanisms (teams 4, 5, 6 and 7);

3) Cellular and molecular approaches of vascular and cardiac dysfunctions related to aging (teams 8 and 9).

The project also includes the creation of an animal facilities platform at the Hôpital Charles Foix in Evry, which is part of the Institute of the Longevity supported by national contracts between the University and the Ministry.

Management team

The proposed director of the B2A unit, Mr Bertrand FRIGUET, will be assisted by a deputy director, Mr Rachel SHERRARD. The organization of the unit anticipates the creation of an executive Committee formed by the assembly of the team leaders and the setup of a *Conseil de laboratoire*/unit Council including elected representative members of researchers, faculties, ingeneers, administrative and technicians staffs, plus some representative of PhD students and post-docs. These collegial structures will be activated as soon as the unit comes into existence administratively. In the mean time the visiting Committee recommended the proposed director to associate more closely the team leaders and staff members regarding the final organisation of the project.

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	18	18	18
N2: Permanent researchers from Institutions and similar positions	17	17	16
N3: Other permanent staff (without research duties)	24 (23.2)	24 (23.2)	12
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	0	0	0
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	8 (7)	8 (7)	8
N6: Other contractual staff (without research duties)	7	7	1
TOTAL N1 to N6	74 (72.2)	74 (72.2)	55

Percentage of producers	***98%***

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	16	
Theses defended	40	
Postdoctoral students having spent at least 12 months in the unit*	7	
Number of Research Supervisor Qualifications (HDR) taken	7	
Qualified research supervisors (with an HDR) or similar positions	23	23

2 • Assessment of the unit

Overall opinion on the unit

Since the project will bring new teams together, it is difficult to anticipate the synergy between these beyond judging the scientific coherence and complementarity of the models and biological approaches. The Committee considers that the project is rather clearly focused on the adaptive processes associated with aging and pathological consequences. The overall productivity of the members of the teams to date is considered to be good but not uniform. Four teams have a very good scientific production record. The publication output of the others, although good, could be improved by targeting high impact factor journals more frequently. Some of the people joining the project are excellent, bringing research of high standing to the unit.

The questions addressed by the different teams are mainly related to basic research, focusing on adaptive processes and aging in particular. However, some researchers and faculties are also involved in more applied research as attested by the many patents obtained in the recent past. Regarding the great societal impact of aging, translational research in particular should be encouraged since the unit will be one of the few units in France aiming to study aging. Similarly, the Committee encourages researchers to include the humanities and social sciences in their multidisciplinary approaches.

Finally, it is worth mentioning that all the members of the proposed research unit seem to support the project strongly and to be enthusiastic about the upcoming collaborations with other groups. Indeed, some of these collaborations already exist as attested by significant common publications between various teams. Others will be encouraged through appropriate incentive. In conclusion the Committee was favorably impressed by the originality and feasability of the proposed project.

Strengths and opportunities

Regarding the federative aspect of the project and the complementarity in the biological approaches from molecular biology to the behavioural level and clinical treatment, there is a real opportunity for developing multidisciplinary studies aimed at better understanding biological and pathological processes related to aging. Since most members of the unit are involved in teaching, the unit will be able to attract undergraduate students onboard and to sensibilize them to studies of aging related processes. Furthermore the contribution of the unit to the federation of research units in the IBPS and related technical platforms will contribute to onsite collaborations in the fields of neuroscience and developmental biology.

Weaknesses and threats

The visibility of the unit as a center for research related to aging will need to be established at the national and international level since most of the teams have not yet positioned their studies in this perspective. However, because most of the individual teams already have good international visibility, it is likely that the upcoming collaborations will lead to high international visibility in aging research. Yet, in this highly competitive field, focusing on selected hot topics will nevertheless be necessary to strenghten the relationships between teams since most of them do not have a common history.

Moreover because of the uneven sizes and compositions of the teams, this could be an opportunity to reinforce the potential of each in a true research community. Competition for limited resources are likely to develop especially between teams closely related to “worthwhile” therapy-related aspects of aging and those involved in more fundamental research of only “academic significance”. Further, because for historical reasons the teams will have access to differential technical support, the Committee recommends that the director and the executive Committee take measures to ensure that the resources of the unit be shared effectively in order to enhance the potential of the unit while reinforcing specific teams with particular potential. The process by which Junior faculty members become associated with research teams is suboptimal and should be improved.

Recommendations

These recommendations for the research unit are related to relative weaknesses of the project as judged by the visiting Committee. More specific suggestions are given through detailed analysis of the teams.

First, since the unit focuses on cellular processes related to aging and adaptation, work must be invested to achieve national and international visibility in these fields along side the current visibility of each group taken individualy.

Second, the visiting Committee recommends that the currently uneven sizes of the teams be reajusted and future opportunities to reinforce emerging groups be exploited. Moreover, it might be necessary to plan the acquisition of further groups with complementary approaches. The team leaders should be directly involved in the selection of Junior faculty members with the expressed aim of their long-term integration into the particular team.

Third, during the transition period it is recommended that the director and deputy-director work actively with all members of the unit to consolidate the project regarding both the research concept and the establishment of a true collegiality within the unit. In general, management structures within the unit and the federated units of the IBPS should be developed to foster creative interactions between teams and individuals at all levels.

Fourth, teams in general should try to publish more frequently in high impact factor journals.

3 • Detailed assessments

Assessment of scientific quality and outputs

The project aims at federating 9 teams coming from pre-existing structures in a new multidisciplinary project focusing on cell biology and aging. The 3 main research domains are related to brain neurodegenerative processes, the aging process of the cardio-vascular system and similar processes related to muscles, studied mainly at the molecular and cellular levels. The scientific level and international visibility of each team taken individually are generally very good, although some of these teams are presently rather limited in their number of researchers.

Assessment of the unit's academic reputation and appeal

Aging is still a research field to be developed in France and such a project is in a good position to carry out important research with high national and international visibility in relation to this socio-economically major problem. Such a research unit could indeed develop a leading position in the field. The teams are already individually strongly attractive. The attractivity of the research unit will come from the visibility of the global project and further interactions between groups. Several papers involving various members of the unit have already been published. At the same time research of high and even excellent standard is carried out by individual groups: it must be safeguarded that this can continue to flourish within the new unit.

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

Aging constitutes a considerable socio-economic challenge in the developed countries. Understanding the basic mechanisms of the process and further proposing some solutions to improve the quality of life of elderly people necessitate interdisciplinary approaches including physiopathology and development of new therapies. Most of the teams in the unit have contracts with important socio-economic players including large pharmaceutical corporations. Some of the teams have developed new processes and filed numerous patents. The development of the *"Institut de la longévité Charles Foix"* (a project led by the University Pierre & Marie Curie) as a part of the unit by a strong connection with *the Hôpital Charles Foix* is a real opportunity to combine basic and clinical approaches in a translational approach of aging including social scientific aspects.

Assessment of the unit's organisation and life

Bringing together 9 teams with different personal history, scientific cultures and research fields constitutes a great challenge for the project managers. The new B2A unit will be a part of the IBPS, itself federating no less than 5 research units. Such a large federation will permit the researchers to access and share excellent technical facilities and forster collaborations between research units and teams. However, because the IBPS itself is a new project, management of the B2A unit is likely to be challenging. The director and deputy director are strongly encouraged to associate more closely their permanent and non-permanent staffs, including technicians, engineers and PhD students, in creating and managing structures to optimize the daily life in the unit. The process by which junior faculty members become associated with research teams should be improved.

Assessment of the unit's involvement in training through research

Without exception the teams forming the unit have great experience in PhD training. Because the research unit will be associated with 3 Doctoral Schools and because of the extensive facilities available to it, PhD students will benefit considerably from working in this new and attractive research environment. However, Assistant-professors and junior scientists are strongly encouraged to prepare their graduation as HDR (Habilitation to direct research).

Assessment of the five-year plan and strategy

The ambition of the research unit is to develop a federative project aimed at further understanding basic mechanisms of aging with cell biological approaches including physiopathology. The coherence of the project is perceptible in the individual project of each team. Because of their great individual potential and desire to work together it can be easily imaginated that the next 5 years will see the emergence of an effective research unit focused on cell biology questions particularly but not exclusively related to aging processes.

4 • Team-by-Team analysis

Team 1 : Photobiology

Name of team leader: Ms Margaret AHMAD

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	0	0	0
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	0	0	0
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	0	0	0
N6: Other contractual staff (without research duties)	0	0	0
TOTAL N1 to N6	1	1	1

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	0	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	0	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team leader has a consistent record of seminal research in relation to the function of the cryptochrome/photolyase superfamily in plants and animals as evidenced by her recent *Annual Review* article. There is every indication that this success will continue and expand in the context of mammalian and aging-related systems in the new unit. The team has published excellent to very good papers during the last 5 years (*PNAS* IF 9.7; 2 *PloS Biol* IF 11.5; *Plant J* IF 6.2; *Mol Plant* IF 5.5; *3 J Biol Chem* IF 4.8; etc.).

Assessment of the unit's academic reputation and appeal

Since her publication featured on the cover of *Nature* some years ago the team leader has grown in scientific stature fostering and often leading international collaborations at the highest level involving diverse questions, systems and methods (X-ray crystallography, transgenic *Drosophila*, magnetoperception, etc.) far beyond her original background in plant science. This conclusion is clearly reflected in her excellent record in grant awards (Human Frontiers Science program (HFSP); The French National Research Agency (ANR); The US National Science Foundation (NSF); etc.).

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

While the team leader reputation as an international female scientist clearly places her as a role-model of some significance, she does not otherwise appear to have made major contribution in this criterion category.

Assesment of the unit's organisation and life

The team leader has successfully managed and organized her research and teaching activities in the USA and France over more than ten years, maintains international connections at all levels in a wide range of disciplines and has an excellent track record of attracting funding from prestigious agencies including HFSP and NSF. She is also coordinator of a current EU Framework Program FP7 application.

Assessment of the unit's involvement in training through research

The team leader has taught in the BIP (*Biologie Intégrative et Physiologie*) Master's program of the UPMC, organized Summer School exchanges between Paris and Pennsylvania State University and successfully supervised numerous Master and PhD project students from France, the USA and Japan. She was an invited speaker of prestigious conferences such as the Gordon Conferences (3 times recently).

Assessment of the five-year plan and strategy

The team leader proposes an ambitious wide-ranging program from fundamental studies of molecular function in the cryptochrome/photolyase superfamily to therapy relevant to magnetobiological studies, thereby providing the new unit with precisely the blend of curiosity-lead fundamental research and novel aging-related studies for which it aims. A danger exists, however, that too many disparate projects will be attempted simultaneously. The team urgently requires at least one permanent additional member as well as technical personnel to achieve its goals.

Conclusion

- Strengths and opportunities

This team displays unique expertise in relation to the cytochrome system. This will be brought to the unit along with related research themes including the biology of photoreceptors, DNA photorepair and circadian timing. Novel input from fundamental *Arabidopsis* and *Drosophila* research, including genetic, 3D structure, spectroscopic and other biophysical methods will also be brought to therapy-related biomedical research.

- Weaknesses and threats

The lack of human ressources with tenured positions beyond the team leader carries the risk that volatile experience in the lab will be lost as researchers leave.

The notion of cytochrome as a "stress transducer" is scarcely justified at the present time and it is not clear what this has to do with aging anyhow. Some preliminary data from the team, however, support a role for cryptochrome/photolyase in oxidative stress for which a role in aging is strongly suggested.

- Recommendations

The team must be guaranteed freedom to retain and exploit its predominance in cryptochrome research.

A permanent position above the postdoc level should be made available to provide the team with long-term stability in its research activities.

Team 2 : Integrative Cellular Aging and Inflammation

Name of Team leader: Mr Bertrand FRIGUET & Mr Mustapha ROUIS

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	2	2	2
N3: Other permanent staff (without research duties)	3	3	3
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	1
N6: Other contractual staff (without research duties)	0	0	0
TOTAL N1 to N6	10	10	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 unit	1	
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

This team originates from 2 previous groups. The team has internationally recognized expertise in the field of oxidative stress and inflammation. Studies are aimed at characterizing protein damage related to aging and its influence on proteasome function. A particular interest is focused on the role of methionine sulfoxide reductase and the function of the thioredoxin system as possible protection mechanisms against apoptosis. The team has published very good to excellent articles during the last 5 years (*PNAS* IF 9.7; *Antioxidants and Redox Signalling* IF 8.5; *Aging Cell* IF 6.3; *Free Rad Biol Med* IF 5.4; *J Biol Chem* IF 4.8; etc.). The team leader has a good international visibility in the field of protein oxidation and atherosclerosis.

Assessment of the unit's academic reputation and appeal

Besides the publications, the national and international visibility of the team is associated with excellent ability to raise funds. Moreover, the attractivity of the team is attested by recent recruitment of one researcher, one assistant-professor and two post-docs in the new project.

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

The team in general displays excellent relationships with industry through numerous contracts. They have obtained 4 patents and they are co-founders of a start-up company.They also contributed to general audience scientific books and to transmission of science to the society.

Assesment of the unit's organisation and life

The research potential of the team is rather important compared to most of the other teams of the unit with 2 full-time researchers and 4 professors and assistant-professors. Given the close thematics separately developed so far a good predictable interaction within the team and with the other teams of the unit is expected. Moreover publications have already been produced with several teams forming the new unit.

Assessment of the unit's involvement in training through research

In the past 5 years the team displayed a very active training activity with 8 PhD thesis defended and 5 current PhD students. The team also trained numerous Master students and hosted 4 post-docs.

Assessment of the five-year plan and strategy

The scientific strategy of the team is appreciated to be good to very good. One of its strenght is that it combines workers from 2 previous thematically-related groups. Consequently, the project focusing on the role of oxidized protein accumulation in aging is considered as innovative and of a high standard. The putative protective role of thioredoxin is to be further documented but it seems to represent a key system against apoptosis.

Conclusion

- Strengths and opportunities

The team is conducting an innovative research program on the identification of proteins that are specifically modified in several conditions of oxidative stress and their regulation by different antioxidant protective systems in the context of the aging processes and arterial inflammation.

The team leader is also the director proposed for the new research unit. As his activity has been focused for a long time on oxidative stress and aging he will have a key role in guiding the activity of the 9 teams toward the theme of aging. The team will also have a leading position for developing collaborations with the other teams. The international visibility and the high motivation of the team leader is certainly a major factor for the development of a visibility of the global project.

- Weaknesses and threats

As the team has a new configuration resulting from the amalgamation of 2 previous groups one of the risks is that the fusion process will be incomplete and that too many projects will be conducted at the same time.

- Recommendations

The team members should fuse their research efforts and themes in order to reduce the total number of projects and to develop close collaborations with other teams of the unit and at the level of the local federation.

Team 3 : Eukaryote Translation

Name of Team leader: Mr Olivier JEAN-JEAN

Workforce

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

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	0	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	0	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	2	2

Detailed assessments

Assessment of scientific quality and outputs

The team has published a total of 14 original articles plus 2 review papers in the reference period. These publications were in highly respected journals in the field of translation regulation (*Plos Genet* IF 8.7, *Nucleic Acids Res* IF 8.0, *Molecular and Cellular Biology* IF 5.5, *RNA* IF 5.1, *RNA Biology* IF 4.9, *Molecular Biology of the Cell* IF 4.9). Several of these publications have an IF > 5 indicating that the research is highly original. The team leader therefore can be considered as having a significant impact on the mRNA translation field. He is indeed a leading reference at international level in mammalian translation termination.

Assessment of the unit's academic reputation and appeal

The scientific results of the team have been produced in many national and international meetings, some of them with high visibility such as EMBO and Cold Spring Harbor Laboratory (CSHL) symposia. The team leader is also often involved in reviewing activities for international granting agencies and most important journals in the field. The team has developed national and international collaborations attested by significant publications in common, especially with an internationally prominent group in Portugal in the domain of translation termination. The expertise of the team leader was also recognized by his contribution to the *Comité National du CNRS (coNRS sections 22 et 21).*

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

Not relevant.

Assesment of the unit's organisation and life

The team leader has led a productive research groups for a long time. Although the team is relatively small, lacks technical assistance and up to now has operated in a very small lab space, the scientific output has been high, reflecting a good atmosphere, high level of collegiality and excellent communication between the team members.

Assessment of the unit's involvement in training through research

The attractivity of the team for PhD students is high. Five PhD students have been trained recently. Master and even bachelor students frequently become associated with the team. The team leader also contributes to teaching activities in the field of molecular biology and theoretical formation in molecular biology (specialized courses).

Assessment of the five-year plan and strategy

All 3 aims of the scientific program are well focused, highly innovative and ambitious. These projects reflect scientific excellence with high impact in the field. The feasibility is very good but would be improved by the provision of technical assistance. The strategy thus enables significant discoveries which will enhance international attractiveness of the team.

Conclusion

- Strengths and opportunities

The team is composed of 2 permanent full-time researchers (HDR) plus 2 assistant-professors. Since mRNA translation is a major component of the regulation of gene expression, including translation termination, processes information will extend and enhance many of the unit’s investigations. The team leader is recognized for his expertise in mammalian translation termination and thus will bring the research tools associated with translational control along with great expertise in molecular biology in general to the new unit. This should lead to collaborations such as those already planned with another team of the unit. Moreover, a new project will be started on RNA integrity and the cytotoxic effect of RNA damage (project funded by the University). The presence in the team of 2 assistant-professors will help the team to acquire further students.

- Weaknesses and threats

As the past and proposed future work represents an excellent project, the international visibility of the team is compromised by its low level of funding. The lack of technical assistance might also represent a limiting factor in future developments.

- Recommendations

Increased scientific communication between teams of the new unit will create new options for collaborations toward the development of original projects. Since this team is the only one in the unit with the theoretical and technical background in the field of mRNA translation, it is expected that this aspect of gene expression will be integrated into various projects of the unit. For example collaboration with team 1 on the translational regulation level dowstream of cryptochrome activation will be highly innovative and could be attractive for funding. Similarly, the control of local translation in neurons in response to physiological and stress signals is still poorly understood. The combined forces within the unit open a window of opportunity for new projects and will contribute to increased national and international visibility and attractiveness of the team and of the whole unit.

Team 4 : Neuronal Cell Biology and Pathology

Name of Team leader: Mr Christian NERI

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	0	0	0
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2	2
N6: Other contractual staff (without research duties)	1	1	0
TOTAL N1 to N6	5	5	4

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The current hypothesis of the team is that the mechanisms that are essential for longevity/cell survival may be key to neuronal endurance/survival during the early phases (before cell death) of the pathogenic process in neurodegeneration with a particular interest for Huntington's disease (HD). Studies of the role of aging-delaying factors focus on the FOXO longevity factors ('FOXO network': sirtuins SIRT1, ß-catenin, uncoupling proteins) in the regulation of neuronal endurance in HD.

Key findings are the general capacity of the SIRT1-FOXO pathway to regulate cell survival in several degenerative diseases (HD, prion disease, oculopharyngeal muscular dystrophy (OPMD)) and the discovery of early-stage neuron survival deficiency in HD as caused by unexpected interplay between neurodevelopmental and longevity-promoting pathways. The team has a very good publication record, i.e. *J Neuroscience* IF 7.5; *Human Molecular Genetics* IF: 7.6; *BMC Genomics* IF 4.1. In collaboration with top international labs the team also produced outstanding publications such as in *Nature* IF 36.3, *PNAS* IF 9.7, or *Human Molecular Genetics* IF 7.6.

Assessment of the unit's academic reputation and appeal

The team leader has an international leading position in the study of longevity/cell-survival factors in neurodegenerative disease pathogenesis using *Caenorhabditis elegans* and Systems Biology. In this respect he was recently invited to numerous selected international conferences such as EMBO conference 2012, Keystone Symposia 2012, etc. ▫he project also benefits from the capacity to innovate and to regroup leading laboratories into international collaborative networks (Associated International Laboratory (AIL) INSERM-Buck Institute-University of Montreal, Euro-HD Network, FP7 grant application) around innovative developments.

The project of the team regularly attracts funding by several organizations including the ANR (2005, 2008), the French Foundation for Medical Research (FRM) (2006-2011), the International Associated Laboratory (LIA) initiative of INSERM (2008-2012), The French Muscular Dystrophy Association (AFM) (2009- 2012), the Euro-HD Network, the Cure HD Initiative (CHDI) Foundation and the Hereditary Disease Foundation.

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

The team has developed recently many patents such as: MOLECULAR PROGNOSIS OF HUNTINGTON'S DISEASE. WO/2012/028718; or USE OF INHIBITORS OF SIRTUINS AND/OR AMPK FOR THE PREPARATION OF A MEDICAMENT FOR THE TREATMENT OF POLYALANINE DISEASES. WO/2008/155390. The team has established a fruitful partnership with industry (GlaxoSmithKline).

Assesment of the unit's organisation and life

The team appears to be well organized and fosters a collegial environment.

Assessment of the unit's involvement in training through research

During the period 2007-2012 the team comprised 9-10 people including 1 PI (the team leader) and 8-9 people holding contractual positions as post-docs, PhD students (6) or research assistants in the field of either biology or bioinformatics. In average, the team offers 2-3 contractual positions (technicians, informaticians, researchers, PhD) every 2-3 years. The PI is involved in Master courses and participates in international summer schools. The team has sufficient critical mass to incorporate additional scientists and stimulate interactions with other members of the unit.

Assessment of the five-year plan and strategy

The program is very ambitious and innovative. Its feasibility is good despite its complexity although additional human and economical resources would be advantageous. The project is likely to improve the current leading international position of the team.

The aims of the proposed project over the next years are to:

- advance understanding of the role and therapeutic value of molecular networks that may be critical to neuronal resistance and survival during the early phases (before cell death) of the pathogenic process in HD;
- use complementary approaches [notably C. elegans, human induced pluripotent stem (iPS) cells and human cohorts] for validating key players in neuron survival and disease modification;
- transfer these validated targets to clinical research for neuron preservation and personalized medicine in HD.

Conclusion

- Strengths and opportunities

The team has an international visibility in the field on studying longevity. The demonstration that SIRT 1-FOXO pathway regulates cell survival in different neurodegenerative disease was indeed a major finding recently. The team leader has an internationally recognized leading position in the field of modelling neurodegenerative diseases and especially of Huntington's disease. The interactions with the *Institut de la longévité Charles Foix* could be a real opportunity for the development of the platform contributing to the screening of new drugs active in *C. elegans.*

- Weaknesses and threats

There is a tendency to develop too many projects at the same time, which might weaken the potential of the team.

- Recommendations

The team will play a critical role in the future in contributing actively to the building of the unit and federating the activity of the different teams because of the transversal interest of its research and animal models.

Team 5 : Degenerative Processes in Neurons and Networks

Name of Team leader: Mr Bernard BRUGG & Mr Etienne JACOTOT

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	3	3	3
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	0	0	0
N6: Other contractual staff (without research duties)	0	0	0
TOTAL N1 to N6	5	5	5

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 unit	0	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	3

• Detailed assessments

Assessment of scientific quality and outputs

This team (formerly "Neuronal Death and Survival" team) is familiar with aspects of neuronal degeneration processes including molecular and cell biology. In 2008 thanks to the ANR Neuro-Grant (*Neurofluidic* project), the team has operated a successful technological shift toward the development of microfluidic systems to study axonal degeneration and neuronal network reconstructions. They focused their research to decipher molecular mechanisms of the dying back phenomenon during axonal degeneration and synaptic disconnection, in particular in Alzheimer's disease (AD).

This team sequentially developed 3 complementary research approaches: the first aim comprised the development of microfluidic tools for cellular neuroscience. Using this technology (Patent PCT/FR2009/001198) they started to study two fundamental research aims such as the molecular mechanism of axonal degeneration, role of mitochondria and the synaptic and trans-synaptic degeneration in reconstructed neuronal networks. The sum of this work gave rise to very good publications (*PNAS* IF 9.7; *J Neuroscience* IF 7.3; *Cell Death &Diseases* IF 5.3; *Apoptosis* IF 4.8; *PloS One* IF 4.1; etc.) and communications in international symposia (2nd French-Argentinean Symposium in Neurosciences; MuTas international conference, Groningen) and 6 patents. Because the team's PIs only joined forces recently, they have no common publications to date. However, the second PI published a number of good papers recently (*FASEB J* IF 5.7; *Lab Chip* IF 5.7; *Cell Death* IF 5.3). Based on the oral presentation, the complementarity of the two PIs looks promising. The potential limitation of the team resulting from the fusion of two groups with technical tools centered on their microfluidic chamber might be transformed by interactions with other innovative and broader technologies and methods represented in the new unit.

Assessment of the unit's academic reputation and appeal

This relatively small team started recruiting new competences. The addition of 2 non-permanent positions will reinforce the group in 2013. It is worth mentioning the limited number of invited conferences at international and national meetings, suggesting that the team is not at present playing a leading role at the international level. There exists a good potential for the near future, however. Several grants have been obtained to fund the proposed research (5 ANR programs; *Fondation de France*; *Fondation Plan Alzheimer*; Wellcome Trust; Specific Targeted Research Projects (STReP) program of EU).

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

The team has shown its capacity to raise national and international funds. The complementarity of the two PIs looks promising and probably not circumstantial. The group has produced numerous patents previously. Consequently, the expertise of the PI joining the team should be a clear added value for the current project.

Assesment of the unit's organisation and life

Permanent positions (2014): 3 Researchers; 1 Professor/assistant Prof; 1 Engineer/technician.

The two PIs show an efficient complementarity that should be validated by joint publications.

Assessment of the unit's involvement in training through research

The team is involved in student training, currently with 3 PhD students and 3 Master students. The entity implements a regular and individualized monitoring of doctoral students and trainees.

Assessment of the five-year plan and strategy

The proposed project takes advantage of the microfluidic approach. Three research aims are planned.· First, the molecular mechanism of compartmentalized neuronal degeneration comprising the propagation of apoptotic/necrotic signals and the role of mitochondria (mitochondrial dynamics, redox metabolism, control of cell death) in somatic, axonal and synaptic compartments. Second, synaptic and trans-synaptic degeneration, focused on extra-synaptic excitotoxicity and dispersion of aggregated proteins. Third, the development of an industry-oriented platform for cultured neuronal networks. They plan to use IPS from Human disorders.

Conclusion

- Strengths and opportunities

The project is coherent and at a national competitive level in the field. Interestingly the team proposes to focus on caspase-2, which is unexpected in view of the background of the PI joining the group. But the fact that such a caspase is not involved in physiological apoptosis but restricted to pathological processes will reinforce the interest to pinpoint its role in cell death. Taken together, it can be expected to reach an internationally competitive level quite rapidly under the conditions of the new unit.

- Weaknesses and threats

The team is newly formed and no common publications have been yet produced by the 2 PIs. The international visibility of the team must be improved.

- Recommendations

Since the PI joining the group had previously published high standing articles it is recommended to focus the project on the aims which are likely to improve the international visibility of the team.

Team 6 : Brain Development, Repair and Aging

Name of team leader: Mr Jean MARIANI & Ms Rachel SHERRARD

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	3	3	3
N3: Other permanent staff (without research duties)	6	6	4
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	2	2
N6: Other contractual staff (without research duties)	0	0	0
TOTAL N1 to N6	16	15	13

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	3	
Theses defended	11	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	4	4

• Detailed assessments

Assessment of scientific quality and outputs

The team follows a number of well-established research lines that have been pursued for several years. Publications have been consistently produced in good quantity in international, peer-reviewed journals of high profile, with cases of excellence (*Neuron* IF 14.7; *PNAS* IF 9.7; *FASEB J* IF 5.7; *Neurobiology of Disease* IF 5.4; *PloS One* IF 4.1; etc.). The concept that previous cellular experience determines the ability for re-establishing specific connectivty is one of the major achievements of the team. Also of wide interest are studies on neuronal aging and the role of the nuclear receptor Rorα in these processes. Interesting developments may come from the analysis of cellular/molecular mechanisms underlying therapeutic application of trans magnetic stimulation (TMS).

Assessment of the unit's academic reputation and appeal

The team (and particularly his senior PI) has wide international reputation in the fields of cerebellum, brain repair and aging. team members are invited to national and international conferences. The team has reasonable funding, but it does not appear to participate in research networks. On the other hand, scientific collaborations with national as well as international partners are extensive. Likewise, the team has good capacities for attracting and recruiting students, postdocs and visitor scientists.

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

The team has some well-established interactions with industry, although the research is not directly aimed at technological development. Of major interest is the strong commitment in the project of the *Institut de la Longevité Charles Foix.* team members participate to extra-academic dissemination events and are part of Committees and associations. Notably, the historical team leader has wide visibility in the extra-academic milieu and he is actively involved in cultural activities and scientific dissemination events. Moreover, the set-up of the extremely performant animal house for transgenic mice at the *Hôpital Charles Foix* will represent a major issue for development of translational research in connection with human aging.

Assesment of the unit's organisation and life

In spite of the rather large size of the team, organization and management appear to be more than adequate for running research and training tasks. The two leaders have established experience in research direction. Many of the members have been working together for several years and the new ones will be easily integrated. The different members of the team would benefit from stronger integration of research activities, but this process appears to be in progress.

Assessment of the unit's involvement in training through research

The team has well-established expertise and roles in different teaching activities at the undergraduate and postgraduate levels. team members have proven training abilities and skills, as also witnessed by the high numbers of PhD students and postdocs that attend the lab. The participation of team members to master courses (and other types of training activities) further expands the opportunities for recruiting good students.

Assessment of the five-year plan and strategy

The five-year plan is clear and detailed. It comprises four distinct projects (some are further subdivided in different lines). Each project is focussed, with defined background, goals and methods. On the whole, the proposed research is original, methodologically updated and timely, representing the natural evolution of the work done during the last five years. Efforts should be done to integrate the work done by different groups and to enhance interactions both at the scientific and methodological levels.

Conclusion

- Strengths and opportunities

The team comprises a group of experts with solid experience and complementary competences ranging from basic science to clinical investigation. The research project for the next five years is timely and innovative. It is based on a number of well-established models and represents the natural continuation of the work done in the past few years. This situation guarantees the feasibility of the proposed experiments and promises interesting results. At the same time, working on such established experimental settings will also favour progressive implementation of new methodological tools and approaches that may lead to address novel questions. Major opportunities for future development of the work done by the team come from the *Institut de la Longevité Charles Foix*, which will provide access to state-of-the-art facilities and platforms, animal models and direct interaction with clinical investigation. It is worthnoting the high degree of automatization of the animal housing, which is presently the most advanced in France. Similarly, potentially interesting interactions may be developed within the Jussieu Campus in the context of the new IBPS.

Another strength of the team derives from the commitment to teaching and training activities. While this may consume significant amounts of the time available to some of the team members, it surely represents a valuable opportunity for selecting and recruiting excellent students that may secure the future evolution of the team.

- Weaknesses and threats

While the four projects are clearly defined and focused, integration between the different parts of the plan is at present less developed. Notably, given the multidisciplinary experience of the participating scientists efforts should be made to increase interactions and collaborations that may lead to developing new ideas. For instance, it may be possible to extend the experiments on olivocerebellar reinnervation to an hippocampal model as to enhance the general impact of the work. In general, however, while the work at the cellular/molecular level is clearly planned and based on solid premises, the immediate translation to clinical practice is less evident. This may be solved when the collaboration with Charles Foix Hospital is operational.

Another concern comes from the “advanced” age of some members of the team. This is not going to be a problem for the next five years, but it will become critical soon after. Accordingly, a careful recruitment policy to favour turnover while maintaing the scientific identity of the team should be initiated during the first term of the project.

- Recommendations

Main recommendations are already outlined in the points above. In summary:

1. Increase integration of the research project and collaboration among team members;
2. Plan a careful recruitment policy to secure turnover of the team;
3. Exploit the opportunities for development offered by the *Institut de la Longevité Charles Foix* and the IBPS.

Team 7 : Cellular Integration of Neuromodulatory Processes

Name of Team leader: Mr Pierre VINCENT

Workforce

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

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

• Detailed assessments

Assessment of scientific quality and outputs

The team developed unique biosensors leading for the first time to the detection of very small amounts of cAMP in tissues. These are cAMP fluorescent sensitive probes that they used in combination with active caged compounds to study spatio-temporal dynamics of cAMP/PKA signaling cascade in neurons, by two-photon imaging microscopy, and in vitro (brain slices) and in vivo (deep brain regions) electrophysiology in genetic models. The major finding of the team is that specific phosphodiesterases determine the final equilibrium of cAMP intracellular concentration and compartmentalization in neurons and cardiomyocytes. They also found that in striatal neurons the steady-state cAMP concentration at rest remains very low in the bulk cytosol thanks to a dynamic equilibrium between cAMP synthesis by cyclases and degradation by phosphodiesterases (PDE), rather than from an on/off switch mechanism. Such a dynamic control allows more flexible adaptive responses. Finally, they showed that striatal medium spiny neurons are equipped with a specific set of signalling molecules (DARP-32 and PDE1/2/10) that enables them to produce powerful and strongly non-linear cAMP/PKA responses. These properties may be linked to some peculiar physiological function of these neurons. These are findings of major importantce in the field. The level of publications of the team is good (*Neuron* IF 14.7; *J Neuroscience* IF 7.1; *Cerebral Cortex* IF 6.5; *J Biol Chem* IF 4.8; etc.).

The scientific project is in the continuity of the previous results. It aims at describing the spatio-temporal changes in cAMP production at a subcellular/dendritic level in striatal medium spiny neurons in response to dopamine (DA) receptor stimulation. The effects of synaptic release of DA will be compared to its tonic global release. The modalities of a crosstalk between dopamine and adenosine receptors will also be examined. An interesting issue will be to understand how does the system adapt to prolonged absence of dopamine receptor signal, such as in Parkinson's disease, and how long treatments with L-DOPA leads to dyskinesia.

The team will develop collaborations to study trans-differentiation of vascular smooth muscle (team 8), compartmentation of cAMP signaling in axon (collaboration with team 5), and to generate new biosensors (collaboration with the real-time molecular imaging company Biospace Lab). The project is excellent and highly competitive at the international level.

Assessment of the unit's academic reputation and appeal

The team is very attractive. The PI has been invited to 13 national and international conferences during the last period, including Jacques Monod and Gordon conferences. He organized a regular meeting for the French cAMP Club and other conferences (Biosensors and Dynamic Imaging, 2010, Paris). The team is part of a LABEX (*Laboratoires d'Excellence* funded by the French *Investisement d'Avenir* progam) and of a GDR (*Groupement de Recherche*) on biosensors and developed numerous national and international collaborations. The team was recently enlarged with the arrival of 1 post-doc and 3 PhD students. Moreover 1 student was recruited as an assistant-professor. The team has raised funds mainly from national calls. For the next reporting period the team should make some significant efforts to apply to international competitive calls.

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

The team is strongly involved in industrial collaborations for developing biosensors. One of the devices developed by the team is now available commercially. The Committee encourages the team to further go in this way.

Assesment of the unit's organisation and life

The team is recognized as performant and has been well funded with 2 ANRs. However, the Committee recommends recruitment of post-docs from abroad.

Assessment of the unit's involvement in training through research

The team recently recruited 3 PhD students. These are very well integrated in the group. The team offers them an excellent environment for training, seminars and courses at doctoral levels. The PI strongly participates in the management of local schools (Doctoral school and *Neuropôle de recherche francilien* (NeRF)), club meetings and students training. It is involved in several Committees including *Conseil National des Universités* (CNU). This testifies a significant involvement in education of PhD students and research training.

Assessment of the five-year plan and strategy

The scientific project is original, innovative and feasible. Equipment and cutting-edge technologies are already set-up and available. Appropriate collaborations have been established with internal and external teams. Although the project is at a highest international competitive level, the issues are nevertheless too descriptive. More insights into cellular mechanisms and pathophysiology should be considered.

Conclusion

- Strengths and opportunities

The team provided an excellent contribution to the understanding of cAMP intracellular signaling, thanks to the development of unique fluorescent biosensors. It seems very attractive as testified by the recruitment of several PhD students and one post-doct, and its participation to 2 very good consortia (LABEX and GDR). It provided excellent training activities for students and post-docs. The project is clearly attractive and very competitive at an international level. The objective of studying cAMP compartmentalization in Parkinson's disease may be an opportunity to developp contacts with pharmaceutical companies.

- Weaknesses and threats

Although very original,studies are mainly descriptive and the Committee suggests deeper investigations in the mechanisms underlying the spatio-temporal pattern of the studied cAMP signals. The team lacks of industrial financial supports. The PI should increase its international visibility in the field of neuroscience.

- Recommendations

International applications for raising funds have to be encouraged. The team should also consider publishing in higher impact journals, which could be obviously possible regarding the approaches of the pathophysiological processes of brain diseases. The team could benefit from recruiting a full-time permanent researcher.

Team 8 : Phenotypic Control of Vascular Smooth Muscle Cells

Name of Team leader: Ms Isabelle LIMON

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	2	2	2
N2: Permanent EPST or EPIC researchers and similar positions	0	0	0
N3: Other permanent staff (without research duties)	0	0	0
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	3	3
N6: Other contractual staff (without research duties)	1	1	1
TOTAL N1 to N6	5	6	6

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The main goal of the team is to identify the molecular and cellular mechanisms that regulate vascular smooth muscle (VSMC) and endothelial cells changes of phenotype in the context of atherosclerosis and cerebral amyloid angiopathy. During the last quadrienal period, the team reported several interesting and original observations. They have done a particularly good job in determining the role of adenylyl cyclase 8 (AC8) in VSMC phenotypic switching and atherosclerosis. Specifically, the team determined a cause-to-effect relationship between AC8 expression and the migratory/inflammatory response of VSMCs. These data identify AC8 as a potential marker of VSMC trans-differentiation. In addition, they reported that Notch signalling controlled the transition of VSMC to an inflammatory state in response to cytokines (IL-1B). Of note the benefit of omega 3 fatty acids on VSCM migration and proliferation is dependent on the notch regulation of matrix metalloproteinase (MMP)-2/-9. Another novel result from the team is the finding that, with respect to angiopathy, the AB1-40 peptide induced VSMC death is independent on MMP activity. The scientific production is considered as very good in regard to the size of the team and its involvement in teaching (9 original articles with 5 major publications in *Aging Cell* IF 6.3, *J Pathol* IF 6.3, *J Cell Science* IF 6.1, *Am J Pathol* IF 4.9, *J Biol Chem* IF 4.8, with the group leader as last author). She and other members of the team are also coauthors of a dozen of scientific papers in very good journals (*Journal of Clinical Investigation* IF 13.0, *Cell Death & Differenciation* IF 8.8, *Molecular and Cellular Biology* IF 5.5).

Assessment of the unit's academic reputation and appeal

Since 2006, this is a small team, which is currently composed of 2 permanent faculties including the team leader, 1 temporary faculty member, 1 contractual technician, 1 postdoctoral fellow, and 2 PhD students. The team will be strengthened by the recruitment of a permanent faculty member and an assistant engineer in 2013. The team appears highly motivated and has been successful in obtaining funding with one ANR grant (on Ac8 project) obtained last year, two industrial grants (collaboration since 2005, a third one has just been renewed). Members of the team were invited to 9 seminars (national or international), 2 international and 2 national meetings (Frontiers in cardio-vascular Biology; The Notch meeting; etc.). Several international collaborations are depicted in the report. Of note, the team also developed local (team 7, local control of cAMP in VSMC, sponsored by ANR) and national collaborations with different basic research teams and is an associate laboratory of the international Transatlantic Cardiovascular Research Center.

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

The team has very good interactions with industry. Indeed, two research industrial contracts were obtained and connected with 2 post-doc positions (2005-2008; 2009-2012). The team is a member of the Alzheimer European consortium PharmaCog, a host lab for biotechnology professions bachelor degree students and participates in Paris Masters Fairs.

Assesment of the unit's organisation and life

The team is recognized as efficient despite the fact that there is no full time researcher. The team is collegial.

Assessment of the unit's involvement in training through research

Through its leader the team is strongly engaged in research training. Notably, the group leader is involved in the direction of studies of the UPMC Master BIP (*Biologie Intégrative et Physiologie*) and the direction of the Physiology and Physiopathology program of the UPMC Master BIP. She has created and coordinated 6 teaching units in Bachelor and Master of Biology programs. The team is member of the UPMC Physiology and Physiopathology PhD school (ED 394) board and is involved in the PhD candidate selection Committee of this Doctoral school. The group leader was also chairman of the UPMC Expert group in charge of recruiting professors, assistant professors and temporary assistant professors in physiology from 2007 to 2011. During the last reporting period, the team supervised 10 master students and 3 PhD students (of which 1 has already graduated). All of the PhD students had the Researcher Minister PhD scholarship. According to the rule of the Doctoral school PhD students are required to publish at least one paper as the first author and to attend at least 2 meetings during their PhD training period.

Assessment of the five-year plan and strategy

The working hypothesis of the project is based on recent results of the team and on preliminary observations. The two major topics are: 1) to continue the characterization of AC8 role in pathological vascular remodellings including atherosclerosis. The use of specific in vivo models such as AC8 ko mice and double ApoE/AC8 ko mice and the generation of SMC-specific AC8 knock-out mice is of great value. The clinical connection of this project will be approached by examining a possible correlation between AC8 expression and the fragility of the human plaque (collaboration with INSERM unit U698, Bichat Hospital); 2) To characterize the cellular and molecular mechanisms of inflammatory cerebro-vascular disease in aged brain. This will be performed within a collaboration with a compagny (Funded by Pierre Fabre Innovation until the end of 2015). The research project on the role of AC8 in VSMC is innovative and original with strong international and external collaboration (ANR grant).

Conclusion

The main goal of the team is to identify the molecular and cellular mechanisms which regulate phenotypic changes in vascular smooth muscle (VSMC) and endothelial cells in the context of atherosclerosis and cerebral amyloid angiopathy. The team has a very good track record and research topics are relevant for both aging and vascular disorders.

- Strengths and opportunities

The team presents an innovative research program on AC8 functions in atherosclerosis comforting its leadership on AC8 in VSMC. The members of the team also display efficient internal, national and international collaborations and they have very good connections with industry. Such collaboration is fruitful regarding funds rising for research. Finally the team shows strong involvement in University teaching and training research (Doctoral school and Master).

- Weaknesses and threats

Besides the ongoing fruitful research the Committee recommends to the team to have more insights into cellular mechanisms of AC8. Moreover, international funding could be increased.

- Recommendations

Given the small size of the team, the project on ABeta and cerebral angiopathy might be reduced. This would increase the visibility of the group on AC8. The team could benefit from recruiting one full time permanent researcher.

Team 9 : Genetics and Physiopathology of Muscle Tissues

Name of Team leader: Mr Zhenlin LI & Mr Mathias MERICSKAY

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	3	3
N2: Permanent EPST or EPIC researchers and similar positions	4	4	3
N3: Other permanent staff (without research duties)	2	2	2
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	0	0	0
N6: Other contractual staff (without research duties)	0	0	0
TOTAL N1 to N6	9	9	8

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	8	
Postdoctoral students having spent at least 12 months in the unit	0	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	5	5

• Detailed assessments

Assessment of scientific quality and outputs

Team 9 was previously part of the UR4-UPMC on Jussieu Campus. This group is interested in understanding the mechanisms involved in age-decline of cardiac and muscular tissues. The team has strong experience in evaluating the role of the SRF (serum response factor) transcription factor and of the filament protein synemin in the striated cardiac and skeletal muscle, smooth muscle cells and endothelial cells, and their dysfunction in muscle diseases, particularly in cardiomyopathies. This work is based on the use of relevant mouse animal models, obtained either by conditional inactivation or overexpressing SRF or synemin.

During the last quadriennal period, the team reported several important and original observations, linking the role of SFR to embryonic cardiomyogenesis, and post-natal hearth growth. SFR is required for post natal cardiac hypertrophy and may play a role in the development of dilated cardiomyopathy, which also involves muscle cratine kinase (MCK) dysfunction and desmin glycation.

Beside its involvement in cardiomyopathies, SRF contributes to visceral muscle contractility, vascular muscular tone and arterial stiffness, and is involved in angiogenesis. Another important observation is that synemin, an intermediate filament protein, is marker of embryonic stem cells, and could control hypertrophy. Finally, projects related to muscle wasting and the existence of a microenvironment surrounding muscle fibers potentially important for muscle regeneration, have been developed.

The group is very active and productive with 33 original articles, 5 reviews and 4 book chapters in the last quadriennal period. This scientific production is excellent (*Dev Cell* IF 14.2, *Gastroenterology* IF 12.4, *Eur Heart J* IF 10.4, *Cardiovasc Res* IF 6.0, J Biol Chem IF 4.7). The team leaders and members of the team are co-authors of scientific papers in excellent journals (*Nature Cell Biol* IF 19.4, *Stem Cells* IF 7.7, *J Cell Sci* IF 6.1, *Mol Endocrinol* IF 4.5). The group is leader in the study of SRF in the cardiovascular system, on synemin and desmin research in neuromuscular diseases and beneficiates of an excellent visibility, assessed by the number of invited conferences at national and international meetings, the ability to raise national funds (2 ANR as PI, 2 ANR as partners, VINCI Italian/French partnership). The arrival of a CNRS researcher is planned in the next mandate.

Assessment of the unit's academic reputation and appeal

The team is in international leading position for SRF and synemin functions, as assessed by the quality of the scientific production, the number of invited conferences (7) and communications at national and international meetings for the team leaders and the members of the team. The group is very active and successful in obtaining grants from national agencies or UPMC. In the last period the team leader coordinated 2 ANR, and is partner of 2 other ANR, and grants from charity fundations (2 contracts with the *Association pour la recherche sur le cancer* (ARC), 4 with the *Association française contre les myopathies* (AFM)). The scientific project is very original and well-balanced, with good complementarity between the two team leaders and the researchers of the team.

The team is well attractive with many international collaborations in USA and Italy (SRF and heart), in UK (SRF and angiogenesis), in Germany (SRF and smooth muscle cells), in Brasil and USA (synemin expression in nerve system and stem cells), in Italy (strong collaborations between Italian groups on muscle cachexia), with several national collaborations. The attractiveness is assessed by the recruitment of 1 professor and 2 assistant professors from 2007, and the arrival of a CNRS researcher in the next mandate. The group hosted 6 post-doc fellows from 2007, 2 are currently present (grants UPMC and ANR UPMC), 7 PhD students and 5 Masters students since 2007.

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

Co-direction of the team will indeed favor efficient scientific relay and perenniality. The team leader coordinated the ANR research program CARFUN-SRF on the function of SRF in the cardiovascular system (ANR 2005-2007), involving 4 teams, and is currently coordinating an ANR research program involving 3 teams (REMODEL-SRF) (ANR2008-2013). He is also the partner of the ANR CARSTIF (ANR 2005-2007), and GRAF on arterial stiffness (2009-2013). The team is partner of a French/Italian research program with 4 teams (MIUR, PRIN 2011-2013). The co-leader organized the 8th Congress Biology of Stem Cells in 2008 (Paris). Together with the team leader they organized the 11th International Congress of the IFR83 in 2011 (Paris). The team has numerous international and national collaborations. It is recognized as an expert for international granting agencies (FWO, Iran National Science Fundation) and for journals (*Cardiovasc Res*, *Journal of Clinical Investigation*, *J Biol Chem*, *Biochim Biophys Acta* …). One member is at the Editorial Board of the *World Journal of Stem Cells*, and guest editor for a spotlight smooth muscle phenotype in *Diseases for Cardiovascular Res*.

Assesment of the unit's organisation and life

The team is co-directed to favor efficient scientific cooperations within the team and guarantee productivity in the long term. The team has 4 full time permanent EPST (*Établissement public à caractère scientifique et technologique*) researchers.

Assessment of the unit's involvement in training through research

Members of the team are involved in teaching at bachelor, master and PhD programs. Professors and full-time researchers (4) are involved in training through research (7 PhD theses defended since 2007, 2 current PhD, 5 Master students since 2007, 6 post-docs, 2 of whom are currently carrying out research in the team.

Assessment of the five-year plan and strategy

The project proposed for the next five years is excellent, ambitious and innovative. It is the logical continuation of the previous work on the genetics and pathophysiology of muscle diseases. Based on their expertise in the field of SRF and intermediate filament function, the group will focus on age-linked muscle diseases, in particular sarcopenia, heart failure, muscle dystrophy and wasting.

The project aims at deciphering the mechanisms involved in age-associated cardiovascular and skeletal muscle diseases, with key questions linking mitochondria activity and the muscle aging process, the decline in ATP generation and reduced energy maintenance, with the intermediate filament and microtubule network. The group will focus on the implication of intermediate filaments and the SRF transcription factor in muscle structure and the regulation of the muscle cratine kinase (MCK).

These studies will be carried out on relevant animal models, in particular cre-lox strategies, tested on old mice lacking or overexpressing SRF, BMIP/Nmrk2 KO and transgenic mice, desmin, vimentin synemin KO old and young mice. All these tools are available in the team and are currently validated for the project.

The project is mainly fundamental academic research, with the objective to develop collaborations with clinicians and therapeutic strategies. Each section appears well suited as a program of research The team expertise, as well as its ability to rise national funds, will be a strength for the application and its feasability.

Conclusion

In summary, this is an original and innovative project, with excellent complementarity between the different team partners.

- Strengths and opportunities

The team presents an innovative and original research program in the study of SRF in the cardiovascular system, and IF function in muscle. Such a program will provide new advances linking IFs, energy and lipid metabolism. Interestingly, the new group brings complementary expertises and skill within the team.Thus the team has a leading worldwide position in the field of SRF and IF function in muscle. In this respect the team, which display efficient collaborations in each domain could also develop some collaborations with the Charles Foix Hospital devoted to gerontology and long-term animal hosting. Furthermore the team has shown a great capability in raising funds for research and has a strong involvement in teaching at Master level and in the doctoral schools.

- Weaknesses and threats

This field of investigation is highly competitive at the international level. Translational approaches are not sufficiently developed.

- Recommendations

The team is encouraged at maintaining its very good level of publications but also to improve its participation to clinical research program through the development of new tools for the diagnosis of heart failure, muscle diseases, sarcopenia obesity, for example.

5 • Conduct of the visit

Visit dates:

Start: December 11th, 2012, at 8h30

End: December 12th, 2012, at 15h00

Visit site(s): Room 501, 5th floor of the building B, Campus Jussieu, 9 quai Saint Bernard, Paris 5, France

Institution: University Paris 6

Address: Campus Jussieu, 9 quai Saint Bernard, Paris 5, France

Conduct or program of visit:

December 11th, 2012

8h30 - 9h00 : Closed-room meeting Committee, presention of AERES by the scientific delegate

9h00 - 9h15 : Starting of plenary presentations, presentation of the evaluation Committee, presention of AERES by the scientific delegate

9h15 - 10h00 : Presentation of results and projects of the research unit (B2A Department) by Jean Mariani & Bertrand Friguet

10h00 - 10h30 : Questions to Jean Mariani and Bertrand Friguet

10h30 - 10h45 : Break/ Debriefing of the Committee

10h45 - 11h30 : team 1

11h30 - 12h15 : team 2

12h15 - 13h00 : team 3

13h00 - 14h00 : Lunch

14h00 - 14h45 : team 4

14h45 - 15h30 : team 5

15h30 - 16h15 : team 6

16h15 - 16h30 : Break/ Debriefing of the Committee

16h30 - 17h15 : team 7

17h15 - 18h00 : team 8

18h00 - 18h45 : team 9

18h45 - 19h30 : Presentation of the Charles Foix Institute of Longevity ("team 10")

December 12th, 2012

8h30 - 9h00 : Meeting of the Committee with researchers

9h00 - 9h30 : Meeting of the Committee with technical and administrative staff

9h30 - 10h00 : Meeting of the Committee with PhDs and postdocs

10h30 - 10h45 : Break/ Debriefing of the Committee

10h45 - 11h30 : Meeting with representatives of Institutions supporting the unit

11h30 - 11h50 : Meeting of the Committee with the Head of B2A department

11h50 : End of visit

12h00 - 13h00 : Lunch

13h00 - 15h00 : Closed-room meeting of evaluation Committee (mandatory)

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

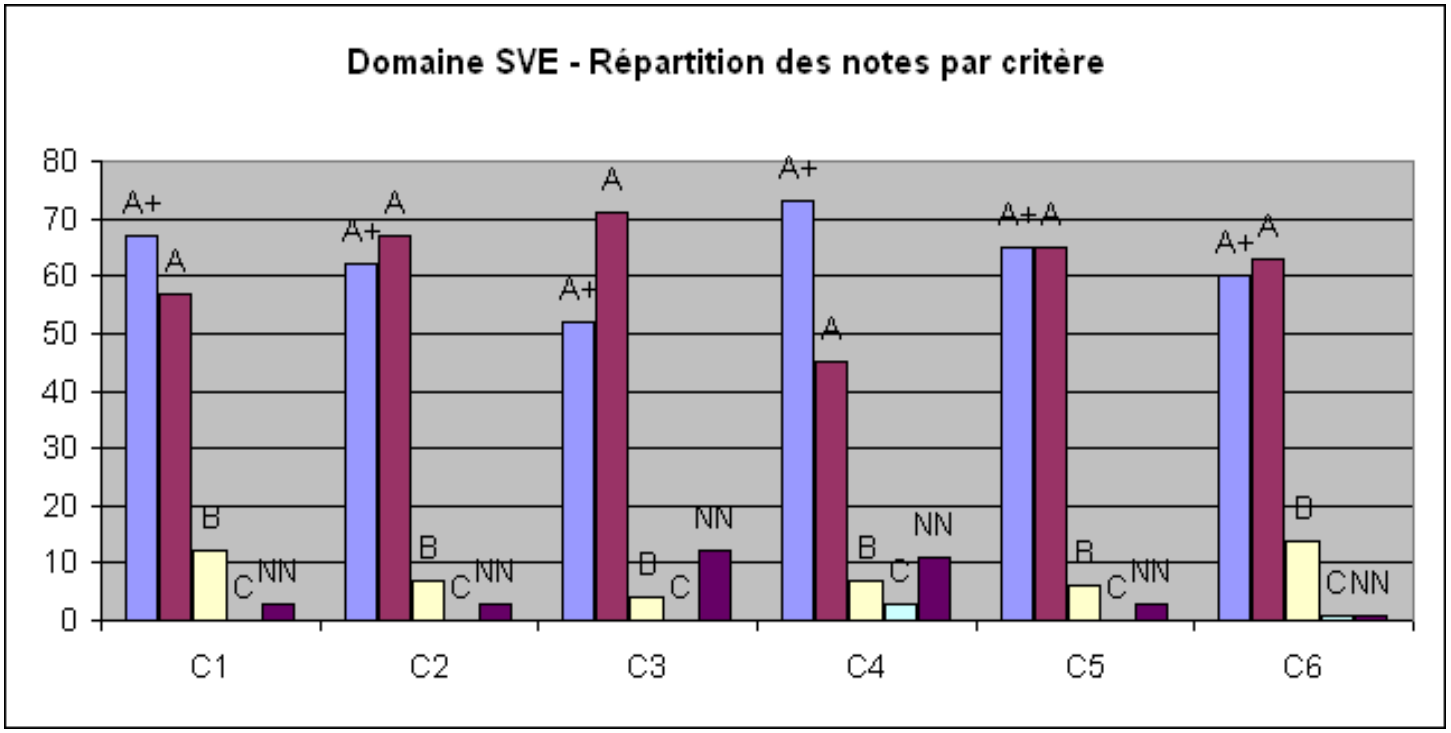
Grades

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 laboratoire Adaptation biologique et Vieillissement, porté par M. Friguet. 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

Response to the AERES Report on the

Unit Biological Adaptation and Ageing-Paris Seine (B2A)

First we would like to thank the committee for their visit and detailed report on our proposed new unit, Biological Adaptation and Ageing (B2A). We are grateful for the time the committee took to understand the broad multi-disciplinary approach that we are undertaking to investigate cellular adaptive processes that contribute to, and underpin, ageing. Moreover, we appreciate that the committee acknowledged the high quality of work undertaken by individual teams and that in combination the teams form a Unit with complementary models and approaches around a coherent project. This coherence will promote the new Unit's identity and international visibility, which, we are confident, will rapidly develop. However to ensure this, the Unit and each team will profit from the advice and comments made by the Committee in order to strengthen their work and the future of the Unit.

Unit's National and International Visibility

The Committee expressed concern that the Unit did not yet have national/international visibility in the field of ageing research. This is not surprising given that the Unit is only under construction and does not come into being until 2014. However as outlined by the committee, most if not all teams have good national and international visibility in their own right, albeit not always in ageing research *per se*. The development of our visibility will be enhanced as several of the Unit's teams are currently very active in National (LABEX), European (EU FP7, COST) and International (LIA) networks dedicated to research into ageing and its associated diseases. Moreover, this visibility as a new unit dedicated to biological adaptation and ageing will be further improved by our coordination of, and/or participation in, an increasing number of local (PRES), national and international networks. An example of this increase is demonstrated by the selection of Pr Mariani's application for the national campaign DHU (Département Hospitalo-Universitaire). In this DHU, FAST (Fight Against Ageing and STress), our unit B2A represents most of the basic science research therein, as well as being deeply implicated in the DHU training programme and new translational perspectives. Finally, the B2A unit is already part of a newly developing national network on ageing that is linked to the European Horizon 2020 KIC initiative on "Healthy Life and Active Ageing".

Management and Unit organisation

The Committee commented that the grouping of 9 teams from different backgrounds and research fields represents a challenge to the Director and Deputy Director and advised that they make particular efforts to "more closely associate their permanent and non-permanent

members". While this comment is true, the challenge is significantly lessened by the desire of the teams' leaders to work together, as is evidenced by new inter-team collaborations which have already been established even before the Unit comes into existence.

Moreover, the Director and Deputy Director have already initiated further efforts to consolidate the project and promote cohesion of the Unit's members so that the management, executive and collegial structures will be already operational when the unit is created in January 2014.

(1) We have established an executive committee "Chefs d'Equipes" which has regular meetings every month. This committee is currently addressing the practicalities of identifying tasks necessary for the Unit to function; e.g. identification of responsibilities such as Health and Safety Officer, Human Resources Officer etc. These meetings will also address the strategy by which the scientific program will be implemented (fostering collaborations, allocation of technical assistance etc).
(2) We have called a general meeting all members (*Assemblée Générale*) in order to establish the structures necessary for daily life in the Unit and identify who will undertake what task: specifically elections for the Unit's management committee (*Conseil de Laboratoire*), writing of the Unit's rules (*Reglementation Intérieure*) and identifying people responsible for experimental legislative requirements (e.g. health and safety, animal ethics, OGM). These developments will foster collegial interactions among the Units members at all levels.
(3) As well as these administrative meetings, our weekly Dataclub for scientific exchange is ongoing. These meetings involve presentations of projects and results usually by PhD students, postdocs and junior faculty in order to foster interactions of the Unit's members over and above those of the team leaders in the executive "Chefs d'Equipes" committee. Moreover, all team members are encouraged to attend, not just the students or team leaders, in order to promote understanding of the Unit's resources at both scientific as well as technical levels.

Recruitment and Staffing

At several points in the review, the Committee expressed concern about staffing levels and the need to equilibrate the unequal team sizes: comments on page 6 (Weaknesses and Threats, 2nd paragraph) and repeated on page 7 (recommendation 2) and page 8 (Assessment of the Units Organisation and Life). The Director and Deputy Director would like to respond specifically:

(1) First, we agree that the sizes of the teams are very unequal. However this historical situation is being addressed by promoting discussion between those technical support staff who have been left without team affiliation due to the reorganisation of the different Units on the Jussieu Campus within the IBPS and the smaller teams that need further human resources.

(2) Second, some of the larger teams are only big because they contain young emerging groups who will develop into independent teams during the next 3-5 years, thus re-equilibrating team size.

(3) Third, the management team, in close connection with the team leaders, has a positive policy for recruitment to support emerging and smaller teams. This policy will also include succession planning for those teams which will lose members through retirement in order to maintain their scientific identity and competitiveness. All teams are encouraged to present researchers to the CNRS/INSERM. However, while the recruitment of faculty is globally directed by teaching needs, the Unit has requested MCU posts for the relatively recent and expanding speciality of the Master BIP, *Biologie du Vieillissement et de la Longevité*, which can provide candidates who can fulfil research needs of most teams. As recommended by the Committee, the recruitment procedure will closely involve the team leaders in order to optimise integration of the new faculty in to the team.

Moreover, there have been ongoing recruitments, including the stabilisation by UPMC in 2013 of three temporary staff (research, administration and finance) and one associate professor who has complementary research approaches and who will start a new group initially under the umbrella of one of the pre-existing teams of B2A.

In addition, the report indicated a concern that the uneven size of the teams would generate "competition for limited resources …. especially between teams closely related to worthwhile therapy-related aspects of ageing and those involved in more fundamental research ……". We are not convinced there will be competition between teams for limited resources. As we demonstrated in our presentation, the great majority of research funding to the Unit comes as research grants to individual teams; not central funds to the Unit. Thus the teams maintain their own research rather than depend on support from the Unit. It is difficult to see where competition will arise. Moreover, what little funding does arrive from the Unit's affiliating organisations (UPMC, CNRS and INSERM) is subject to an obligatory percentage donation to the Institut de Biologie Paris Seine and has to provide common resources such as cleaning contracts and resources common to many teams (eg A2L2 facility, tissue culture and histology). What is left is distributed in a formulaic process and is thus not subject to inter-team competition.

Paris, 2nd April 2013

Pr Bertrand FRIGUET

Pr Rachel SHERRARD

Teams Reponses

The team leaders thank the committee for their comments and will incorporate the recommendations which have been made. In addition some team leaders wish to add further comments specific to their own team.

Team 1: Ahmad

Dr Ahmad agrees fully with the commission (AERES) that her team would benefit strongly from additional permanent members. To this end she is confident that the B2A unit will fully support her efforts to recruit staff including; (1) UPMC personnel (both Faculty and/or research officers), either those existing without lab affiliation or new staff; and (2) the application of a CR1 researcher she has presented to the CNRS.

In addition, Dr Ahmad is confident that the Unit will ensure her scientific freedom and control of her scientific and intellectual property.

Team 5: Brugg/Jacotot

Drs Brugg and Jacotot are pleased that the committee acknowledged the very recent combination of the 2 PIs into a single team, which provides an important scientific complementarity. However, they wish to reply to the committee's concern about their lack of mutual publications. Despite work in different organisations, Drs Brugg and Jacotot do in fact have a common publication; albeit one that is not conspicuous, being before the current quadrennial (Lecoeur et al 2004, Apoptosis 9:157-69). Moreover, Dr Jacotot has co-published with the unit UMR7102 Neurobiologie des Processus Adaptatifs in which Dr Brugg works (co-author Jean Mariani: Cell Death Dis. 2011; J Neurochem. 2007; Apoptosis 2005; Apoptosis 2004), indicating that he has productive thematic links with the neuroscience community.

Finally, Drs Brugg and Jacotot are a little surprised by the comment on page 23 that the focus on caspase-2 is "unexpected". They feel that this is "not unexpected", as E. Jacotot, has a strong background and recent good publications on caspase-2 (including 4 research article in 2011-2012: Annals Neurology, IF = 9.6, Cell Death Dis x2, Pediatric Res).

Team 6: Sherrard/Mariani

Prs Mariani and Sherrard thank the Committee for their review. They acknowledge the necessity of succession planning and have already implemented an active program for recruitment of new researchers and junior faculty; it is presenting candidates to the CNRS and Fondation "Plan Alzheimer" and is requesting a junior faculty to support its 3 professors. In addition they wish to add that the potential translation of the team's research to clinical practise has been greatly reinforced by the opening of the *Institut de la Longévité* where experiments are currently underway, but also the recent success of the DHU FAST (see

above), which greatly strengthens the links to clinicians, including geriatricians, and the application of basic science to improving patient care.

Team 8: Limon

Pr Limon wishes to add the comment that her team is already being reinforced by a full-time researcher, CNRS CR1.

Team 9: Li/Mericskay

Drs Li and Mericskay are pleased that the committee recognised the originality of their project. They agree that their translational approaches are insufficiently developed and will aim to do this by taking advantage of access to clinicians and aged patients at the Charles Foix hospital and benefit from the intellectual and clinical resources recently acquired through the DHU FAST.