Laboratoire de physiologie cérébrale

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Laboratoire de Physiologie Cérébrale

Under the supervision of the following institutions and research bodies:

Université Paris Descartes

Centre National de la Recherche Scientifique

January 2013

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

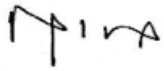
Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head



Pierre Glaudes

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: Laboratoire de Physiologie Cérébrale

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

- Grading table of the team: Synaptic Transmission in the Cerebellum

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

- Grading table of the team: Optical Probing of the Cerebellar Circuit

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

- Grading table of the team: Glutamatergic Transmission in the Cerebellum

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

- Grading table of the team: Synaptic Transmission in the Hippocampus

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

- Grading table of the team: Genetic Expression and Neurological Diseases

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

- Grading table of the team: Biophysics of Glial transmission

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

Evaluation report

Unit name:	Laboratoire de Physiologie Cérébrale
Unit acronym:	
Label requested:	CNRS, Université Paris Descartes
Present no.:	UMR 8118
Name of Director (2012-2013):	Mr Alain MARTY
Name of Project Leader (2014-2018):	Ms Isabel LLANO

Expert committee members

Chair:

Mr Dominique MULLER, Université de Genève, Geneva (Switzerland)

Experts:

Mr Yann BARRANDON, Ecole Polytechnique Fédérale de Lausanne (Switzerland)

Ms Valérie CREPEL, INSERM, Marseille (*CoNRS representative*)

Mr Florian LESAGE, Institut de Pharmacologie Moléculaire et Cellulaire, Sophia Antipolis (*CNU representative*)

Mr Thomas OERTNER, Institute for Synaptic Physiology Center for Molecular Neurobiology Hamburg (Germany)

Mr Carl PETERSEN, Ecole Polytechnique Fédérale de Lausanne (Switzerland)

Mr Dmitri RUSAKOV University College London (UK)

Mr Trevor SMART, University College London (UK)

Scientific delegate representing the AERES:

Mr Laurent GROC

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

Mr Stefano MARULLO (Université Paris Descartes)

Mr Bernard POULAIN (CNRS)

1 • Introduction

History and geographical location of the unit

The unit was created 10 years ago and renewed in 2009 for 4 years. It was at the time constituted of 6 teams. Three teams will not be renewed in the current project. Three other teams will however join the new unit project: CHEVALEYRE team, an ATIP/avenir team who already joined one year ago; the DJIAN team and the OHEIM/ROPERT team who will join in 2014. All six teams will be located at the St-Pères.

Management team

Mr Alain MARTY has served as unit leader during the last report period. He will now be replaced by Ms Isabel LLANO for the next period.

AERES nomenclature : **SV1-LS5**

SVE1_LS5 Neurobiology

Workforce

Effectifs de l'unité	**Nombre au 30/06/2012**	**Nombre au 01/01/2014**	2014-2018 **Nombre de produisants du projet**
N1 : Enseignants-chercheurs titulaires et assimilés	2	2	2
N2 : Chercheurs des EPST ou EPIC titulaires et assimilés	8	14	14
N3 : Autres personnels titulaires (n'ayant pas d'obligation de recherche)	5	9	9
N4 : Autres enseignants-chercheurs (PREM, ECC, etc.)			
N5 : Autres chercheurs des EPST ou EPIC (DREM, Post-doctorants, visiteurs etc.)	6	8	8
N6 : Autres personnels contractuels (n'ayant pas d'obligation de recherche)			
TOTAL N1 à N6	**21**	**33**	**33**

Taux de produisants	***100 %***

Effectifs de l'unité	Nombre au 30/06/2012	Nombre au 01/01/2014
Doctorants	5	
Thèses soutenues	10	
Post-doctorants ayant passé au moins 12 mois dans l'unité *	8	
Nombre d'HDR soutenues		
Personnes habilitées à diriger des recherches ou assimilées	9	

2 • Assessment of the unit

Strengths and opportunities

The evaluation committee has been very much impressed by the high scientific quality of the teams and of their projects. Globally, this unit has reached a high level of excellence and international recognition in the analysis of synaptic mechanisms, a domain in which they have developed approaches at the forefront of current scientific experimentation. The committee is convinced that this will allow them to remain among the world leading research groups in this field. This is attested as well by the high quality of their publications and by the excellent level of funding that they have achieved over the past period.

A major strength of the unit is the high level of thematic and technological cohesion, with a strong focus on functional analyses of synaptic mechanisms. Most teams share complementary approaches that include electrophysiological recordings, optical calcium imaging, optogenetics and uncaging methodologies. This gives a very high potential for interactions between groups, a hallmark of the functioning of the unit as attested by the numerous publications contributed by several teams of the unit.

Another important strength of the unit is the capacity and interest of many teams to develop new tools and technological approaches. The uncaging methodologies developed by one team have not only an extremely interesting potential for addressing important synaptic issues within the unit, but they also have a more global impact in terms of interactions with industry and the development of tools for the research community. The optical imaging approaches developed by two other teams are also at the forefront of the research in their field and make it possible to really advance scientific frontiers and maintain a high level of competitiveness.

The unit has also gaineda high international visibility in terms of training opportunities due to the involvement of one PI in the electrohysiology section of Woods Hole Neurobiology course and the important roles played another PI in the Paris and Plymouth electrophysiology courses. Another important strength of the unit is linked to the excellent management provided by the current director over the past period. The choice to keep the size of teams rather small as to increase interactions has been clearly very beneficial. Also the general co-direction approach taken between senior team leaders and younger colleagues seems to work perfectly to the satisfaction of all and provides an interesting opportunity to promote the emergence of new team leaders. Overall the general impression of the committee is that this unit has delivered far more than what could be reasonably expected from its size.

Weaknesses and threats

A number of difficulties could significantly affect the functioning of the unit over the coming period and could represent potential threats for the unit:

- the unit will have to stop its activities for several months due to an electrical renovation of the building and of their lab spaces. This is a major setback for all competitive research groups and the committee hopes that it will be possible to keep this period to a minimum.

- the unit will welcome two new teams for the next period and space reallocation and reorganization will be necessary for this. Additionally, the ATIP team is expected to move in order to work in proximity to the other teams. The committee is convinced that this proximity of lab spaces is extremely important to warrant the success of integration of these new teams and hopes that the transformations required for these reallocations will be made possible.

- administrative problems may affect the integration of specific team members. In particular, a professor at university Paris Diderot with a strong teaching activity could bring much more to the functioning of the unit and increase his interactions if he could obtain a professorship from the University of Paris Descartes. Another pending issue concerns the situation of a member of one team who is an Inserm engineer and would need to be transferred to the CNRS in order to be able to continue her work with her team. The committee hopes that solutions will be found to resolve these problems.

One difficulty that the unit will have to face is the integration of the new teams. While two of them share many technological and thematic questions with the members of the other teams, the situation of the third new team is special and not so straightforward. The potential for bringing currently missing genetic and molecular knowledge to the unit by the arrival of this new team represents a really very significant addition to the unit. Interactions are also expected through the development by this team of a project on the toxicity of Huntingtin aggregates. However the committee felt that the the work on the basonuclin aspects are also a very original and important research aspect that should be pursued. However, this work is far from the themes currently developed within the unit and the

difficulty or challenge will be to preserve the pioneering position reached by the new team in this very specific field while ensuring contributions to the general functioning of the unit as a whole.

Recommendations

The availability of master and PhD students has been raised as one difficulty faced by the unit. To address this issue, the committee suggests that some emphasis should be given to the development of more global neuroscience master and PhD programs. The current difficulties of the teams of the unit to find master and PhD students is probably partly linked to the absence of such an organized and high visibility program. This will need concerted efforts involving not only teams of the unit but also a more global concertation with other neuroscience units to create an attractive program. Such programs exist in many other universities and could be very valuable to the unit.

Integration of the new teams in the current functioning of the unit will clearly be a major challenge for the next period. Specific steps could be important to facilitate this integration. Relocation of the teams within the unit lab spaces is an obvious requirement, but other steps that could also be beneficial involve the development of specific common projects, regular meetings between team leaders and the organization of journal clubs within the unit to create regular contacts between team members.

Several teams within the unit have expressed their interest to address issues relating to synaptic properties and network functions. Several teams have also started to analyse functional properties through imaging approaches at the level of cell assemblies. The committee shares the opinion that a future recruitment of a junior group leader in the field of neuroscience modelling could represent an interesting option for further developing the unit and would encourage the new director to continue proceeding in this direction.

3 • Detailed assessments

Assessment of scientific quality and outputs

The productivity of the future unit is outstanding with about 80 publications over the last 5 years from the 6 teams. There are numerous publications in high standard journals for which unit members are last author, including 2 Neuron papers, 5 PNAS papers and 10 J. Neuroscience papers. Another important index of the scientific quality of the team is the number of methodological papers highlighting the important emphasis placed by the unit in the development of new techniques and approaches.

Assessment of the unit's academic reputation and appeal

The international reputation of the leaders of the unit is outstanding. They are considered as world leaders In the field of synaptic transmission, they are invited to high profile conferences such as the Gordon conference; they are in charge of important international training programs such as the electrophysiology section of Woods Hole neurobiology course. One PI has also a strong international reputation in the field of uncaging technologies to which he has made substantial contributions. He is also well known for his organization and running of the Paris and Plymouth electrophysiology courses. In terms of recruitments, the unit has succeeded in attracting two excellent young researchers who will team-up together as co-PIs.

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

While the unit mainly addresses fundamental questions in the field of synaptic physiology, the innovative work of one team leader has allowed the creation of important contacts with the industry in the field of uncaging technologies. The work of this team leader has also strongly contributed to provide the scientific community with important new tools.

Assessment of the unit's organisation and life

The unit has been very well managed over the last period. They have regular scientific meetings (biweekly progress report). They have specific meetings of the permanent researchers to discuss scientific projects and science policy (once a month). Teams have usually remained of a small size to increase interactions. Most teams also are co-directed, a situation that increases exchanges within teams and promotes the potential for younger researchers to share responsibilities. The unit has several technical platforms that are shared; there is a dedicated person within the unit for safety issues. Finally the unit benefits from many other structures and common facilities coordinated at the level of the IFR (Institut Fédératif de Recherche).

Assessment of the unit's involvement in training through research

The members of the unit are involved in several teaching programs: these include the Neuroscience M2 program at St-Pères to which the entire unit contributes and various other teaching at Paris Descartes or even at Paris Diderot. One team member has notably contributed to develop an MD/PhD program for medical students. In addition to these pregraduate aspects, the unit is implicated in the organization of several postgraduate workshops or courses. In particular, one team leader organizes yearly a workshop on electrophysiology and imaging techniques and he contributes as well to a practical international course in Plymouth, UK. One team leader is in charge of the electrophysiology section of Woods Hole neurobiology course. Together this represents an important input of the unit to pre- and postgraduate training.

Assessment of the five-year planand strategy

The evaluation committee has been very much impressed by the scientific quality of the different projects developed by the team members. All projects presented are based on solid scientific preliminary data; they involve state-of-the art technological approaches (multi-patch electrophysiological approaches, presynaptic calcium imaging, uncaging technologies, optogenetics, in vivo imaging) for which the unit has gained a high international visibility; many projects are based on collaborative interactions.

4 • Team-by-team analysis

Team 1 : Synaptic Transmission in the Cerebellum

Name of team leader: Mr Alain MARTY & Mr Brandon STELL

Workforce

Effectifs de l'équipe	Nombre au 30/06/2012	Nombre au 01/01/2014	2014-2018 Nombre de produisants du projet
N1 : Enseignants-chercheurs titulaires et assimilés	1	1	1
N2 : Chercheurs des EPST ou EPIC titulaires et assimilés	2	2	2
N3 : Autres personnels titulaires (n'ayant pas d'obligation de recherche)			
N4 : Autres enseignants-chercheurs (PREM, ECC, etc.)			
N5 : Autres chercheurs des EPST ou EPIC (DREM, Post-doctorants, visiteurs etc.)	2	2	2
N6 : Autres personnels contractuels (n'ayant pas d'obligation de recherche)			
TOTAL N1 à N6	**5**	**5**	**5**

Effectifs de l'équipe	Nombre au 30/06/2012	Nombre au 01/01/2014
Doctorants	2	
Thèses soutenues	2	
Post-doctorants ayant passé au moins 12 mois dans l'unité	4	
Nombre d'HDR soutenues		
Personnes habilitées à diriger des recherches ou assimilées	3	

• Detailed assessments

Assessment of scientific quality and outputs

This team has specialised for many years in understanding the network and synaptic behaviour of inhibitory interneurons in the cerebellum. In terms of outputs and novel discovery, the previous work is generally of the highest quality, reporting seminal findings with papers in high quality journals (e.g., Neuron, PNAS, J Neurosci). The discovery of preminis, the use of uncaging technology and ability to resolve single site signalling are important contributions, which also form the cornerstones of the future proposals. These proposals are innovative and will add substantially to our understanding of the basis of neurotransmitter signalling in the cerebellum, not only at the level of synaptic inhibition, but also fundamentally at single synapses.

Assessment of the team's academic reputation and appeal

Members of the laboratory are actively promulgating their research in high quality journals and are asked to present to international audiences and collaborate with internationally renowned laboratories. This laboratory is regarded as an internationally leading lab in the field of GABA signalling. The team has also just received one of the prestigous ERC advanced research grants that will cover the coming period.

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

This aspect is not an appropriate area where the laboratory can easily contribute.

Assessment of the team's organisation and life

Nothing specific to mention.

Assessment of the team's involvement in training through research

Doctoral training is evidently of the highest quality and, in collaboration, a widely recognised high quality imaging and electrophysiology course is also organised to the benefit of students and post-docs in Paris. Training programmes for PhD students are evident. Mentoring of early career staff seems well developed.

Assessment of the five-year plan and strategy

The future proposals are innovative and likely to lead to significant breakthroughs in our understanding of signalling in the cerebellum. The laboratory is considered a world-leader in this area and now, by using caged compounds and precision imaging, the questions that are posed will reveal new fundamentally important aspects about chemical neurotransmission. This is particularly relevant to the single site and single synapse studies that are envisaged. Close interactions between groups ensure a common set of research goals, aided by the small group size.

Conclusion

●Strengths and opportunities:

This is an outstanding team with major strengths: - Excellent track record; - ERC grant holder;- seminal contributor to fundamental aspects of neurotransmission. Mr MARTY is a world-leader in his field; - Excellent innovative research ideas.

●Weaknesses and threats:

The committee did not observe any weaknesses

●Recommendations:

Proceed with current research plans as before, publishing in high quality journals

Team 2 : Optical Probing of the Cerebellar Circuit

Name of team leader: Ms Isabel LLANO & Mr Thibault COLLIN

Workforce

Effectifs de l'équipe	Nombre au 30/06/2012	Nombre au 01/01/2014	2014-2018 Nombre de produisants du projet
N1 : Enseignants-chercheurs titulaires et assimilés	1	1	1
N2 : Chercheurs des EPST ou EPIC titulaires et assimilés	2	2	2
N3 : Autres personnels titulaires (n'ayant pas d'obligation de recherche)			
N4 : Autres enseignants-chercheurs (PREM, ECC, etc.)			
N5 : Autres chercheurs des EPST ou EPIC (DREM, Post-doctorants, visiteurs etc.)	2	2	2
N6 : Autres personnels contractuels (n'ayant pas d'obligation de recherche)			
TOTAL N1 à N6	**5**	**5**	**5**

Effectifs de l'équipe	Nombre au 30/06/2012	Nombre au 01/01/2014
Doctorants	1	
Thèses soutenues	3	
Post-doctorants ayant passé au moins 12 mois dans l'unité	2	
Nombre d'HDR soutenues		
Personnes habilitées à diriger des recherches ou assimilées	3	

• Detailed assessments

Assessment of scientific quality and outputs

The team focuses on obtaining optical measurements of the activity of the cerebellar circuit and its different elements. In vitro fluorescence calcium imaging of the axons of molecular layer interneurons revealed the presence of presynaptic NMDA receptors on these axons (Rossi et al., 2012), extending previous work from the same lab showing the presence of AMPA receptors on these axons (Rossi et al., 2008). Investigation of the functional role of axonal ionotropic receptors is novel and of broad interest. In an important technical advance for the group, they began in vivo calcium imaging of molecular layer interneurons, which is technically demanding because of high firing rates and strong parvalbumin buffering in these neurons. The in vivo investigations provide an exciting direction for future research, which is planned to expand in the next years. From 2008-2012, both group leaders published a total of 5 papers in J. Neurosci. (2x), J. Neurophysiology, J Physiology and PLoS One.

Assessment of the team's academic reputation and appeal

The team leader is a highly respected scientist enjoying an excellent international reputation. She is the coordinator of an ANR grant "INNET - Functional properties of the cerebellar interneurone network" with collaborations with other group leaders of the unit. She was a member of the ANR-Blanc commission 2005-2009. She coordinates the electrophysiology part of the highly-respected Neurobiology course at Woods Hole, USA. This is an important and prestigious role. The team has attracted excellent international collaborators including postdoctoral fellows.

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

N/A This aspect is not an appropriate area

Assessment of the team's organisation and life

Nothing specific to mention.

Assessment of the team's involvement in training through research

The group leader is a diligent and careful advisor of doctoral students, who receive excellent mentorship and close supervision (4 PhD students, 3 of whom finished their PhDs during the period 2008-2012). She is in charge of the electrophysiology part of the Neurobiology course at Woods Hole, USA. This is a highly respected international neuroscience school and it is excellent that she is involved in organizing this important course. Both group leaders participate in the teaching of the Neuroscience M2 program and in the teaching of an international Paris Neuroscience School on electrophysiology and imaging. They are strongly involved in excellent international research training programs.

Assessment of the five-year plan and strategy

The team will continue to focus on 'Optical probing of the cerebellar circuit' both in vitro and in vivo. The in vitro experimental plans are to further investigate the roles and distributions of ionotropic glutamate and GABA receptors across the axons and dendrites of molecular layer interneurons. Further experiments will test the involvement of L-type calcium channels in neurotransmitter release from molecular layer interneurons. Technical development of genetically-encoded calcium indicators targeted to different neuronal compartments through fusion-proteins, will provide new opportunities for making specific measurements and will likely help subsequent in vivo studies. The in vivo experimental plans are to test for an excitatory role of GABA on axons of molecular layer interneurons and parallel fibers, which the lab has so far described in vitro. Further experiments will examine the role of metabotropic glutamate receptors in vivo, which have been found to have profound impact on molecular layer interneurons in vitro. As a next step, basket cell axon terminals on Purkinje cells will be imaged in awake mice performing simple behaviors. The longer-term perspective is to optically investigate the synaptic interactions driving cerebellar neural circuit function during behavior. This research program bridging in vitro and in vivo methods is the perfect goal for this laboratory and the development of in vivo imaging an important new challenge.

Conclusion

●Strengths and opportunities:

Excellent track record of important discoveries and technological developments. Good funding record. Advances with respect to *in vivo* imaging are excellent and at the frontier of neuroscience research.

●Weaknesses and threats:

No specific weaknesses identified.

●Recommendations:

The in vivo imaging is particularly exciting and we suggest that this frontier research program should be given the highest priority for this team.

Team 3 : Glutamatergic Transmission in the Cerebellum

Name of team leader: Mr David OGDEN and Ms Céline AUGER

Workforce

Effectifs de l'équipe	Nombre au 30/06/2012	Nombre au 01/01/2014	2014-2018 Nombre de produisants du projet
N1 : Enseignants-chercheurs titulaires et assimilés			
N2 : Chercheurs des EPST ou EPIC titulaires et assimilés	2	2	2
N3 : Autres personnels titulaires (n'ayant pas d'obligation de recherche)			
N4 : Autres enseignants-chercheurs (PREM, ECC, etc.)			
N5 : Autres chercheurs des EPST ou EPIC (DREM, Post-doctorants, visiteurs etc.)	2	2	2
N6 : Autres personnels contractuels (n'ayant pas d'obligation de recherche)			
TOTAL N1 à N6	**4**	**4**	**4**

Effectifs de l'équipe	Nombre au 30/06/2012	Nombre au 01/01/2014
Doctorants		
Thèses soutenues		
Post-doctorants ayant passé au moins 12 mois dans l'unité	2	
Nombre d'HDR soutenues		
Personnes habilitées à diriger des recherches ou assimilées	2	

• Detailed assessments

Assessment of scientific quality and outputs

The team has a very good publication record (13 publications in the last 5 years, including high impact journals like PNAS and Neuron). A major biological discovery was published in 2010, a novel inhibitory interaction between AMPAR current and mGluR1-evoked slow EPSCs via tyrosine phosphorylation. Past and ongoing projects are well focused biologically (cerebellum, parallel fiber-Purkinje cell synapse, mGluR signaling) and technically advanced (development of caged compounds and fast microscopy). The team pushes the development of uncaging technology on the chemical side (novel cages optimized for one and two-photon exciation), instrumentation (remote focusing microscopes etc.) and synaptic physiology in a highly interdisciplinary fashion.

Assessment of the team's academic reputation and appeal

Mr David OGDEN is considered a world leader in the field of photo-uncaging of compounds.In addition to their own research, the team is clearly an essential collaborator for the unit, as evidenced by the large number of collaborative projects and publications in the last years. Mr David OGDEN coordinated an EU STREP project until 2010, is now coordinator of ANR Blanc TP-Photolysis. The team is small, but international and very efficient, with excellent connections to the UK neurobiology scene.

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

Contacts with a supplier of life sciences reagents for commercialization of novel caged compounds. Commercial availability is essential to enable wider use of the compounds developed by the team, this is an important contribution for the neuroscience community. Patents have been filed for 2p and X-ray caged compounds.

Assessment of the team's organisation and life

Nothing specific to mention.

Assessment of the team's involvement in training through research

Mr David OGDEN is co-director of the Paris School of Neuroscience (18 students/year). In addition, he organizes and teaches every year two 2-week workshops at the MBA in Plymouth, UK (Optical techniques, Microelectrode techniques), which is a highly regarded practical training course running for 30 years. This major effort has also increased the international visibility of the team.

Assessment of the five-year plan and strategy

Three major directions are proposed: 1) Glutamate receptor signaling on Purkinje cell dendrites in situ 2) Advanced microscopy setups for uncaging 3) Development of caged antagonists, improved 2p and X-ray cages. The proposals are innovative and ambitious. The possibility to optically stimulate individual synapses opens up the exciting possibility to investigate transmitter receptor properties and localization in situ.

Conclusion

●Strengths and opportunities:

Combining high level chemical, optical and biological expertise in a single team. Perfect match between technique and biological question. The projects are clearly creative. Importantly, the team is composed of scientists that are essential collaborators for many other teams in the unit.

●Weaknesses and threats:

Too much diversity in methods development could dilute the focus of the small team. Setups that are used for methods development cannot be used simultaneously to acquire biological data and address biological questions.

●Recommendations:

Exploit the strength of uncaging technology to address biological questions of fundamental importance.

Team 4 : Synaptic Transmission in the Hippocampus

Name of team leader: Mr Vivien CHEVALEYRE & Ms Rebecca PISKOROWSKI

Workforce

Effectifs de l'équipe	Nombre au 30/06/2012	Nombre au 01/01/2014	2014-2018 Nombre de produisants du projet
N1 : Enseignants-chercheurs titulaires et assimilés			
N2 : Chercheurs des EPST ou EPIC titulaires et assimilés	2	2	2
N3 : Autres personnels titulaires (n'ayant pas d'obligation de recherche)			
N4 : Autres enseignants-chercheurs (PREM, ECC, etc.)			
N5 : Autres chercheurs des EPST ou EPIC (DREM, Post-doctorants, visiteurs etc.)			
N6 : Autres personnels contractuels (n'ayant pas d'obligation de recherche)			
TOTAL N1 à N6	**2**	**2**	**2**

Effectifs de l'équipe	Nombre au 30/06/2012	Nombre au 01/01/2014
Doctorants	2	
Thèses soutenues		
Post-doctorants ayant passé au moins 12 mois dans l'unité		
Nombre d'HDR soutenues		
Personnes habilitées à diriger des recherches ou assimilées	1	

• Detailed assessments

Assessment of scientific quality and outputs

A young team with a PI starting his own project only from April 2011 and thus cannot yet be fully evaluated on his own scientific contribution. The past work of both PIs as postdocs is outstanding with 2 Neuron papers, 1 J. Neurosci paper for one and 3 PNAS and 2 Neuron papers for the other. The team production since its start in 2011 include 3 papers, including a Cell paper for which Mr Vivien CHEVALEYRE is co-author and a paper in Cellular and Molecular Life Science that is the first publication fully contributed by the team. The work of Mr Vivien CHEVALEYRE focusses on the study of the CA2 area of the hippocampus, where they analyze the mechanisms of opioid-mediated depression at inhibitory synapses in CA2, the role of mGluR4 and presynaptic NMDA receptors and the regulation of rythmic activity by the supremammillary nucleus. The projects are original and supported by strong preliminary data.

Assessment of the team's academic reputation and appeal

Mr Vivien CHEVALEYRE has obtained the prestigious and very competitive ATIP/Avenir grant in 2011. The team is implicated in local and international collaborations. They both have been invited to give 4 seminars in France over the last two years.

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

N/A

Assessment of the team's organisation and life

Nothing specific to mention.

Assessment of the team's involvement in training through research

The team contributes to a workshop on optical imaging and electrophysiology. They also participate as coordinator of the Neuroscience seminars of Paris Descartes University. Currently the team includes 1 PhD student who is regularly supervised by the two leaders.

Assessment of the five-year plan and strategy

The project of the team focusses on the Ca2 region of the hippocampus and will address several distinct questions. One will concern a new form of plasticity of inhibitory transmission mediated by opioid receptors. A second project will be to assess the specific role of mGluR4 receptors in regulating the excitatory/inhibitory balance through the availability of a selective agonist. A third project is to examine the possible existence and physiological role of presynaptic NMDA receptors by using a calcium imaging approach. Finally a last goal will be to examine the role of supramammillary nucleus projections on hippocampal oscillatory activity using an optogenetic approach under in vitro but also under in vivo conditions.

These projects are ambitious and at the cutting edge of available methods and techniques. The team has the necessary expertise and financial support (ATIP/Avenir) to achieve their goals. The projected milestones are realistic and address important issues relating to the properties of synaptic transmission and plasticity in the hippocampus. The project on the supramammillary control of hippocampal activity is particularly appealing and the possibility of an in vivo development makes this project very original, novel and ambitious.Due to the excellent expertise of the team and the potential for interaction with the other members of the unit, the feasibility looks good and will likely provide important new information.

Conclusion

●Strengths and opportunities:

Very promising and dynamic team. The collaboration between the two leaders is excellent and very complementary. The choice to focus on the CA2 area is very original and important. The combination of electrophysiology and optogenetics with a possible in vivo development makes the project very innovative.

●Weaknesses and threats:

The team is still relatively small and might need further support to progress with his ambitious projects

●Recommendations:

It could be useful for the team to enhance interactions with other national or international groups that might bring collaborations and additional grant support.

Team 5 : Genetic Expression and Neurological Diseases

Name of team leader: Mr Philippe DJIAN

Workforce

Effectifs de l'équipe	Nombre au 30/06/2012	Nombre au 01/01/2014	2014-2018 Nombre de produisants du projet
N1 : Enseignants-chercheurs titulaires et assimilés			
N2 : Chercheurs des EPST ou EPIC titulaires et assimilés	3	3	3
N3 : Autres personnels titulaires (n'ayant pas d'obligation de recherche)	2	2	2
N4 : Autres enseignants-chercheurs (PREM, ECC, etc.)			
N5 : Autres chercheurs des EPST ou EPIC (DREM, Post-doctorants, visiteurs etc.)			
N6 : Autres personnels contractuels (n'ayant pas d'obligation de recherche)			
TOTAL N1 à N6	**5**	**5**	**5**

Effectifs de l'équipe	Nombre au 30/06/2012	Nombre au 01/01/2014
Doctorants	2	
Thèses soutenues	3	
Post-doctorants ayant passé au moins 12 mois dans l'unité	1	
Nombre d'HDR soutenues		
Personnes habilitées à diriger des recherches ou assimilées	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The team has an excellent publication record (18 papers in the last 5 years with two PNAS papers in 2008 and 2009, one paper in J. Cell Biol in 2007), but mainly outside the neurobiology field. Their main contribution in recent years has been the discovery of basonuclins, proteins expressed in various tissues including epidermis, cornea and reproductive germ cells. By generating knockout mice for basonuclin2, they have uncovered an important role of this protein for the maintenance of spermatogonial stem cells in testis. In ovaries, they find that basonuclin2 represses the multiplication of epithelial cells, a function that could relate to an implication of the protein in ovarian cancers. Together the committee was impressed by the solidity and quality of these observations and the potential importance that they represent. As a second research interest, the team is also focussing on the mechanisms of aggregation of expanded huntingtins. By studying microaggregates in the brain of patients, they have identified several types of inclusions, some with a probable beta-sheet enrichment that they suspect to be toxic. Their overall contribution to this topic has been more modest so far but represents one of the directions through which interactions with the other members of the unit could be generated.

Assessment of the team's academic reputation and appeal

The team can clearly be considered as an international leading research group in the basonuclin field. Despite this however it has not been as visible on the international scene. The group leader has served for 14 years as director of the IFR 95 and has made an outstanding job creating common facilities and supporting the development of the direct units and contribute to the reputation of the research site.

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

N/A

Assessment of the team's organisation and life

Nothing specific to mention regrading the team organisation and life.

Assessment of the team's involvement in training through research

The team has trained a sizable amount of Master and PhD students over the last years. The group leader is directly teaching the Master course of Biologie-Pharmacotox at Paris Descartes.

Assessment of the five-year plan and strategy

The proposed project builds on the two main directions taken by the team: a further characterization of the functions of basonuclins and the mechanisms of toxicity of aggregated polyglutamine expansions. The projects on basonuclins is a direct continuation of the excellent work carried out so far and proposes to examine in more details the role of basonuclin2 in ovarian cancer and stem cell function. They will use a silencing approach in mice and human cells and will study the expression profile under these conditions. The proposal is straightforward and expected results are important with a potentially high clinical relevance.

The project on the toxicity of aggregated polyglutamine expansions is also a direct continuation of their current work indicating the possibility that these aggregates form beta-sheets and could be toxic. They will now use culture systems and use synthetic polyglutamine as seeds to promote aggregation and study their toxicity in IPS cells. The issue is important and the competences for carrying out the proposed experiments are present in the team. Support is also expected to be obtained from the unit for some functional measures such as calcium imaging as an early sign of toxicity.

Conclusion

●Strengths and opportunities:

Strong track record; leading role in the discovery of basonuclins and of their functions; very interesting and important preliminary results regarding the basonuclin project.

●Weaknesses and threats:

The integration of the team into a neuroscience unit will remain a main challenge for the years to come. Support from the institutions to resolve issues related to space reorganization and the situation of one team member will be important for this integration to be a success. The benefits that the team will bring to the unit in terms of expertise in genetics and molecular approaches is however real and important and justifies the move. On the other hand, it seems less clear how much the expertise of the other members of the unit will help and be useful for the development of the team's projects.

●Recommendations:

Despite their integration in a neuroscience unit, the committee felt that the basonuclin project should remain a priority within the research projects of the team. Also with the quality of the results obtained so far, the committee felt that a more ambitious attitude to international communication could probably increase the international visibility of the team.

Team 6: Biophysics of Glial transmission

Name of team leader: Mr Martin OHEIM & Ms Nicole ROPERT

Workforce

Effectifs de l'équipe	Nombre au 30/06/2012	Nombre au 01/01/2014	2014-2018 Nombre de produisants du projet
N1 : Enseignants-chercheurs titulaires et assimilés			
N2 : Chercheurs des EPST ou EPIC titulaires et assimilés	3	3	3
N3 : Autres personnels titulaires (n'ayant pas d'obligation de recherche)	1	1	1
N4 : Autres enseignants-chercheurs (PREM, ECC, etc.)			
N5 : Autres chercheurs des EPST ou EPIC (DREM, Post-doctorants, visiteurs etc.)	3	2	2
N6 : Autres personnels contractuels (n'ayant pas d'obligation de recherche)			
TOTAL N1 à N6	**7**	**6**	**6**

Effectifs de l'équipe	Nombre au 30/06/2012	Nombre au 01/01/2014
Doctorants	1	
Thèses soutenues	2	
Post-doctorants ayant passé au moins 12 mois dans l'unité	3	
Nombre d'HDR soutenues		
Personnes habilitées à diriger des recherches ou assimilées	2	

• Detailed assessments

Assessment of scientific quality and outputs

The team will join the unit in 2014. The scope of past research was two-fold. One focus was on the methodological development of super-resolution optical microscopy involving improved TIRF imaging methods, and on the implementation of adaptive optics techniques to optimise 2P excitation yield in turbid brain tissue. The other was a concentration on the functional properties of central synaptic circuits and on the Ca2+-dependent signal exchange between astroglia and neurons. The overall research output in terms of publication record has been strong, at the level of international recognition, with several papers in leading journals: one in PNAS USA (IF=10), one Nano Letters (IF=13), three J Neurosci (IF=7), further papers in J Physiol, Biophys J, BJP, Opt Express, Langmuir, and others.

Assessment of the team's academic reputation and appeal

Ms Nicolle ROPERT have contributed significantly to neuroscience research, and the outcome related to the neuroscience theme in this group appears to have a strong impact in terms of published findings. Mr Martin OHEIM have made significant contributions to the development and dissemination of novel optical tools, and Mr Martin OHEIM has had an outstanding record of invited international presentations (~51 over 5 years).

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

The team has one patent filed that may be of great value for non-academic outcome.

Assessment of the team's organisation and life

Nothing specific to mention.

Assessment of the team's involvement in training through research

The group leaders and staff have trained two PhD students and eight undergraduates over the reported period.

Assessment of the five-year plan and strategy

Astroglia-neuron communication has rapidly emerged as an important topic in neuroscience research because it challenges the traditional view postulating that major brain functions rely exclusively on "wired" neural circuits. The novelty and potential impact in this direction is high, and the outlined strategy combining optogenetic and high-resolution optical registration methods in the context of astrocyte-neuron signalling appears promising. The super-resolution microscopy developments are potentially important.

Conclusion

●Strengths and opportunities:

Strong track record of publications and grants; importance, novelty and timeliness of scientific vision, cutting-edge optical and electrophysiological approaches

●Weaknesses and threats:

Much emphasis on cultured astroglia, sub-optimal integration between optics and in situ physiology.

●Recommendations:

It would be useful to define more focussed objectives for exploring very diverse aspects of astroglial signalling. Also the developments towards more in situ analyses of astroglial function are highly encouraged.

5 • Conduct of the visit

Visit dates:

Start: 17 January 2013 at 8h50

End: 18 January 2013 at 16h00

Visit site(s):

Institution: Faculté des St Pères

Address : rue des St Pères, 75005 Paris

Conduct or programme of visit:

January 17, 2013

8:50 to 9:15	Visiting Committee closed meeting
9:15 to 9:30	Mr Laurent GROC (AERES), Mr Dominique MULLER (committee): presentation
9:30 to 9:45	Mr Alain MARTY: Past activity of the Unit
9:45 to 10:00	Ms Isabel LLANO: Projects of the Unit
10 :00 to 10:45	Team #1 (Mr Alain MARTY, Mr Brandon Stell)
11 :15 to 12 :00	Team #2 (Ms Isabel LLANO, Mr Thibault COLLIN)
12:00 to 12:15	Discussion of Teams 1-2 (Visiting Committee closed meeting)
12:15 to 13 :00	Lunch
13 :00 to 13 :45	Team #3 (Mr David OGDEN, Ms Céline AUGER)
13 :45 to 14 :30	Team #4 (Mr Vivien CHEVALEYRE)
14 :30 to 14 :45	Discussion of Teams 3-4 (Visiting Committee closed meeting)
15 :00 to 15 :45	Team #5 (Mr Philippe DJIAN)
15 :45 to 16 :30	Team #6 (Mr Martin OHEIM, Ms Nicole ROPERT)
16 :30 to 16 :45	Discussion of Teams 5-6 (Visiting Committee closed meeting)
16 :45 to 17:15	Parallel meetings :
	Meeting with PhD students and postdoctoral fellows
	Meeting with engineers, technicians and administrative assistants
	Meeting with permanent researchers (except team leaders)
17:15 to 18:00	Interview with past and income directors (Ms LLANO/Mr MARTY)

January 18, 2013

9:00 to 11:00	Poster exhibits (possible team visits)
11:00 to 12:00	Meeting with the institution (“tutelles”) representatives
12:30 to 16:00	Closed discussion
16:00	End of the visit

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

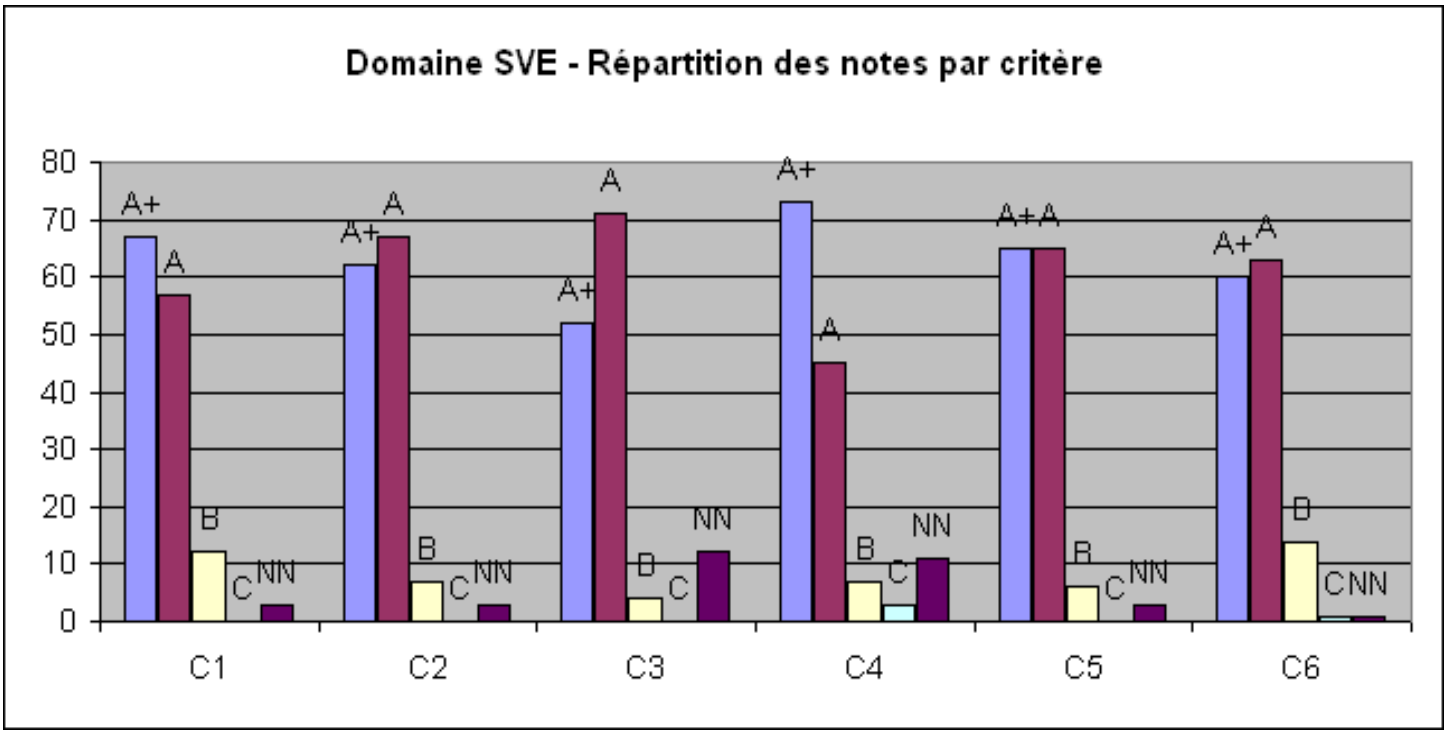
Grades

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

Percentages

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

Histogram



7 • Supervising bodies' general comments

UNIVERSITÉ PARIS DESCARTES

Vice Président du Conseil Scientifique

Paris le 09.04.2013

Vos ref : S2PUR140006252 –
Laboratoire de Physiologie Cérébrale
- 0751721N

Monsieur Pierre GLAUDES
Directeur de la section des unités de recherche
Agence d'Evaluation de la Recherche et de l'Enseignement Supérieur
20, rue Vivienne
75002 PARIS

Monsieur le Directeur

Je vous adresse mes remerciements pour la qualité du rapport d'évaluation fourni à l'issue de la visite du comité d'expertise concernant l'unité « Laboratoire de Physiologie Cérébrale »

De même que le Directeur de l'unité, Isabel LLANO, le Président et moi-même n'avons aucune remarque particulière à apporter.

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

Le Vice Président du Conseil Scientifique

Stefano Marullo, DM, DesSci

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