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

Department for the evaluation of research units

# AERES report on unit:

## Neuroscience Paris Seine - IBPS-Neuroscience

## 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

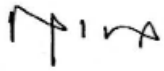
Research Units Department

President of AERES

**Didier Houssin**

Research Units Department

*Department Head*



**Pierre Glaudes**

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

# Grading

Once the visits for the 2012-2013 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).
This score (A+, A, B, C) concerned each of the six criteria defined by the AERES.
NN (not-scored) attached to a criteria indicate that this one was not applicable to the particular case of this research unit or this team.

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

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

- Grading table of the unit: Neuroscience Paris Seine - IBPS-Neuroscience

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

- Grading table of the team: Genetics of autism

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

- Grading table of the team: Neuronal Signaling and Gene Regulation

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

- Grading table of the team: Cortical Networks and Neurovascular Coupling

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

- Grading table of the team: Glial Plasticity

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

- Grading table of the team: Normal and pathologic glutamatergic systems

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

- Grading table of the team: Neurophysiology and behavior

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

- Grading table of the team: Pathophysiology of Psychiatric Disorders

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

- Grading table of the team: Development and degeneration of spinal motor neuron

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

- Grading table of the team: Neuronal Networks and Physiological Rhythms

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

- Grading table of the team: Development of the spinal cord organization

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

- Grading table of the team: Neuroplasticity of Reproductive Behaviors

| C1 | C2 | C3 | C4 | C5 | C6 |
|---|---|---|---|---|---|
| NN | A | NN | A | A | B |

- Grading table of the team: Axonal Growth and Regeneration

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

- Grading table of the team: Navigation, Memory and Aging

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

- Grading table of the team: Development and Plasticity of Neural Networks

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

- Grading table of the team: Gene Regulation and Adaptive Behaviors

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

# Evaluation report

| | |
|---|---|
| Unit name: | Neuroscience Paris Seine - IBPS-Neuroscience |
| Unit acronym: | IBPS-Neuroscience |
| Label requested: | CNRS INSERM UPMC |
| Present no.: | Creation |
| Name of Director (2012-2013): | Creation |
| Name of Project Leader (2014-2018): | Mr Hervé CHNEIWEISS |

# Expert committee members

| | |
|---|---|
| Chair: | Mr Jean-Philippe PIN, Université de Montpellier |
| Experts: | Mr Serge AHMED, Université Victor Segalen Bordeaux 2 |
| | Ms Julie BAKKER, Liège, Belgique |
| | Mr Yuri BOZZI, University of Trento, Italy |
| | Mr Andrew COPP, London, Great-Britain |
| | Ms Britta EICKHOLT, Berlin, Germany |
| | Mr Eckart GUNDELFINGER, Magdeburg, Germany |
| | Mr Yann HUMEAU, Université Bordeaux 2 |
| | Mr Jose NARANJO, Madrid, Spain |
| | Mr Yoland SMITH, Atlanta, USA |
| | Mr Enrico TONGIORGI, Università di Trieste, Italy |
| | Ms Joëlle CHABRY, Valbonne (representative of INSERM CSS) |
| | Ms Stefania MACCARI, Villeneuve d'Ascq (representative of CoNRS) |
| | Mr Marc SAVASTA, Grenoble (representative of CNU) |

## Scientific delegate representing the AERES:

Mr Patrick BLADER

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

Mr Bertrand MEYER, UPMC

Mr Bernard POULAIN, INSB/CNRS

Ms Anne ROCHAT, INSERM

# 1 • Introduction

## History and geographical location of the unit

The research unit "Neuroscience Paris Seine – IBPS Neuroscience" is part of the research federation "Institute of Biology Paris Seine", located in the Cassan building, Quai St Bernard, in the UPMC main campus (2700m$^2$ available, half already renovated). It is then part of a large neuroscience campus in the center of Paris, that includes the "Institut du Cerveau et de la Moëlle" (ICM), the "Institut de la Vision", the "Institut du Fer à Moulin", the "Collège de France" and the "Institut de Biologie de l'ENS" (IBENS), all at walking distance from each other.

IBPS Neuroscience originates from a complete reorganization of biological research present within the main UPMC campus. This reorganization led to the creation of 5 departments associated with a common high tech facility platform (imaging, proteomic, genomics,…). For the next period, each department will constitute an independent research unit, one on these being "IBPS Neuroscience"; they will be all together associated in a large federation.

IBPS Neuroscience will bring together 15 research teams originating from two local CNRS/INSERM/UPMC units: "Physiopathology of Central Nervous System Disorders" and "Neurobiology of Adaptative processes", with the addition of one team coming from the University Paris Descartes (Centre for Psychiatry and Neuroscience). This new unit will be created by merging different research teams addressing fundamental questions in neurophysiology that are aimed at providing key information of the normal and pathological brain by applying a wide range of approaches from molecular, to cellular, behavioral and pre-clinical level.

Among the 15 proposed teams, 5 result from the fusion of pre-existing teams (E7, E10, E11, E14, E15), while 3 are emerging teams (E1, E8, E11). All teams worked already according to the future organization of the unit at the time of the site visit, illustrating the coherence of the ensemble, as well as the numerous interactions already established among them, demonstrating the added value of this new organization. Prior to the site visit, the organization has been validated by the scientific advisory board of the IBPS Paris-Seine federation of units.

## Management team

The IBPS Neuroscience is constituted of fully independent research teams. The unit management team is composed of the director, a main secretary assistant, a board of team leaders and an Institute council. Advise will be obtained from an external Scientific Advisory board common to the IBPS federation.

The Director is responsible for taking the main decisions regarding the organization, and strategic orientation of the research unit. He also represents the Institute locally, within the University, as well as nationally at the CNRS and INSERM, and internationally.

The board of group leaders headed by the director, takes the main decisions regarding scientific programs and organization, and discuss the strategic and scientific orientations of the institute. It meets monthly.

The Institute Council is composed of elected and nominated personnel representing the various categories (researchers, technicians and engineers, students and post-docs) and is involved in installing and executing the rules established by the UMPC, INSERM and the CNRS. It is headed by the director. During the Institute council meetings (3 a year) the main organization points are discussed and validated.

The administrative management is supported by an administrative staff of 6 persons including a general secretary.

A Health and Security Committee is in charge of the establishement and application of the health and security rules within the unit

The internal rule book, to be finalized and accepted by all units of the IBPS federation, will have to be finalized before the end of 2013.

The proposed director of the unit, Dr Hervé CHNEIWEISS, has been leading his own research team for many years, first at the Collège de France, and for the last period at the Centre for Psychiatry and Neuroscience within the Ste Anne hospital. He is trained as a medical doctor in neurology. He is still acting as a neurologist, in a service of neuro-oncology.

Although his actual laboratory is not yet located at UPMC (being at the university Paris Descartes), Dr Chneiweiss demonstrated a perfect view of the scientific development ongoing within the 15 research teams included in this project. He participated in the discussions that have occurred since 2010 and that led to the present proposal for the structural organization of biological research at UPMC. His leadership is well recognized by all scientists, researchers and technicians being part of this proposal, as demonstrated by his internal election as the future director of this unit. His previous experiences in leading research, his strong involvement in translational medicine, and his medical practice as a neuro-oncologist, makes him an excellent candidate to lead this unit and to bring it to the best level, integrating the technological know how and the basic neurophysiological concepts being studied towards a more translational direction.

## AERES nomenclature

SVE1 Biology, health - LS5 Neurobiology

## 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 | 22 | 23 | 21 |
| **N2:** Permanent researchers from Institutions and similar positions | 32 | 36 | 30 |
| **N3:** Other permanent staff (without research duties) | 1 | 1 | 0 |
| **N4:** Other professors (Emeritus Professor, on-contract Professor, etc.) | 2 | 0 | 2 |
| **N5:** Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.) | 22 | 19 | 17 |
| **N6:** Other contractual staff (without research duties) | 0 | 0 | 0 |
| **TOTAL N1 to N6** | 79 | 79 | 70 |

| Percentage of producers | ***88.61 %*** |
|---|---|

| Unit workforce | Number as at 30/06/2012 | Number as at 01/01/2014 |
|---|---|---|
| Doctoral students | 54 | |
| Theses defended | 54 | |
| Postdoctoral students having spent at least 12 months in the unit* | 30 | |
| Number of Research Supervisor Qualifications (HDR) taken | 9 | |
| Qualified research supervisors (with an HDR) or similar positions | 32 | 39 |

# 2 • Assessment of the unit

## Strengths and opportunities

IBPS Neuroscience is located in close proximity to many other Neuroscience institutes, with complementary expertise and aims, in the center of Paris. The IBPS Neuroscience regroups very good to excellent research teams in basic neurophysiology, with programs oriented towards understanding the bases for neurological and psychiatric diseases. Overall, scientists at IBPS Neuroscience have demonstrated their abilities to conduct outstanding research at the molecular, cellular, system and behavioral levels, with some well established connections with the clinic. Cutting edge technologies have been set up, that include the use of optogenetic tools in living animals, proteomic analyses, ultrasound microscopy, innovative mouse genetic approaches, the use of viruses in *in vivo* studies, innovative behavioral analyses and tools. These constitute a well balanced combination of expertise. In addition, IBPS scientists have access to a number of facilities organized as platfoms shared by the different units of the IBPS federation, and headed by one team leader of IBPS neuroscience. As such, all teams will have access to cutting edge techniques and know how offering them an exellent environment to conduct science at a highly competitive level.

The research teams, although coming from three distinct units, have already established strong collaborations between themselves, creating an excellent scientific atmosphere that will be essential to maintain, and promote scientific quality, and also to allow technology transfer between the teams. Many of the research teams are part of the labex PsyBiol, or the IHU Pep-Psy, offering the IBPS neuroscience a number of possibilities to further develop translational programs, with a better connection to the clinic. A number of national and international collaborations have been established with outstanding laboratories, again reinforcing the attractiveness of the unit.

IBPS Neuroscience is well integrated within the university, being located on the main campus, in close contact with the students. More than one third of the scientific staff is composed of either professors or assistant professors, with important teaching responsabilities, including the head of the Neuroscience PhD program of UPMC. Although affecting the time dedicated to research, such a strong involvement in teaching duties offers the entire unit the ability to attract the best students from this internationally recognized university. This attractiveness is well illustrated by the large number of graduate students (50 at the time of the visit, 91 in total over the past evaluation period), not only coming from Paris, but also from abroad (30%).

The staff scientists, engineers and technicians are well motivated, with a real enthusiasm in being more involved in the construction of this unit. They represent a critical mass to conduct the proposed project. The staff is well balanced between leader scientists, professors, and young assistant professors and researchers, a number of them have been recruited recently, thereby offering good opportunities for the future.

IBPS Neuroscience is unique among all neuroscience units in France in being active in the history of neuroscience and epistemology. Such an important research activity certainly offers the members of the unit a unique opportunity to have a better view and analysis of neuroscience research and its impact on our society. This will have important beneficial consequences on how their research will be conducted in the future.

In conclusion, IBPS neuroscience has a number of opportunities to reach outstanding goals in basic to translational neurophysiology, being part of the excellent Paris neuroscience community, offering a good combination of know how and cutting edge technologies, being deeply involved in training students at every university level, and offering scientists an excellent atmosphere to conduct research. Its involvement in translational and clinical studies will certainly grow thanks to the connection to the labex BiolPsy and Pep-Psy IHU. Together, these represent excellent opportunities for IBPS neuroscience to attract young and motivated scientists at any level of their career.

## Weaknesses and threats

IBPS neuroscience is located in an old building within the UPMC campus that is currently being renovated. The ongoing work will certainly continue over the next few years, creating a number of problems to conduct research, especially given the apparent lack of information given to each individual research team affected. It was reported that renovation work led frequently to loss of electrical power, that it caused dust and significant noise disturbances, which resulted in an increased difficulty to organize and conduct research over several days. This problem appears to be particularly pertinent for those teams involved in organising behavioral studies.

The space limitation, and the ongoing renovation will prevent the IBPS Neuroscience from attracting new groups within the next few years.

Many of the research programs are based on the use of animals, and the actual animal facilities located on the roof of the building will have to be removed for legal reasons. Although two alternatives have been proposed, none of them are satisfactory. The first proposal is to use a new animal facility located at Charles-Foix Hospital, 7 kms away. Although such a facility may be used to maintain mouse lines, it will not be possible to use it for day to day experiments, since the laboratory equipment is located at the UPMC campus. The second alternative is the construction of a new but temporary animal facility on the campus. However, although funding for the construction has been obtained, these do not extend to cover equipment and personnel, bringing the future research programs of the IBPS neuroscience in a rather delicate situation.

The budget of the unit raised on external grants remains low, in regard to the quality of the science being done at the institute. External fundings is heterogenous among the teams, with a few groups being well funded, while others having almost no external funds guaranteed for the next years such that their projects are in danger. In particular funding from European Resources is not overwhelming.

Although a few teams have gained an international reputation, as illustrated by two groups having a position at McGill University, Montreal, and another one leading an international consortium on a specific brain disease, the overall international visibility can be improved. Only few international meetings have been organized by members of the unit, and there have been only few invitations to prestigious international meetings, participation to international board meetings, or members of the editorial board of well recognized journals in the field. Attractivity of foreign students and post-docs is good (30% of the graduate students and 40% of the post-doctoral fellows are foreigners).

Most teams demonstrate good to oustanding scientific productivity, although there is still a significant proportion of researchers (2 out of 36) with a lower output.

The engineer, technical and administrative staff appears to be adequate, albeit on the low side (some groups have very little technical support). However, the absence of any personnel in charge of informatics (network, storage, computer maintenance) limits any possible development of this aspect. This certainly puts in danger the large amount of information including images and video that need to be securely saved and processed, and limits the development of a better visibility of the Institute through the web.

## Recommendations

The quality of the scientific production may be improved in some teams, and care must be taken to stimulate everyone to be actively involved in research programs, such that the percentage of "producing" scientists is increased. Projects must be lifted to the best level by integrating all expertise found in the unit and the associated platforms, offering ways to improve the quality of the publications, even though the number of publications might decrease.

Most research teams have already established strong collaborations within the unit, but these might be improved by taking advantage of the multidisciplinary expertises of the different members within the unit and the number of technologies available within the unit and the different platforms. Further application of multidisciplinary approaches in individual research projects will certainly be fruitful in the near future, to reach high impact publications, and to help raise external funding, in particularly from European sources.

A number of novel and cutting edge techniques are being developed. Such constant activity in technology development has to be maintained, and may be improved by embracing currently less explored approches such as genomics, epigenetics, *in vivo* imaging technologies, as already illustrated by some groups.

The external support to the unit must be improved. A number of teams have low external support, and overall, few ANR grants have been obtained. Improving the quality of the publications, and taking advantage of the multidisciplinary approaches will certainly improve the quality of the projects, increasing the success rate in grant applications to the ANR and ERC. Networks with other European countries should be reinforced, offering possiblities to participate in EU programs.

The above recommendations should also help improve the international visibility of the unit, but this must be associated with more international actions such as organization of symposia, organization of international meetings, conferences and schools. International attractiveness may benefit from such actions, especially if associated with the use of English for most communication within the unit.

Some efforts are being made to connect the unit to the pharmacological and biotechnical world. This can be improved possibly through a better connection to the valorisation services, including the local SATT (Société d'Accélération de Transfert de Technologies) in order to stimulate more researchers to protect their findings. This should also open new possiblities to the graduate students and post-docs for their future career by stimulating them to work in pharmaceutical industry or biotech companies, or even to create their own company.

The internal management should be improved with i) dedicated roles of the management staff and common services, ii) a clarification of the budget allocation to the common expenses and teams, iii) a better information and involvement of the personnel regarding the scientific strategy and decisions and iv) clarification of the conditions for the creation of novel and/or emerging teams, and on the strategy to be used to attract new team leaders.

The organisation of the administrative staff, as well as the personnel working in the common services, will have to be defined. Such an organisation will have to be carefully planned within the year 2013. The management of the Security and Health, Genetically Modified Organisms and use of chemicals will also have to be organized properly, especially because people in charge of these different aspects of the laboratory security are coming from two different laboratories, with possibly different practice. The name of the person in charge of these responsibilities will have to be defined, advertised to every one, and clearly indicated in the organizational chart of the unit.

# 3 • Detailed assessments

## Assessment of scientific quality and outputs

The science performed by the teams that will compose IBPS Neuroscience is well concentrated on the understanding the basics of neurophysiology, well oriented towards neurological and psychiatric disorders. The research carried out covers many aspects from the molecule to behavior, via cellular and neuronal networks studies. It covers a combination of multidisciplinary approaches. This makes IBPS Neuroscience quite unique among the neuroscience Institutes in the center of Paris, with some overlaps with the Fer à Moulin Institute, but quite different from the clinically oriented ICM, the Institut de la vision, or the IBENS mostly dedicated to pure basic science at the molecular and developmental level.

The scientific output of the unit is very good to excellent, with about 400 publications in international journals, mostly within the best journals of the field (such as Journal of Neuroscience and Biological Psychiatry), and a few in top journals (2 Science, 1 Nature, 4 Nature Neuroscience, 1 Nat Rev Neurosci, 1 Nat Genetics, 3 Mol Psy, 6 PNAS led (first or last author) by the members of the different research teams with the unit, and more when considering collaborative publications led by other laboratories).

Among the major findings of the unit, one can mention: 1) the identification of new genes, such as shank2&3 and neurexin1 involved in autism; 2) the identification of the role of vGluT3, a vesicular glutamate transporter found in cholinergic, serotoninergic and GABA ergic neurons, where it fullfils two functions, the increased concentration of the neurotransmitter in the vesicles, and the ability of the neurons to co-release glutamate with its transmitter; 3) the role of alpha4 subunits of the nicotinic receptors in the reinforcing effect of nicotine; 4) the low-affinity transporter OCT2 plays an important role in mood related behaviors such as anxiety and the response to stress; 5) the GTPase atlastin, involved in early-onset hereditary spastic paraplegia (HSP), controls spinal motor axon architecture by inhibiting the BMP pathway; 6) demonstration of the importance of the brain androgen receptor in activating male sexual behavior in the mouse; 7) the important role of the cerebellum in the building of the body representation in space; 8) glucocorticoid receptors in dopaminoceptive neurons facilitates cocaine seeking and are responsible for social aversion induced by chronic stress. Such findings nicely illustrate the capacity of the IBPS neuroscience research groups to conduct outstanding programs at the genetic, molecular, cellular and more integrated levels, thereby offering an ideal environment to conduct integrated projects from the molecular to the behavioral level.

Research conducted at IBPS Neuroscience is based on a large panel of techniques, many groups use up to date electrophysiological set ups, with patch clamp recordings and cell imaging associated with the use of transgenic animals and viral infection to manipulate gene expression. Novel in vivo imaging based on ultrasound measurements very recently developed will be implemented by a young researcher who just joined the Institute. Three groups have been implementing optogenetic approches, even in vivo, in living animals, and a very talented chemo-biologist recently recruited will bring very innovative tools based on the development of light-activated receptors that he developed during his post-doc. A micro-patterning technique has been developped (nano-enableTM system) to study axonal growth. Other technologies being used include up to date genetic approaches based on genome wide sequencing, innovative mouse genetic approaches, and epigenetic analyses based on ChIPseq technologies. Two groups also affiliated at McGill University in Montreal bring along important tools, such as access to a human brain library, which, associated with collaborations initiated with clinicians, will allow better connections between clinical studies and analyses of human samples.

## Assessment of the unit's academic reputation and appeal

The national reputation of the various teams that compose IBPS Neuroscience is very good, with many collaborations established in France. Two third of the already existing teams (not taking into account the newly created ones) belong to the Ecole des Neuroscience de Paris (E2, E4, E5, E6, E13, E14, E15), and to the Labex “BioPsy” (E2, E5, E6, E7, E13, E14, E15), while a few are part of the IHU “PEP-Psy”. This quality is also illustrated by the relatively good level of funding coming from national grant agencies reaching 1.1M€ in 2012. Many team leaders are also involved in national Scientific councils, such as those of the CNRS-INSB, the CoNRS sections in neuroscience, the INSERM section of Neuroscience, the FRM, the AERES, the CNU sections in neuroscience, cell biology and physiology (E2, 3, 4, 8, 9, 10, 13, 14 & 15).

The scientific quality of the research teams that compose the IBPS Neuroscience is very well perceived at the international level. About half of the teams’ research papers are cited more than 200 times a year (E01-E05, E07, E15) with some being cited 550 to 700 times a year (E01, E07 and E15). This good international visibity is also confirmed by invitations of staff scientists from most teams to present their research at international meetings (with a mean of 5

invitations per team over the period, up to 15 for the best, though very few in outstanding conferences such as Gordon conferences). A number of long term effective collaborations with foreign laboratories are well established, with McGill (Montreal, Canada) British Columbia (Vancouver, USA), Cardiff (UK) Universities, as the best examples, but other more recent and granted collaborations have been established with Yale University, (USA), Brazil and Belgium. Several members are also members of editorial boards of international journals, most in good journals in the field (Frontiers series). Teams leaders are also involved in international organizations such as the executive committee of the European College of Neuropsychoparmacology, the Autism Genome Project International consortium, and the future director is a member of the Brazilian Academy of Sciences. A couple of high profil review articles have been prepared upon invitation (Nat Rev Neurosci, TINS, …), and team leaders have been involved in organizing a number of international meetings (2 in France and 3 abroad) and 8 symposia in international meetings. Aside from an ITN consortium leaded by the future director, and a young HFSP grant, no other international grants (FP7, ERC, HFSP) have been obtained.

The IBPS Neuroscience has been able to attract young and promising scientists who get positions at the CNRS, INSERM or UMPC. As noted above, some of them bring state of the art technologies that will certainly benefit to many teams in the Institute.

IBPS Neuroscience has also been able to attract a number of foreign graduate students (31 out of 91), post-docs (19 out of 45), as well as professors (6 in total) from various countries, including Brazil, Italy, Lebanon, Ireland, Russia, and Spain.

IBPS Neuroscience scientists received a number of prices including Chevalier de la Légion d'Honeur (2), Bronze medal from the CNRS (2) and the prestigious Award of the European College of Neuropsychopharmacology (in 2009).

Two scientists are also in the board of the French Society for Neuroscience.

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

The staff scientists of IBPS Neuroscience are deeply involved in public communication, with several researchers being involved in the organization of the DANA Alliance "Brain awareness week" in Paris over the last few years, and others even participated in such events outside of Paris. Four leaders had a good media visibility with interviews on radio and TV on topics like ethical issues in neuroscience, memory and space orientation, addiction, virtual reality as a new diagnostic tool for Alzheimer's patients. A strong involvement of the future director in ethical (member of the INSERM Ethic committee) and scientific political issues (member of the advisory board for science and technology choices to the French Parliament and Senate) has to be noted.

The unit is also unique in its investment in the history of neurosciences and epistemology, with a research group attached to the direction.

The connection with the industry is good, with a few collaborative contracts (6 in total, with companies including Sanofi, Servier, P Fabre, Quantum GÈnotype), 6 patents, and 2 licences. A project for creating a company is on the way, with discussion already well engaged with INSERM transfer.

Six groups have established interactions with clinicians for genetic studies, programs on neurodegenerative disorders (Huntington, Alzheimer), and in Neuro-oncology. This is expected to be increased within the next years due to a number of new programs being initiated through the Labex BiolPsy and the IHU Pep-Psy.

## Assessment of the unit's organisation and life

It must be mentioned here that IBPS Neuroscience will be a new unit created in January 2014, and as such does not officially exist yet. Accordingly, the evaluation of the unit's organization and life can only be analyzed based on what has already been set up and organized, but it is clear that the final details of the organization will be prepared the year before the creation of the unit.

The scientific organization of the unit has been well planned, and validated by an external scientifc board common to all units of the IBPS federation. It is organized around 3 main areas: 1) Neural development, plasticity and regeneration; 2) Dynamics of neuronal networks and cognitive processes, and 3) Cellular and molecular basis of neuroadaptation, each covering both studies of neurological and psychiatirc disorders. Such an organization is not intended to separate the unit into three independent "laboratories", but rather to give a better visibility to the research projects being covered within the unit. Of note, these research topics mix teams coming from the two main original units. As a good demonstration of the overall scientific exchanges between every team of the unit is the number of common publications (16) and ongoing collaborations between teams from different areas.

The general organization of the Institute has been set up over the last years, and was very well received by the committee. The committee very much appreciated the very good spirit and friendly atmosphere within the entire unit. The IPBS neuroscience is composed of i) independent research teams (on average around 10 people per team) that decide on their scientific programs and are responsible for obtaining funds to conduct their research, ii) common facilities and iii) an administratif staff. The management is organized around three main boards, i) the board of group leaders where the main scientific decisions are discussed, ii) the Institute council composed of representatives of all the categories of personnel where the internal organization and problems are discussed, and iii) a health and safety committee. An external scientific advisory board, common to the IBPS federation of units, has been invited to prepare the new organization of the unit, and will be invited to evaluate the teams' activity at mid term of the next period, and to give advice regarding the recruitment of new teams.

The scientific life at IBPS Neuroscience is based on regular "data" meetings, internal and external seminars. Meetings are organized every week within each team.

The discussion with the staff scientists and the engineers, technician and administrative personnel confirmed the very good atmosphere within the unit, and their enthusiasm in participating in the creation of this new unit. The engineers and technicians are very positive regarding their involvement in the scientific projects, their work being well recognized in the publications (co-authorship) and in the participation to meetings despite the difficulties due to budget constraints. Although, as described below, a number of points were raised, the committee appreciated their demand to be more involved in a better organisation of the unit through the creation, for example, of specific small committees in charge of specific questions. These discussions revealed a number of points that will need to be taken into acount in the near future, with more transparency and an increased vertical flow of information. Among the issues raised are i) a better clarity of the future management with the organization of the administration and common services, ii) some information regarding the use and sharing of the internal budget, both recurrent and grant budgets, iii) more information regarding the strategy to recruit new teams, researchers and professors, iv) more information regarding the scheduling and organization of the refurbishment of the building, and especially the animal facility, and iv) the lack of personnel dedicated to informatics and the web. More space for social interactions (cafeteria), and scientific meetings (larger seminar room) would be much appreciated. The staff scientists also insist on the creation of a new web site for the Institute, and a rapid finalization of the internal rule book. They all expressed their difficulty regarding the lack of information on the refurbishment of the building and the problem with the animal facility.

The discussion with the post-docs and graduate students revealed a very good atmosphere within the unit, and most of them were positive about the quality of their supervision and the access to state-of-the-art technlogies. They appreciate the recently established data meetings, and all have the possibilty to attend national or international meetings. The committee noticed some important points regarding the graduate students, although these concerned mostly the Graduate school: a demand for an external scientific advisor and the requirement that every student receive a salary up to the thesis defense. One potential problem is that most of the data meetings are being held in French whereas a good proportion of the PhD students and postdocs are foreigners. This does not stimulate interaction. A decision should be made that all data meetings are going to be held in English.

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

Being located within the UPMC campus, and with 40% of the staff scientists being professors or assistant professors, IBPS Neuroscience is deeply involved in teaching. Professors from IBPS neuroscience also have strong responsabilities in the neuroscience teaching organization at UMPC: Director of the faculty of biology, Director of the PhD Program "Cerveau, Comportement, Cognition", Director of studies of the Master of Integrative Biology and Physiology (BIP), Director of the Neuroscience Program of the Master BIP.

A large number of graduate students are being trained within the IBPS Neuroscience teams (91 over the period, with 30% coming from abroad). Thanks to a connection with Brazil established by the future director, IBPS Neuroscience has been able to attract 4 students from this country. Every student get their PhD degree in 3-4 years, and most continue in research as post-doctoral fellows, mainly abroad. Among the former graduate students, 15 have secured a position, 8 in france (4 in academic institutions, and 4 in private companies) and 7 abroad (4 in academic institutions, and 3 in private companies, most of the others being still in science as post-doctoral fellows abroad. This represents a good success regarding the current possibilities of positions in France.

Relatively few post-doctoral fellows were hired during the period (25, which represent a means, over 5 years, of about one post-doc a year per team). This is consistent with the level of external fundings raised by IBPS Neuroscience.

## Assessment of the five-year plan and strategy

The overall research plan for the future is of excellent quality for most teams, as detailled below, with many interactions between the teams within the future unit, as well as with other teams of the IBPS, making use of the common facilities. The unit will make use of a combination of state of the art new technologies, from new optogenetic tools, to innovative behavioral studies and mouse genetics, through up to date electrophysiological studies and imaging technologies. The research programs will cover studies in basic neuroscience and is organized into two vertical axis: 1- Pathophysiology of Psychiatric Disorders, and 2- Pathophysiology of Neurological Disorders, each part of three horizontal axes: 1- Neural development, plasticity and regeneration, 2- Dynamics of neuronal networks and cognitive processes, 3- Cellular and Molecular basis of neuroadaptation. This general scientific organization helps to clarify the main topics that will be studied, will favor interactions between teams, and is organized in such a way that this will not split the institute into independent sub-units.

This is very positive, and reflects major efforts made during the preparation period, in relation to the creation of IBPS and the different Institutes that will compose this site. However, the general strategy of the IPBS Neuroscience could well be improved to increase the attractiveness, and orient the teams towards more challenging projects that may include more integrated programs based on systematic analyses, including “-omics” approaches. The bases for such programs are there and could well be reinforced. We encourage the director, together with the team leaders to go forward, and define major strategic research areas of expertise, with more ambition to gain higher international visibility, and attractiveness. This will also be critical to help team leaders to raise more funds, not only from France, but also from Europe since the potential is there. A general internal policy regarding the creation of new or emerging teams, as well as the opening of new space to attract new team leaders with specific scientific expertise that will reinforce the ensemble, has to be established. The committee is aware that such a strategic plan has been limited due to the actual difficulties regarding the renovation of the building, and the problem with the animal facility. But the sooner these reflections are engaged, the better it will be, especially in creating hope and enthusiasm among the staff scientists.

# 4 • Team-by-team analysis

**Team 1 :** Genetics of autism

Name of team leader: Ms Catalina BETANCUR

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

| 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 (post-MD) | |
| 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

Team E1 is actively involved in investigating the genetics of autism, which represents an emerging field in neuropsychiatric research. Recent work contributed to the discovery of new autism-associated mutations (e.g. SHANK3), and to defining autism as a highly heterogeneous neurodevelopmental disorder involving synaptic dysfunction. The team had excellent scientific output as it published 44 papers since 2007, including a relevant number of studies in high impact journals (e.g. 3 Nature, 2 Nature Genetics, 2 Biol. Psychiatry, 1 PNAS) and had a high scientific impact in the international scientific community.

## Assessment of the team's academic reputation and appeal

The E1 team leader has an excellent international reputation. She has been actively involved in management of the Paris Autism Research International Study (PARIS) and the Autism Genome Project (AGP; an international network devoted to the discovery of autism-related genes). As shown by her last authorship in a Nature paper published by the AGP in 2010, the team leader has a prominent role in this network. She also participated to the set-up of a next generation sequencing facility at the Hopital Henry Mondor in Creteil, that will be instrumental for her team's future work. The high reputation and quality of her research work on autism has been acknowledged by an important NARSAD 2010-2012 grant, her membership in the editorial board of the journal Molecular Autism, 10 presentations at international conferences and the organization of the 2013 meeting "Wiring the brain" at Cold Spring Harbor Laboratory (US). In 2012, the team leader has been invited as a Faculty member of the Neuroscience School "Neurobiology of Autism Spectrum Disorders" (Italy).

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

The interaction of Team E1 leader with the social, economic and cultural environment has been characterized by the active participation to the life of autism patients associations (including the Phelan-McDermid Syndrome Association), as well as intensive appearance on different media (TV, newspapers). No patents/start up activities arose from her research so far. This is a very good activity.

## Assessment of the team's organisation and life

Team 1 has a very limited number of members (2 PhD students flanking the Team Leader, no postdocs). However, its organization and life is solid; the work is carried out through collaborations, both external and internal at IBPS-Neuroscience.

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

Despite her long-standing academic activity (>10 years), the team leader has a relatively limited research training experience (4 master students, 3 PhD students, 2 technicians, 2 psychologists), that clearly reflects the small size of her research group through these years. Technical training of graduate students is mainly achieved through collaboration, with limited chance that the knowledge remains within the team. University teaching (lecture courses) is not documented. Team E1 did not show attractiveness for foreign postdocs; her documented training activity is limited to few French PhD students during several years of activity.

## Assessment of the five-year plan and strategy

The five-year research plan proposed by Team E1 is well conceived and logically stems from the previous, solid results obtained by the team. From extensive and up-to-date genetic studies (including CNV and exome sequencing studies) on large and well-characterized collections of patients and controls, the proposed research aims at identifying and subsequently characterizing novel autism-associated genes. The proposed experimental strategy is multidisciplinary and is based (especially for the functional characterization of novel autism genes) on collaborations (already ongoing) with other IBPS-Neuroscience groups. The five-year strategy by Team E1 is essentially proposed as a basic research approach (i.e. identification and functional characterization of autism-associated genes). The potential impact of these studies on applied research (i.e., development of novel therapeutic strategies for autism) is not immediate nor easily foreseeable, and will mostly depend on the type of identified genes, and the quality/level of their functional characterization that the Team will be able to achieve in these five years, but overall this was judge as very good to excellent.

## Conclusion

- Strengths and opportunities:

Major strengths of the group are the excellent and internationally competitive CV of the team leader, and her excellent background in autism research. Another strength is the solid and up-to-date five year scientific plan.

- Weaknesses and threats:

The small size of the group and the absence of experienced postdocs in the team are seen as weaknesses and threats for the future development of the group. Other potential threats are the limited availability of funding, as well as serious problems with infrastructure (small lab size, ongoing renovation of the building, insufficient animal house). The very limited experience in academic teaching by the Team leader is also seen as a weakness, potentially reducing attractiveness of the group. Another potential threat is represented by the limited experience in technologies for functional validation studies (Team 1 is essentially a molecular genetics group). Last, but not least, high competitiveness of the autism research field is also seen as a serious threat for the team.

- Recommendations:

Team E1 research strategy is clear, and presents logical and consistent scientific objectives. The overall judgement of the proposed “emerging team” E1 is clearly positive, but some implementation is needed to ensure the accomplishement of all the proposed middle- and long-term goals. Specifically, the committee recommends (in order of importance): i) to increase and differentiate as much as possible the funding requests at European and international level; ii) to increase the size of the group, making efforts to recruit experienced postdocs; iii) to increase visibility at the University level, e.g. giving lecture courses (this will allow to attract students in the lab); iv) to keep very tight and continuous collaborations inside IBPS-Neuroscience, so to increase the feasibility of the in vitro/in vivo functional validation studies; v) introduce novel techniques for in vitro/in vivo functional validation studies.

# 4 • Team-by-team analysis

**Team 2 :** Neuronal Signaling and Gene Regulation

Name of team leader: Ms Jocelyne CABOCHE and Mr Peter VANHOUTTE

## 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) | | | |
| **N4**: Other professors (PREM, ECC, etc.) | | | |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | 1 | | 1 |
| **N6**: Other contractual staff (without research duties) | | | |
| **TOTAL N1 to N6** | 5 | 4 | 5 |

| Team workforce | Number as at 30/06/2012 | Number as at 01/01/2014 |
|---|---|---|
| Doctoral students | 8 | |
| Theses defended | 5 | |
| 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 | 2 | 2 |

# • Detailed assessments

## Assessment of scientific quality and outputs

Team E2's research program aims at deciphering the intracellular cascades that govern cerebral plasticity and long-term behavioral alterations resulting in drug addiction and neurodegenerative disorders (i.e. Huntington disease model). Over the past 5-year period, the team mainly focused on striatal neurons that control movement execution, reward-dependent learning and cognition. The team is a pioneer in the characterization of the role of kinase activation-dependent signaling pathways in gene transcription, neuronal plasticity and cerebral functions. As a significant and original result, they described close relationships between dopamine and glutamate receptors, which trigger Erk-dependent intracellular signaling pathway activation leading to behavioral responses. Techniques used and scientific approaches are broad, complementary and highly relevant ranging from genomic studies, cellular and behavioral characterizations. The whole work carried out by members of Team E2 is coherent, valuable, and of excellent quality, and has lead to significant outputs in terms of publication and valorization (2 patents). Altogether 27 peer-reviewed manuscripts were published *plus* an additional 10 peer-reviewed papers published by members of the team in collaboration with authors outside of the team. Papers have been consistently produced over the past 5-year with very good to excellent impact factors, including Biol Psychiatry (2), Mol Psychiatry (1), J Neurosci (3), Hum Mol Genet(1), FASEB J(1).

## Assessment of the team's academic reputation and appeal

Team 2 has definitely gained an excellent international reputation for work on intracellular cascades occurring in addictive and neurodegenerative disorders. This is underscored by an increasing number of citations and numerous invitations in national and international conferences (10 in total) including the prestigious Gordon Research Conferences. One of the team leaders was a member of organizing comitees and chairwoman of two international conferences. Remarkably, Team 2's leaders have established internal and international high quality and effective collaborations including with laboratories in Canada, Spain, Switzerland, Italy and USA, showing that work led by this team establish the reference in the field. Moreover, Team 2 members participate in a significant number of scientific boards and executive committees (6 in total) and networks including the "Bio-psy" Labex. Finally, one of the team leaders was scientific advisor of the AERES from 2008 to 2010 and recipient of the CNRS Award for Scientific Excellence (PES).

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

Over the past 5 years, the team has filed 2 patents. Both team leaders are scientific advisors of a biotech company in the context of the valorization of one of their own patent illustrating an excellent connection with industrial application of their work. An excellent connection with clinician and patient organizations has been established.

## Assessment of the team's organisation and life

Overall, the governance is excellent and efficient. The team will be co-directed in the next 5-years by two well recognized scientists, both experienced team leaders who have studied for several years intracellular signaling pathways and subsequent transcription regulations in neuronal cells in physio-pathological situations. The allocation of human and financial resources between the two research areas namely "neurodegeneration" and "addiction" is balanced. Likewise, members of the team exhibit excellent complementarity, that is required for both projects. One can suppose that the co-direction has every chance of success since both researchers have already co-led the "Signalisation intracellulaire et Neuroadaptations" research group (UMR INSERM 952 CNRS 7224) since 2010. The position of one team member has been recently stabilized, as an Assistant Professor, thanks to the recent award of a Chair of Excellence. The team composition is well balanced between experimented senior researchers (2), junior researchers (2) i.e. assistant professors, technicians (2) all having permanent positions and post-docs (3) and Ph.D students (5).

Research grants have been successfully obtained throughout the previous 5 years; however, the major ones will end by the end of 2013. Given the excellent publication record of the team, further grant successes can reasonably be expected soon.

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

Senior researchers of team 2 currently train 4 PhD students. Five students have defended their Ph.D. thesis over the last five-year period. Several members of the team 2 are involved in training courses in a permanent or occasional manner. Team leaders participate in master classes, in the jury of thesis vivas and hold academic responsibilities, further illustrating the very good training activity of the team.

## Assessment of the five-year plan and strategy

The proposed studies aim at further characterizing the molecular and cellular mechanisms underlying the plasticity of striatal neurons induced by pathological dysfunctions or drug abuse. Elegant and relevant approaches, set up through collaborative works or by the team itself, will be implemented in order to characterize molecular events involved in neuronal plasticity. The proposed project is based on the preliminary works of the previous years, and incorporates new and sophisticated techniques such as a three-dimensional automated morphometric analysis. To achieve their goals, a nice combination of techniques and skills are currently set up ranging from *in silico to in vivo* experiments. Although the field is highly competitive, the five-year project is ambitious and well designed and should lead to significant advancement of basic knowledge as well as high impact factor publications and development of patentable molecular tools.

## Conclusion

- Strengths and opportunities:

In summary, major strengths of the team 2 include: i) number and quality of publications ii) achievements with high patentable potential, iii) excellent ability to raise funds, in the past, iv) supervision PhD students, strongly oriented towards publications and autonomy, v) complementarities of team members, vi) good combination of skills and techniques, and vii) relevance of the established collaborations.

- Weaknesses and threats:

The major weakness relates to the future grant funding of the team. To deliver on the research program, expected grants need to be obtained. Uncertainties remain concerning the construction of new and larger animal facilities; this may affect the work of the team.

- Recommendations:

A strategy for obtaining sufficient funding should be considered. Owing to the collaborative network already established, EU funding could be considered. Strengthening links with a biotechnology company seems to be a real opportunity to fund, at least partly, the research program.

# 4 • Team-by-team analysis

**Team 3 :** Cortical Networks and Neurovascular Coupling

Name of team leader: Mr Bruno CAULI and Bertrand LAMBOLEZ

## 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 | 3 | 4 | 3 |
| **N3**: Other permanent staff (without research duties) | | | |
| **N4**: Other professors (PREM, ECC, etc.) | | | |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | 3 | 2 | 1 |
| **N6**: Other contractual staff (without research duties) | | | |
| **TOTAL N1 to N6** | 8 | 8 | 6 |

| Team workforce | Number as at 30/06/2012 | Number as at 01/01/2014 |
|---|---|---|
| Doctoral students | 6 | |
| Theses defended | 3 | |
| Postdoctoral students having spent at least 12 months in the unit | 3 | |
| Number of Research Supervisor Qualifications (HDR) taken | 2 | |
| Qualified research supervisors (with an HDR) or similar positions | 3 | 4 |

# • Detailed assessments

## Assessment of scientific quality and outputs

The team's objectives – neuro-glio-vascular interactions in the cerebral cortex - reflect the team's organization around the two "high profile" researchers of the team who have different initial backgrounds that will co-manage the team. The activity report and interviews convincely demonstrate the added values of this convergence of expertise on this brain structure (cerebral cortex) with shared methodological tools. The team appears as being extremely well established experimentally, with a lot of running methodologies including cutting edge optogenetic manipulations and genetically encoded tools to assess important neuronal and glial signaling pathways. One can also notice that required materials are both available within the team but also in shared platforms, the construction of which being strongly supported by the team leaders.

The team is strongly collaborating with local, national and international groups, most of them being fruitful in term of publications. Accordingly, the scientific production over the period is very good, with 28 identified publications, 13 of them being peer review articles from the group *per se* (9 first or last author, including 3 J Neurosci. and 2 Cereb Cortex). Recently, the team has succeeded in obtaining significant funding from the ANR in both of the team's main scientific topics, and the next added component is also well financed for the 2012-2014 period.

## Assessment of the team's academic reputation and appeal

The team belongs to the Equipex Ultrabrain, and is part of the "Ecole des Neurosciences de Paris" and of the IHU Institut des neurosciences translationnelles de Paris. One of the co-leader had strong national investment by its participation to the committee of the 25$^{th}$ section of the CNRS and to several AERES committees (6 over the period). The other co-leader received the bronze medal of CNRS, and organized or chaired several sessions in international meetings. Both have highly cited scientific production (about 50 citations/article). Locally, the team has contributed to the establishement of several shared platforms (2P-microscopy, holography, Optogenetics and ultrasound imaging). They have succeeded in recruiting a CR2 staff researcher and will be joined by an experienced scientists who has developed complementary *in vivo* methods.

The team members are reviewers for moderate to high impact journals (Cereb. Cortex, PNAS, J. Neurosci.). The large size of the team raises the point aout the absence of publications in IF>10 journals from projects developped within the group. However, as said above, the team collaborates with several national and international renowned investigators and appears to be well implanted within the host institute. Therefore, the team is very attractive and has an excellent visibility at the national and international levels.

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

No mention of participation in important social or cultural events was present in the report. Also, no contribution of the team to the development of or collaboration with private companies was provided. Thus, this criterion was not evaluated.

## Assessment of the team's organization and life

The team has – through the building of several platforms – access to equipments crucial for its activity and also recruited young researchers developping their own research. The co-leadership of the team seems to be well managed so far with ongoing intra team collaborations (as assessed by co-authored publications). The integration of a new scientist with novel expertise appears as being well prepared within the organization diagram, some allocation of new space being garanteed by the institute director. The team, which currently includes 9-10 people, will grow to 14 by 2014. It was also noticed that the team is among the most succesfull of the whole institute in getting external grants. Thus, this team is a very strong and dynamic component in the institute life, that is considered very good regarding this criteria.

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

The team has strong involvement in teaching, essentially due to the two UPMC lecturers (each 192h/year). Other team members participate to master courses (UPMC, ENS, ESPCI). Over the past period, the team has trained 22 students and post-docs. Additionally, two team members obtained their habilitation during the period. In the report, it is mentioned that 90% of lab members who left the lab during the period pursued their scientific career/studies. This excellent lab management training and strategy was also clearly visible during the interview of both team leaders.

## Assessment of the five-year plan and strategy

Based on past activities and the decision to stop some high-competition projects (neuronal classification of cortical circuits), the project, which includes the topic of the newly integrated scientist, sounds very integrative and turned toward combinations of in vitro and in vivo cutting edge techniques. The objective is to examine the coordinated activity of several components of the cortical circuit, in normal and pathological conditions. Among the 6 main lines, several are based on unpublished observations, and others appear as low risk being mostly based on available techniques that need to be applied on specific questions. The global project is very well-funded scientifically and adjusted to the working power of the team and to the existing techniques in the institute. Overall, the five-year plan and strategy put forward by the team is excellent: solid, very well-designed, innovative, and should lead to significant advances in the field of cortical network and neuro-vascular coupling.

## Conclusion

The team provided a fair analysis of its own strengths, opportunities and potential threats. It sounds that the threats were well taken into consideration and that the project is adjusted to deal with the “risk of dispersion”.

- Strengths and opportunities:

The team is well-equipped and has all the necessary expertise to achieve its scientific goals. It was recently joined by two young talented researchers whom technical expertise will complement and extend that already well-established within the team. These are clear opportunities for developping new cutting edge approaches and asking formerly unaccessible scientific questions. Globally, the team is well structured and embedded in a rich network of national and international collaborators that will further increase its future opportunities. Finally, it is well-implanted in the local neuroscience community which should also add to its opportunities.

- Weaknesses and threats:

Being in such a big structure may provide strong help in administartive duties, but it was noticed and discussed that because the team anticipates a 50% growth, some additional technical help may be necessary in the coming years. The successfull integration of a new technical expertise into the team brought through the arrival of a new staff scientist, will strongly depend on the capacity of other team projects in developing transversal questions that include the new analytical level for such whole brain imaging.

- Recommendations:

The host laboratory should consider the recruitment of a permanent technician/assistant.

# 4 • Team-by-team analysis

**Team 4 :** Glial Plasticity

Name of team leader: Mr Hervé CHNEIWEISS and Ms Marie Pierre JUNIER

## 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 | 2 | 2 | 2 |
| **N3**: Other permanent staff (without research duties) | | | |
| **N4**: Other professors (PREM, ECC, etc.) | 2 | | 2 |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | 1 | 1 | |
| **N6**: Other contractual staff (without research duties) | | | |
| **TOTAL N1 to N6** | 6 | 4 | 5 |

| Team workforce | Number as at 30/06/2012 | Number as at 01/01/2014 |
|---|---|---|
| Doctoral students | 3 | |
| Theses defended | 5 | |
| 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 | 3 |

# • Detailed assessments

## Assessment of scientific quality and outputs

The work carried out by this team on the cell biology of glioblastoma tumours is pioneering in many aspects and very valuable. The group has made relevant contributions in basic aspects like i) the definition of new properties of glial stem cells, ii) the discovery of their self-renewal capabilities, fundamental for cancer progression and resistance to chemotherapies, and iii) the analysis of their interactions with the endothelial microenviroment. Moreover, the group has very important translational contributions including i) new GSC markers with diagnostic value (the mutation in the IDH1 gene), ii) the discovery of the effect of miR-302-367 on GSC differentiation and, iii) three drugable candidates able to stop GSC proliferation that are awaiting clinical trials.

In summary, very good cell biology research, strongly based on state of the art technologies like proteomics and metabolomics, with potentially oustanding translational results. Very good publication record (50 publications in this period), some of them in top journals in the field (contribuiting authors 2 papers in Stem Cells and Oncogene; collaborating in 2 Stem Cells; EMBO Reports; Cell Death & Diff.). Good funding although excessively fragmented.

## Assessment of the team's academic reputation and appeal

The leaders of the team have received 16 invitations, half of them in international meetings (10th IUBMB; 9th Euroglia meeting).

One team leader is deputy director of an EU ITN Marie Curie program. The members of the Group participate in a significant number of scientific councils (European Genetic Foundation, InSB, OPECST, FRM, CSS06, PROSTEM.), networks and editorial boards (Medecine/Sciences, Progress in Neurobiology, International Journal of Ethics). The visibility of the team is good.

The team has very good interactions with other French groups and with other groups outside France. The collaboration with the French groups has been very important in the scientific output of the team. Also, the collaboration with a group in Geneva has been very successful in terms of publications.

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

The team has filed 3 patents. One of the leaders is very active in the social/public promotion of science, participating on a regular basis in radio programs, is member of the Ethics Committee of INSERM and member of the advisory board for science and technology of the French House and Senate. The team has 12 publications aimed at the general public and one of the co-leaders has 5 publications on the ethics of science.

The team has created a unique collection of GSC cell lines derived from glioma of great interest for the scientific community as well as for screening purposes in biotech companies.

In summary, the team has an excellent interaction with the social, ecomomic and cultural enviroment.

## Assessment of the team's organisation and life

The team has a co-direction that seems to work very efficiently, with a correct distribution of responsabilities. They are further strengthened by 2 university lecturers, 1 neuropathologist, 1 scientist from College de France, 2 visiting scientists and 2 post-doctoral fellows which, all together, garanties an excellent management and supervision of the students. Furthermore, the team has 5 engineers/technicians that take responsabilities in the different technical facilities and platforms of the unit. Currently, as for other teams in this unit, the work is compromised because of the excessive spreading of the research facilities.

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

The team has an important number of PhD students (10) and other students (2). Both PhD students and other students occupy relevant positions (first and second authorships) in 11 publications out of the 13 corresponded directly by either co-leaders of the team. The students also benefit of authorships in other collaborative papers of the team.

The group has graduated 6 PhD studies in the evaluation period. The leaders participate in different masters and hold several academic responsabilities.

## Assessment of the five-year plan and strategy

The team has plans to strengthen its international networking, especially within the EU, which could open new possibilities for funding. The main aim for the five-year plan is to unravel the molecular mechanisms that restrict the stem-like potential, and consequently the tumorigenicity of GSC. The model will profit from the ability of the cluster of microRNAs (miR-302-367) to commit GSC to an irreversible non stem-like state and will use metabolomic approaches to unravel the molecular pathways involved in this cell cycle arrest process. The team has promising preliminary results and two by-products of neurotransmitters pathways, seems to be able to reproduce the inhibition of GSC stem-like properties. Plans are to transfer to the clinic potential compounds able to target GSCs and to develop the use of these metabolites for optical imagery in neurosurgery.

The planning is excellent, coherent with the research line of the group and is ambitious, though feasible. Strong preliminary data makes the 5-years plan realistic.

## Conclusion

- Strengths and opportunities:

Well established research line, in which the team is a pioneer and holds a strong position in the field. Reasonable opportunities to transfer to clinic the results of the research in an area devoid of appropriate therapeutic tools and eagerly awaiting them. Appropriate set of collaborations to guarantee successful development of the project in a near future.

- Weaknesses and threats:

The geographic spreading of the research facilities is negatively impacting the work of the group. This situation might not be easy to solve due to present economical constraints. Funding from local sources probably compromises too much time in paperwork with little benefit for the research.

- Recommendations:

The team is strongly encouraged to increase the international networking, especially within the EU and to gain access to additional funding sources.

# 4 • Team-by-team analysis

**Team 5 :** Normal and pathologic glutamatergic systems

Name of team leader: Mr Salah EL MESTIKAWY

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

| Team workforce | Number as at 30/06/2012 | Number as at 01/01/2014 |
|---|---|---|
| Doctoral students | 5 | |
| Theses defended | 2 | |
| Postdoctoral students having spent at least 12 months in the unit | 4 | |
| Number of Research Supervisor Qualifications (HDR) taken | 0 | |
| Qualified research supervisors (with an HDR) or similar positions | 2 | 3 |

# Detailed assessments

## Assessment of scientific quality and outputs

The team originally discovered the third vesicular glutamate transporter (vGLUT3) that is expressed in neurons expressing other neurotransmitters or modulators. They also discovered a quite unexpected function for these transporters in regulating filling of synaptic vesicles with acetylcholine and serotonine (vesicular synergy). It was mainly work of the team leader that showed that vGLUT3-expressing neurons serve important functions in regulating modulatory processes in the brain including those mediated by acetylcholine and serotonine. In addition the team has made efforts to dig into pathological implications of vGLUTs both as biomarkers (Morbus Alzheimer, Morbus Parkinson) and as causes of disease (e.g. deafness) due to mutations. The scientific contribution of the team to the understanding of glutamatergic functions in the brain is enormous. The work of the group is published in top journals of the field including J. Neuroscience and Nature Neuroscience (discussed in F1000). Altogether 48 papers were published during the reporting period by five (previous, current and future) senior team members and the PI. In summary, the scientific achievements are qualified as outstanding and ground-breaking, in particular because of the discovery of vGLUT3 functions.

## Assessment of the team's academic reputation and appeal

The high visibility of the team leader is also documented by an invited review in Nat Rev Neurosci that he signed as the first author. There, novel ideas and concepts about the function of co-release of transmitters are discussed indicating that the PI is among the opinion leaders in the field. This is underscored by a high number of invitations to international meetings (13) and seminars (27, 11 of them abroad) and steadily very high numbers of citations. The team leader is an internationally highly visible scientist who is well integrated into networks of excellence (ENP, BIOPYS, LABEX and FondaMental). Moreover, he is collaborating with other internationally leading figures in the field and has a double affiliation with UPMC and the McGill University, Montreal (Canada).

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

The discovery of biomarkers and human pathology-causing mutations is of potential social, medical and economic interest. However, currently no activities have been undertaken in this direction.

## Assessment of the teams's organization and life

The governance is very good and efficient. The team leader with his double affiliation to UPMC and the Douglas Hospital Research Center at McGill is predestined to provide a rich international environment for his team. Certainly this way the team profits from the influence of different cultures of science. The team leader developed a clear concept of the group structure and how the senior scientists will backup his frequent absence due his the double affiliation. Moreover the experienced researchers provide different and complementary types of technological know how and expertise – a very solid basis for successful future work.

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

The group hosted recently quite a number of trainees (14), master students (12) and PhD students (7). This is an appropriate number well in balance with the number of seniors and postdocs. Most PhD students got very good postions in academia. One of the seniors staff of the team is teaching as assistant prof. at UPMC. Overall there is a very stimulating research environment for students and postdocs.

## Assessment of the five-year plan and strategy

The team aims at deepening the understanding of the complexity of the glutamatergic neurotransmitter system in mammals. Based on their excellent previous work this is a well-taken, very ambitious but feasible undertaking. The team is in the position to indeed provide strong and medically relevant contributions to our appreciation of this central excitatory transmitter system. The comparative study of animal models and humans is considered as a particular strength the team’s research goals.

Specifically the team wants to assess the role of (i) VGLUT3 in the auditory system; (ii) VGLUT3 in the striatal cholinergic interneurons in regulating reward and addiction; (iii) VGLUT3 expressed in 5-HT neurons that are involved in the regulation of anxiety behaviors and sleep; (iv) VGLUT3 in GABAergic interneurons – i.e. in a subclass of basket cells where it is expressed; (v) VGLUT1-3 in ageing and cognition by investigating rodents and human for the correlation of glutamatergic parameters (mainly VGLUTs) and states of cognitive impairment; (vi) VGLUT3 in psychiatric disorders (because a potential association of the VGLUT3 locus SLC17A8 with neuropsychiatric diseases including schizophrenia, major depression and bipolar affective disorder); additionally, (vii) the pharmacochemistry of VGLUTs – that is currently poorly understood – shall be investigated in collaboration with a team of chemists. This will become of high medical relevance.

The team leader described a very clear and straight forward concept of the distribution of the planned work between the Paris and Montreal laboratories. While research on striatal cholinergic neurons and on 5-HT functions as well as on the pharmaco-chemistry will be performed at UPMC, biomarker studies in humans and the role of vGLUT3 in GABAergic interneurons is planned for the Canada lab. The research program is considered as outstanding. The committee is convinced that major progress in the appreciacion of mammalian (including human) brain physiology and pathology can be expected.

## Conclusion

- Strengths and opportunities:

These include: i) strong multidisciplinary approaches to a highly relevant topic, ii) studies on both animal models and humans to understand brain function and disease, and iii) international connection by double affiliation of team leader to UPMC and McGill with ambient access to research facilities and materials (including relevant patients and human brain material).

The team has a broad technological expertise including anatomy (including ultra-structure and cell biology), protein biochemistry, electrophysiology, animal behavior, human studies including pathology, psychiatry, human genetics, pharmaco-chemistry that is provided either by the team members or national and international collaborators.

- Weaknesses and threats:

The double affiliation may also cause problems. Good governance structures have to be maintained to deal with these issues. Currently funding of the group does not mirror the scientific output.

- Recommendations:

Access to relevant infrastructure and facilities (e.g. mouse facility) must be provided. Major efforts should be made to acquire national and international (EU, ERC) extramural funding.

# 4 • Team-by-team analysis

**Team 6 :** Neurophysiology and behavior

Name of team leader: Mr Philippe FAURE

## Workforce

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

| Team workforce | Number as at 30/06/2012 | Number as at 01/01/2014 |
|---|---|---|
| Doctoral students | 1 | |
| Theses defended | 0 | |
| Postdoctoral students having spent at least 12 months in the unit | 4 | |
| 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

Overall, the scientific quality and outputs of this small-sized team (1 permanent researcher in the past period, 2 in the next period) are excellent (16 publications including 6 high-profile publications: 1 Nature, 1 Science, 1 Molecular Psychiatry, 3 PNAS). The research of the team mainly focuses on the dopamine-based neurobiology of both normal and pathological decision-making, using nicotine addiction as a paradigmatic example of the latter condition. Since nicotine is the main active ingredient of tobacco and since tobacco is the second preventable cause of premature death in the world, the societal impact of this research is potentially immense.

Specifically, by combining a variety of cutting edge methods (gene KO technology, in vivo gene rescue vectorology, in vivo electrophysiology, statistical analysis of behavior), this team has greatly contributed to our current understanding of how different VTA nAChRs differentially regulate phasic and tonic VTA dopamine signaling and how this differential regulation differentially impacts decision-making, particularly the decision to repeatedly take nicotine.

Finally, this team was also very successful in obtaining competitive grant funding (2 ANRs, 1 Prix Fondation Bettencourt and 1 FRC), amounting to about 1 million euros over the past period. As a result, it acquired all the necessary equipments for its current research activity and its future project.

### Assessment of the team's academic reputation and appeal

Though this team has only emerged recently, it has acquired a very good national and international reputation. The team leader has been invited to give talks at 6 international meetings, including 1 plenary conference at the Hong-Kong Polytechnic University, and lectures at 7 national or international academic institutions.

It has also attracted a talented young researcher who recently obtained a permanent researcher position (CR1) at INSERM and who will join the team in 2013. The scientific quality of this young researcher is also excellent (e.g. 1 Nature Meth, 1 Nature Chem).

The team belongs to the Labex Bio-Psy and is an active member of the steering committee board of several neuroscientific societies and organizations. The team leader has also served as an expert reviewer for several funding bodies, including the ANR.

Finally, the team collaborates with several renowned scientific investigators from different prestigious national (e.g. Institut Pasteur; ENS) and international (e.g. UC Berkeley, CA; LMU Munich; Oxford Univ) universities or academic institutions.

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

The team’s interaction with the social, economic and cultural environment is good but could be increased in view of society’s interest in tobacco addiction. The team provides its expertise in statistical analysis of behavior to two private companies. It has also participated to 3 national public debates on drug addiction (i.e. “Bar des sciences”).

### Assessment of the team's organization and life

The team’s organization and life has been so far very good. It succeeded to find its unique scientific niche in the host lab and to build new productive collaborations with the other teams of the host lab (e.g. 1 Science with the team E15, 1 Mol Psy with team 2 and 3).

The team has secured all the equipments (5 electrophysiological setups) for its current research activity and its future research project. In 2013, it will be joined by 1 permanent young researcher and plan to grow to 10 people by 2014.

However, some of its future activities (notably those involving the use of behavioral assays) may be hampered by space limitations in the host lab. In addition, the team has currently no permanent research assistant which may become a problem in the future.

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

The team's involvement in training through research is very good. Over the past period, the team has trained through research 4 master students, 2 PhD students and 4 post-docs.

The team was also involved in teaching activities in 6 master programs (2-3 hours per year per program).

## Assessment of the five-year plan and strategy

The 5-year plan and strategy are excellent and highly original. The plan is structured around 3 major goals: 1. Deciphering functional specialization of different VTA DA cell subpopulations; 2. Defining dopamine-related genetic and environmental risk factors for nicotine addiction; 3. Understanding how firing activity of VTA dopamine neurons controls normal and addictive decision-making. These goals are in continuity with previous research from the team but extend it in entirely new directions. Each goal is solid scientifically and involves a reasonable dose of risk-taking. If everything goes well, however, this project should be feasible within 5 years. One particularly risky and exciting research subgoal concerns the adaptation of 'classical' optogenetic tools to make originally 'blind' nAChRs sensitive to light. This novel technology will allow researchers to turn on or off VTA nAChRs to study their involvement in nicotine reward and addiction. Its successful application promises to lead to some breakthrough discoveries in the field. Another original and timely subgoal is to study nicotine self-administration in a context where mice live and are free to choose among different other options. Such context is clearly more relevant for modeling human addiction than the standard experimental setting which offers no other choice than the drug.

## Conclusion

- Strengths and opportunities:

The scientific project is original and ambitious. It promises to deliver new insights into the dopamine-based neurobiology of nicotine reward and addiction.

The team leader is highly capable and has shown a high degree of flexibility and creativity in coping with challenging situations in the past. The team is well-equipped and has developed cutting-edge techniques to achieve its ambitious goals.

The team is relatively young and attractive. It was recently joined by a young talented researcher whom novel expertise will enrich the team.

Finally, the team is embedded in a solid network of renowned collaborators. It is also well-implanted in the local neuroscience community (e.g. Labex Bio-Psy) which should increase its opportunity to create new productive collaborations.

- Weaknesses and threats:

The lack of a permanent research assistant and the limited experimental space allocated to the team may eventually hamper the good development of some aspects of its project (e.g. those that rely on behavioral assays).

- Recommendations:

Every effort should be made by the host lab to help this team to recruit a permanent research assistant.

The team should consider to increase its interaction with the social, economic and cultural environment.

# 4 • Team-by-team analysis

**Team 7 :** Pathophysiology of Psychiatric Disorders

Name of team leader: Mr Bruno GIROS

## 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 | 3 | 1 |
| **N2**: Permanent EPST or EPIC researchers and similar positions | 6 | 5 | 6 |
| **N3**: Other permanent staff (without research duties) | | | |
| **N4**: Other professors (PREM, ECC, etc.) | | | |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | 5 | 4 | 5 |
| **N6**: Other contractual staff (without research duties) | | | |
| **TOTAL N1 to N6** | 12 | 12 | 12 |

| Team workforce | Number as at 30/06/2012 | Number as at 01/01/2014 |
|---|---|---|
| Doctoral students | 6 | |
| Theses defended | 14 | |
| Postdoctoral students having spent at least 12 months in the unit | 3 | |
| Number of Research Supervisor Qualifications (HDR) taken | | |
| Qualified research supervisors (with an HDR) or similar positions | 3 | 5 |

# • Detailed assessments

## Assessment of scientific quality and outputs

The scientific productivity of the team has been very good in the past 5 years. For many years, this team has been a leader in the field of psychiatric disorders, mainly aimed at understanding the pathophysiology and identify new therapeutic targets for schizophrenia and depression. To do so, they have used a wide array of complementary molecular, genetic, pharmacologic and behavioral tools to develop mice models relevant for these disorders, with the ultimate goal of moving their basic pre-clinical work to patients. In order to achieve this goal, the team has built strong collaborations with various psychiatric units and Departments in France and Canada.

In the past five years (2007-2012), the team published a total of 73 peer-reviewed manuscripts (including 7 from members of the collaborative team), which is very good for such a large team (12 in Paris, plus a few in Montreal). An additional 22 peer-reviewed papers were published by members of the team in collaboration with authors outside of the team. The papers were published in very good to excellent journals with significant impact factor (Nature NS, J. Neurosci., Neuropsychopharmacology, Biological Psychiatry, etc…).

A weakness is the lack of significant external funding from ANR or other foundations in France or Europe. Small external funding and awards were gained by some team members. In order to help solve the problem, the team leader mentioned that he will aim at the publication of a lower number of papers in higher impact journals during the next funding period. One the main problems that could jeopardize the team's effort in achieving the goal of getting external funding is the poor animal housing condition the team has to deal with.

## Assessment of the team's academic reputation and appeal

The team's academic reputation and appeal is excellent. Many team members have been invited as speakers in national and international conferences (41 in total). Some organized and chaired national conferences (6 in total). A few are members of Editorial boards of scientific journals (2) and have participated in evaluations of international grant agencies. The team leader was awarded Chaire de Recherche du Canada-Neurobiology of Psychaitric disorders at McGill Univ (Montreal, Canada)-5 months/year. One staff scientist was awarded a Scientific Price from the Bodossakis Foundation. Some team members are part of INSERM scientific council. The team leader is a member of SAB-Instituts des Neurosciences, Montpellier, Fondation de France, President Autism Committee, Member and President FRSQ postdoctoral awards, Member Canadian Institute Health and Research-CIHR. One staff scientist has been a panel member to evaluate Research Team Proposals in Science and Technology-CONYCIT in Chili. The team leader and others review grant applications for National (INSERM, APHP, AERES, FRC, ANR etc…) and international (CIHR, FRSQ, Welcome Trust, Greek Ministry of Education) funding agencies. Many team members review papers for journals with good impact factors.

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

N/A

## Assessment of the team's organisation and life

The team's organization and life is excellent. It is an excellent team of scientists with complementary expertise. They have established strong collaborations with Psychiatric Depts in France (Creteil, Salpêtrière) and Canada (Douglas hospital, Montreal), which provide them the opportunity to translate their work to the clinic. The team belongs to the labex Bio Psy and the DHU Pep-Psy. The team leader has shown convincingly that he is able to manage very well the supervision of both the Montreal and France research teams. Together, these two locations and teams offer him the possibility of exploring a broader range of expertise and research areas than would be possible at a single site. Overall, the research program is highly translational, ranging from basic to clinical sciences, which adds strength to the general organization of this team.

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

The training through research has been excellent to outstanding. Forteen PhD students have graduated from the team in the past 5 years. Four students remain in the team. Nine postdocs have been part of the team (5 have now left). Six unit members have significantly contributed to teaching in courses in Med School, Biochemistry and Master BIP.

## Assessment of the five-year plan and strategy

The proposed research plan and strategy for the next five years is very good. Two main axes of research: schizophrenia and depression for next five years. The research plan is well explained and the main goals of proposed studies is clear. The schizophrenia research plan focuses on the role of DA dysregulation, which is not new because DA has long been known as a main target of schizophrenia. Although this may appear as a weakness because of limited innovation, the team is going after non-conventional targets such as D1 dopmaine receptors. Looking at the role of DA in LTP and LTD is also of interest and relatively new despite the fact that DA role in cognition has long been known. The research plan for the depression research program is highly innovative through investigations of new research areas. The success of the five years strategy is dependent on stronger infrastructure support, mainly for animal facilities, and a stronger incentive of the team leader.

## Conclusion

- Strengths and opportunities:

These include: i) an outstanding Group leader with an excellent national and international reputation as scientist and team leader. This provides excellent visibility and recognition of the team at the national and international levels; ii) the scientific productivity of group leaders and some team members is really good to excellent, iii) collaboration with clinical psychiatric departments and access to patients in France and Canada represent excellent opportunities for translational research with important clinical relevance; iv) the expertise of the different team members is complementary which allow to share expertise and address broad scientific issues in the field of schizophrenia and depression.

In addition, the scientific environment is solid, which may lead to future collaborations and the development of new research axes. There is a solid expertise in molecular biology, genetics and development of new mice models based on DAT interacting proteins may pave the way for new unexplored avenues that could be explored as targets for schizophrenia.

The possibility of testing D1 antagonist in schizophrenic patients may open up some new treatment avenues. The “novel” areas of research explored for depression add some innovative value and significance to the proposal. The dual position in Montreal is a strength and has been very productive so far. The team leader explained well how he handles both laboratories and what the main goals of this collaboration are. This allows him to expands his research program taking into consideration the limited resources available in Paris.

- Weaknesses and threats:

- Eternal funding is limited. Problems getting funds from ANR must be solved.

- Working conditions are problematic. Animal facilities must be improved to allow continued growth.

- Limited support and infrastructure in France. May jeopardize the future success of the team.

- The focus on DA dysfunction as the main drive for schizophrenia is risky because it has been so heavily studied. Limited novelty is a concern. The depression area of research is stronger and more innovative.

- Although interesting experiments are proposed using sophisticated molecular, pharmacological and electrophysiological approaches, there is limited discussion of the potential impact of this work towards improvement of therapeutic strategies for schizophrenia and depression.

● Recommendations:

- Getting external funding from ANR should be a priority.

- Increase impact of published papers.

- Continue develop strong bonds with McGill University in Montreal.

- Seek stronger institutional support for animal facilities. This problem must be solved to ensure the future of the team.

# 4 • Team-by-team analysis

**Team 8 :** Development and degeneration of spinal motor neuron

Name of team leader: Ms Jamilé HAZAN

## Workforce

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

| Team workforce | Number as at 30/06/2012 | Number as at 01/01/2014 |
|---|---|---|
| Doctoral students | 1 | |
| Theses defended | 0 | |
| 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 | 1 | 1 |

# • Detailed assessments

## Assessment of scientific quality and outputs

This is a newly emerging team whose research is on an upward trajectory. The most notable output has been a highly influential paper in *Nat Neuroscience* in the last 2 years. The studies described in this paper, and in the other recent outputs of the team, reflect high quality science that is illuminating the role of genes that cause spastic paraplegia in humans. The approach has been to take known causative genes for spastic paraplegia and investigate their function through knockdown or over-expression in zebrafish. The work has revealed that several of the spastic paraplegia genes have a unifying function in the regulation of receptor trafficking within the cell, with a specific regulatory role on BMP signaling by the atlastin gene. In addition to the *Nat Neuroscience* paper, the team has published five other papers including in the high impact factor journals *Neurology* and *Amer J Pathol*.

## Assessment of the team's academic reputation and appeal

While the team leader is a relatively new group leader in her current field, she has a strong track record from her previous work in identifying the causative genes for spastic paraplegia, where she published many papers. Having retrained in developmental neurobiology, she now needs to build a new reputation in this field. She has made a good start, as her team is well connected through productive collaborations in UK and USA, as well as with other groups in France. These connections are evidence of a growing reputation, internationally, for the research in this team. The expertise of team leader in using the zebrafish model to determine the mechanisms underlying spastic paraplegia in humans is clearly of great appeal to both clinical and non-clinical collaborators, within and outside the Department of Neuroscience. Moreover, the work has many different ramifications, and so can appeal to a variety of areas of developmental and genetic neuroscience. These include the areas of BMP signaling (of great importance in many different developmental fields), vesicular trafficking, microtubule dynamics, and the regulation of axon growth and guidance in spinal motor neurons.

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

The team leader makes considerable contributions both to the organisational aspects of science in France, and to public engagement through her work with patient groups. She has been CNRS delegate for the Lab Council (Conseil de Labo) of UMR Inserm U952/CNRS 7224/UPMC since Jan 2009 and, in September 2012, she became an expert member of the Inserm section for Neuroscience (CSS6). She belongs to the Permanent Delegation (DP) of this committee. She contributes actively to liaison with patient groups, through her membership of the common Scientific Council of three French patients' associations, namely the "Association Française de l'Ataxie de Friedreich" (AFAF), "Connaître les Syndromes Cérébelleux" (CSC) and the "Association Strümpell-Lorrain" (A S-L).

## Assessment of the team's organisation and life

Team 8 is an 'emerging team' within the proposed Department of Neuroscience. The leader has only just started the team, and will head a small group that consists of an experienced resarch fellow and two PhD students. This decision to promote the leader to group leader has been taken with agreement of the majority of other team leaders and clearly indicates the perceived importance and potential of her recent research. The team has funding to support its research currently, but this does not appear to be financially large. Starting in 2012 are a 35K support grant for a 3-year PhD studentship, a 20K grant for consumables and equipment, and a 32K grant for consumables. Hence, it appears that 87K is the amount available over a 3-year period to support research in the team.

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

Two Masters' students have trained with the leader in recent years, one becoming a current PhD student. Indeed, the leader places great priority on student training and is clearly an excellent mentor who strongly encourages students to enter a research career. She is a member of the teaching staff of the ED3C PhD School, and has organised the annual meeting for 2$^{nd}$ year students, and well as participating in the annual meeting for 3$^{rd}$ year students. This is very important work and indicates a culture within the team that values student training. The team will provide an exciting environment for students to work in, and to carry out research projects.

## Assessment of the five-year plan and strategy

The plans for the next 5-year period are impressive, and build upon the promising research of the last few years. Four areas of new investigation are planned. First, to examine the mechanisms by which Atlastin regulates BMP signaling. The hypothesis is that BMP receptor trafficking is the level of regulation and the team will carry out a number of studies to test this idea. Second, the team will determine how BMP signaling may regulate spinal motor axon guidance, and why its disturbance leads to defects, as in spastic paraplegia. The work has already demonstrated that dorsomorphin, a BMP signaling inhibitor, can reverse the effects of morpholino-knockdown of *atlastin* in zebrafish, and alleviate the neurological phenotype. They will now determine if this is mediated via the canonical or non-canonical branches of the BMP signaling pathway. Third, they will follow up the observation that the two alternatively spliced isoforms of Spastin have different effects cellularly, and in producing a neurological phenotype in fish. This is an important extension of the spastin research to date. Fourth, Fidgetin-like-1 will be assessed for its mechanism that leads to a motor axon guidance phenotype, thereby illuminating a further cause of spastic paraplegia in humans. Altogether, these are well planned studies that capitalise on the successes of the team in recent years, make use of their expertise with the zebrafish model, and continue to develop international collaborations. Hence, further research into this group of genes may contribute importantly to an understanding of basic cell biological mechanisms, as well as determining the causes of spastic paraplegia.

## Conclusion

- Strengths and opportunities:

A very promising research team that has emerged from studies of the genetics of human spastic paraplegia (leader's research area prior to 2007). Now, with considerable expertise in use of the zebrafish experimental model, the team has already demonstrated the ability to determine cellular and molecular mechanisms, and to follow up on these using incisive experimental approaches. Excellent collaborations are in place and these represent opportunities for more rapid progress than could be achieved by the team itelf, which is relatively small (two senior staff and two PhD students). A strong research plan is proposed that should lead to new discoveries and high quality publications – for example, a paper is in revision for *J Cell Biol*. Leader displays very clear thinking about her research goals – she wishes to investigate in depth the underlying biological mechanisms that unite a few of the genes causing spastic paraplegia, rather than performing a more superficial assessment of many genes. Her commitment to training is an additional strength, as is her contributions to public engagement through two French associations representing the interests of patients with neurological disorders such as spastic paraplegia.

- Weaknesses and threats:

The small size of the team could be a weakness, but with productive collaborations this does not need to be so. There is a relatively urgent need to secure further funding to support the team in the next few years. The team's size appears to have been limited not only by financial issues but also by lack of space, and the provision of dedicated research space for the team is a priority. Zebrafish facilities are essential for this team's work, and good progress has been made by sharing of facilities with the Developmental Biology Department. However, concerns about the timetable for a new animal facility are a potential threat.

- Recommendations:

Support for this new team is essential if it is to achieve success in a relatively short period. This will include assistance to the team leader in seeking additional funding - great benefit would result if the team could be integrated into a European Network to ensure both collaboration and financial support. There is also a need to add new staff members - the highest priorities are a technician to enable the team leader to concentrate more on leadership and innovation, and a cell biologist to provide expertise in this area, which is of importance to the future research. The team leader also needs dedicated laboratory space, and uninterrupted high quality animal facilities. Overall, It will be important for the Department of Neuroscience to provide early assistance to the leader, both financial and infrastructural (including increased space) in order to allow this new group to establish itself quickly and productively, and to fulfil its evident promise.

# 4 • Team-by-team analysis

**Team 9 :** Neuronal Networks and Physiological Rhythms

Name of team leader: Mr Régis LAMBERT and Ms Nathalie LERESCHE

## 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 | 2 | 2 |
| **N2**: Permanent EPST or EPIC researchers and similar positions | 1 | 1 | 1 |
| **N3**: Other permanent staff (without research duties) | | | |
| **N4**: Other professors (PREM, ECC, etc.) | | | |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | 1 | | |
| **N6**: Other contractual staff (without research duties) | | | |
| **TOTAL N1 to N6** | 3 | 3 | 3 |

| Team workforce | Number as at 30/06/2012 | Number as at 01/01/2014 |
|---|---|---|
| Doctoral students | 2 | |
| Theses defended | 2 | |
| Postdoctoral students having spent at least 12 months in the unit | 4 | |
| 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's research concerns the mechanisms underlying sensory information processing in thalamic networks, as well as the slow rhythmic activities occurring in the thalamocortical loop when the subjects are disconnected from the external world, as during sleep or absence seizure. This is an important topic to understand how intrinsic properties and functionnal network connectivity support the thalamic function during different physiological brain states (sensory processing and sleep), and in some neurological or psychiatric diseases such as absence epilepsy and schizophrenia. Special attention is given on the role of the low-threshold calicum T-type current.

A total of 11 papers (10 research papers and 1 review) have been produced by the team during the past 5-year period. These papers have been of very good quality (1 PNAS, 2X J Neuroscience, 1 J. Physiol and 1 Int J Neuropsychopharmacol) but the number of papers could be considered as moderate taking into account the number of post-docs and PhD students involved (9 in total). However, the group, and in particular one of the co-leader, has been successful in obtaining research funding (2 ANR as PI, CNRS European Associated Laboratory and PEPS CNRS Biologie-Mathématique-Informatique (2012-2013)). Most of the papers are co-signed by the co-leaders. In summary, the scientific quality and output of the group are good.

## Assessment of the team's academic reputation and appeal

The team seems to be well-established and has a good expertise from basic biophysics to *in vivo* physiology. During the last 5 years, two international collaborations are mentioned, with partners in the UK and USA. An Associate Professor from Seoul has been invited in the team for two months in 2008. Three national collaborations are also mentioned (UNIC, UPR 2191, Paris and IGF CNRS UMR 5203-Inserm U661, Montpellier). One of the co-leader is co-director of the LEA CNRS, has been invited two times to give talks at international conferences (SFN 2007, Symposium in Cardiff, 2011), has acted as the "chargée de mission" for Neurosciences at CNRS, was the organizer and chairman of a FENS symposium in 2010 "Molecular, cellular and network basis of thalamocortical dynamics" and is a member of the editorial board of Journal of Neuroscience Methods. The other co-leader is also co-director of the LEA CNRS and has been invited to give one talk at an international conference (Workshop in Kyiv, Ukraine on 2008). Many poster presentations are mentioned. However the international visibility of the team could be improved although one co-leader has high level of teaching and administrative responsabilities.

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

There is little in the team's document to provide information in this area. The team, probably does not seem to consider the possibility to interact with economical entities. No programmes for technology transfer towards industrial exploitation of their research results are mentioned, nor communication to the public. However, both staff scientists of this team have heavy duties either in administration, or teaching.

## Assessment of the team's organisation and life

The team will continue to be co-directed in the next 5-year period by the same co-leaders. The lab space and facilities seem to be adequate to conduct their research although it is mentioned that the team has a limited access to the two-photon microscope that is shared with two other groups. By obtaining grants from FRC and Bettencourt Schueller Fondation, the team, in collaboration with three other in the unit, has developped a laboratory dedicated to the analysis of mouse models of human diseases allowing microcircuit mapping, electrophysiological recording in freely moving animals combined to optogenetic tools to study behavior through control of neuronal activity.

Five post-doctoral fellows have been hired during the last 5 years and four PhD student have been trained by the team. One former PhD student/post-doctoral fellow in the team has been recruited as MCU at UPMC in 2012 and will integrate the staff of the team for the next five years. An IE was recruited in 2012. So there is a good influx of students and post-doctoral fellows. The team will be supported by two full time permanent postions, one MCU and one IE. However no post-doctoral fellows will arrive next year. For the next 5 years, the team will be composed of 1 Prof and 1 lecturer (MCU) with high teaching duties, 1 DR1 CNRS, plus 1 IE, 2 Ph.D. students and 1 master student.

In summary, this team has a very good unit's organisation and life.

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

Training was one strength of the team during the past 5-year period: 5 post-docs, 4 PhDs and several Master (M1 and M2) students. All PhD students were co-directed by both leaders of the team and two of them have now finished and have already found a job.

- One co-leader is the current director of studies of the Master of Integrative Biology and Physiology (BIP) program at UPMC, responsible of the Master of Integrative and Cellular Neurosciences and Chief coordinnator of the Bachelor "Life Science" (undergraduate program in Biology). He has also lot of adminitrative responsabilities and he is member of the National University Council (CNU), section 69 – Neuroscience since 2012. He was promoted PU 1st class in 2011 and "PES"(Prime d'Excellence Scientifique) awarded in 2010.

- The other co-leader is "Chargée de mission" for Neurosciences at the Institute of Biological Sciences (INSB) since 2006 and in charge of the interdisciplinary programs between INSB and the CNRS Institutes of Mathematics and Informatics (Program PEPS Biology-Mathematics-Informatics) since 2010. She was promoted DR 1st class at CNRS in 2011 and "PES" awarded in 2010.

- One young lecturer has been recruited at UPMC. He is associate faculty member Faculty of 1000.

In summary, the team has a very good involvement in PhD and Post-docs training.

## Assessment of the five-year plan and strategy

The main research focus is on the analysis of the thalamic functions during physiological or pathological conditions by trying to understand how intrinsic properties of thalamic neurons interact with their functional network connectivity. The project is built on important previous studies which have characterized *in vitro* multiple inhibitoy mechanisms within the thalamo-corticothalamic network.

The objectives of the project have the following aims:

1) To understand how inhibitory and excitatory synaptic input interact with intrinsic properties of thalamic neurons to condition whisker information processing in the thalamus with a focus on T current which could compensate trial-to-trail and cells-to cells fluctuations in the membrane potential levels and contribute to thalamic sensory response. Another question will address the role of the spatial and temporal cortical activity in the prediction of sensory responses of thalamic neurons.

2) To understand the complex relationship between T current density and sleep oscillations and how T currents mediate sleep related synaptic plasticity. This work will consist to an *in vivo* approach combining microdialysis for pharmacological studies, electrophysiological and EEG recordings.

3) To study within the thalamocortical loop the role of T currents in the synchronus spike-and-wave discharges involved in absence seizures in epilepsy by manipulating the Cav3.1 channels. GAERS rats and pharmacological model of absence seizures (GHB model) will be used.

4) To uderstand if alterations of the synaptic transmission could be involved in schizophrenia through NMDA receptor inactivation strategies.

All these objectives will be achieved using a multidisciplinary strategy that includes *in vitro* and *in vivo* electrophysiological approaches, two-photon calcium imaging *in vitro*, dynamic clamp, and molecular biology based strategies.

The plan involves the strategic collaboration with different international laboratories. The team has local academic connections which warrants recruitment of PhD students. However the project appears ambitious for this small team and should be focussed.

## Conclusion

● Strengths and opportunities:

The team is dynamic, built on 4 permanent (1PU, 1MCU, 1DR and 1IE); 2 PhD students and 1 master student and has good expertise from basic biophysics to *in vivo* physiology.

The quality of scientific publications is good as well as funding. There is a translational approach of the research questions (sleep, epilepsy, schzophrenia..). The development of a laboratory dedicated to the analysis of mouse models of human diseases using techniques combining a multidisciplinary strategy that includes *in vitro* and *in vivo* electrophysiological approaches, two-photon calcium imaging *in vitro*, dynamic clamp, and molecular biology based strategies, is a very good tool and helpful.

● Weaknesses and threats:

The overall scientific production could have been better in regard to the personnel involved. The project seems ambitious with probably too many questions. Funding supporting the project is not clearly identified.

The visibility of the team is moderate and should be improved. The team leaders have too little international invitations.

● Recommendations:

Improve the international visibility of the group by participating to international conferences and seminars. It may be possible to improve the number and the quality of publications. Keep the link with translational research, problably some effective interactions with clinicians will help. Some focus is necessary for the next five-year plan and strategy.

# 4 • Team-by-team analysis

**Team 10 :** Development of the spinal cord organization

Name of team leader: Mr Pascal LEGENDRE and Mr Jean Marie MANGIN

## Workforce

| Team workforce | Number as at 30/06/2012 | Number as at 01/01/2014 | 2014-2018 Number of project producers |
|---|---|---|---|
| **N1**: Permanent professors and similar positions | 5 | 3 | 4 |
| **N2**: Permanent EPST or EPIC researchers and similar positions | 2 | 2 | 2 |
| **N3**: Other permanent staff (without research duties) | 2 | 2 | |
| **N4**: Other professors (PREM, ECC, etc.) | | | |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | 1 | 1 | 1 |
| **N6**: Other contractual staff (without research duties) | | | |
| **TOTAL N1 to N6** | 10 | 8 | 7 |

| 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 | 1 | |
| 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's research aims are to understand the origin of the spinal cord neuronal activity, as it arises in the embryonic and fetal periods of development. This is an important topic for investigation with implications for an in-depth understanding of normal nervous system development. It also has relevance to disease processes that affect early neuronal development and degeneration. The work of the different members of the team during the past 5 years has been of significant quality, with papers consistently produced in high impact journals of the neuroscience field, including *Nat Neuroscience* (x2), *J Neuroscience* (x7) and *Glia* (x3). Altogether, members of the team have produced 36 papers during the 5-year period - an impressive output rate. Moreover, there has been a steady achievement of research grants throughout the previous 5-year period. Several grants, most notably the Young Investigator Grant to one of the co-leader, will continue into the coming years.

## Assessment of the team's academic reputation and appeal

Both co-leaders have a very good international reputation for work on the origin of early neuronal activity in mammals. They have received a fair number of invitations to speak at conferences and have an impressive list of international collaborators, including laboratories in USA, Germany, Belgium, UK and France. This suggests that eminent groups in all of these countries are keen to participate in joint research projects with the group. The appeal of the team's research lies in several aspects of its work: (i) a focus on the events of early spinal cord development that generate neuronal electrical activity where there was none before; (ii) considerable and long-standing expertise in single cell patch clamp analysis that enables both neurons and non-neuronal cells to be assessed for activity; (iii) a willingness to incorporate powerful genetic approaches to mammalian development, particularly as indicated by the use of Cre-loxP technology to inactivate key genes and to ablate specific cell types (via conditional diphtheria toxin, DTA, expression).

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

There is relatively little evidence that the team has made a significant contribution in this area. One of the co-leader has served on INSERM Scientific Councils over an extended period.

## Assessment of the unit's organisation and life

The team will be co-directed in the next 5-year period by an experienced team leader who has worked for a number of years in the field of early spinal cord neuronal activity, and a new team leader who was recruited recently. The latter is making the transition from postdoctoral fellow to principal investigator. This co-director arrangement will ensure succession planning for the team in the coming years. The new co-leader is supported by a Young Investigator Grant and brings specific new experience of glial cell biology to the team, which will greatly benefit the future research program. Within the team are several experienced postdoctoral scientists, including one who has considerable electrophysiology expertise and another who has contributed importantly to the team's previous work on neuronal gene expression. Hence, there is multi-disciplinary experience and expertise within the team for the next 5-year period, with sufficient personnel, and a good management to conduct the proposed research.

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

The co-directors plus postdoctoral scientists intend to train a new generation of PhD students in the coming years, with 5 trained over the review period; 2 of which have now graduated. Moreover, the team demonstrates a real example of scientific advancement, in the progression of a staff scientist to become co-team leader from a postdoctoral position. It is hoped that the career progress of the other senior scientists in the team will similarly be promoted, either within the university or elsewhere. It would be expected that students on Master courses participate in the research through short-term projects. This is not discussed in detail, but would be a beneficial way to ensure training through research at the most junior level.

## Assessment of the five-year plan and strategy

The 5-year plan of research is clearly thought out and well structured. Three projects are described, the first of which aims to further elucidate the mechanisms regulating early neuronal activity in the embryonic spinal cord (axis 1) while the second and third investigate the role of non-neuronal cell types (microglia and NG2 cells respectively) in interaction with the developing motor neurons. The proposed studies build closely on the preliminary evidence of the previous years' research, and incorporate exciting new techniques such use of optogenetic methods and use of Cre-DTA to ablate specific cell populations. The new work will build upon existing strengths in electrophysiological recording, with innovative use of the 'open book' preparation for recording. The experiments included in the 5-year plan should ensure further significant advancement of knowledge and high impact publications.

## Conclusion

- Strengths and opportunities:

Strengths include the well-established scientific area of enquiry, with many recent achievements in terms of publications and ambitious research plans, with use of exciting new technologies. The multidisciplinary expertise and the range of seniority within the team – especially the promotion of a co-director role – are additional strengths. The collaborations undertaken by the team represent opportunities to expand the range of research areas that can be covered in the coming years.

- Weaknesses and threats:

The team is included in the Vertical Axis that relates to both Mental Illness and Neurological Disease. However, there is no indication in the team's plans that the research will be applied at a more disease-focused level. Instead, the concentration appears to be solely on the fundamental biological mechanisms. While is not a weakness per se, it is perhaps a current limitation of the team's research program and vision. In order to deliver on the research agenda, it seems likely that additional grants would need to be achieved, and there is a risk to the program if this is not forthcoming. There is a major dependence on high quality animal facilities, mainly mouse, and this represents a threat in view of the uncertainty surrounding the Department's animal facilities in the coming years.

- Recommendations:

Additional collaborations, particularly clinical, should be established to provide a more translational outlet for the group's research. It is essential that the new co-leader is seen externally as leading the NG2 work, with senior authorship on publications. It will also be important for him, as team co-director, to participate personally in the Unit's board of team leaders. Clarity about the building program and future animal facilities should be provided to the team co-directors from the University authorities.

# 4 • Team-by-team analysis

**Team 11 :** Neuroplasticity of Reproductive Behaviors

Name of team leader: Ms Sakina MHAOUTY-KODJA

## 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) | | | |
| **N4**: Other professors (PREM, ECC, etc.) | | | |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | 1 | 1 | 1 |
| **N6**: Other contractual staff (without research duties) | | | |
| **TOTAL N1 to N6** | 4 | 4 | 4 |

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

# • Detailed assessments

## Assessment of scientific quality and outputs

The main scientific achievement of the team has been the identification of the role of Androgen receptors in testosterone effects specifically in the brain, then without interference of its peripheral functions. This goal was achieved through the generation of a mouse line in which the AR gene has been deleted exclusively in the brain, using Cre-loxP technology. The approach opens new possibilities for understanding the role of AR and testosterone in the brain. They have shown that this system plays a critical role in the differentiation of several pathways necessary for the establishment of the adult sexual behavior. More recently, they show that the adult brain is highly sensitive to bisphenol A (BPA) that mimics oestrogenic activity. They show that AR may be a target for BPA. In parallel, they show that oxytocin maturation deficiency, due to alteration in the transcription factor Maged1, is associated to abnormal male sexual behavior.

The scientific quality of the 2 groups at the origin of this team (one coming from team E15 and the other from team E7) is good to very good. 17 papers during the last 5 years, 1 JNeurosci, 3 Endocrinology, 1 Hum Mol Genet and 1 Brain. Overall this represents a good scientific production.

## Assessment of the team's academic reputation and appeal

Two staff scientists have been invited to conferences (7) and have presented communications in meeting (2) with associated review papers, 5 selected communications, and they have organized one symposium. This illustrates a good academic reputation for the team leader. The group raised enough funding over the last few years to conduct their research: ANR CES (2009-2012), Afsset APR (2009-2012), Programme Interdisciplinaire de Recherche CNRS (2009***),*** Comité mixte inter-universitaire franco- algérien (2005-2009), Contrat interne IFR 83-Biologie intégrative.

A graduate student won prizes for her work from “Société d’Andrologie de Langue Française” and from “Société de Neuroendocrinologie”, and a post-doctoral fellow had the 2012 prize from the “Société de Neuroendocrinologie”. National and international collaborations with research partners have already been developed and will continue with the same partners or with new collaborators.

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

Conferences were given, oriented towards a more general audience by two members of the team, at the African School UNESCO-IBRO in 2010. No information was given regarding any link with the industry.

## Assessment of the team's organisation and life

This emerging team results from the merger in January 2011 of two groups, one coming from E7 team, and the other from team E15. This merger was approved by the team leaders of the future Institute Neurosciences Paris-Seine. The team is composed by 1 DR2 CNRS, 1 Prof UPMC, 1 MCU UPMC, 1 permanent technician UPMC, 1 assistant-engineer (CDD), 1 Postdoc and 2 PhD students. During the last period, 1 additional postdoc and 5 PhD students were supervised by the three scientists of the team. Weekly meetings and a very close interaction between all the members of the team allowed i) to set up a common functioning and organization and ii) to publish a first common paper and submit a second one.

The funding obtained, as indicated above, allowed the recruitment of two technicians and 1 post-doctorant (CDD contracts) since 2009. The team’s goal is to hire a researcher on a permanent position. Prior to the merger, members of this team have published some common papers, so the team seems to be well organized.

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

Two scientists in the team are members of many committees involved in the of training of students as well as some administrative functions (President of the « Conseil des Enseignements de l’UFR de Biologie » ; Member of Directoire des Formations de l’UPMC (since March 2012), Member of the Conseil de l’Institut de Formation Doctorale, Member of the Conseil de département de la Licence Sciences du Vivant, Member of the EFU de l’Ecole Doctorale « Cerveau, Cognition, Comportement ». Coordinator of “stage de formation continue”: « Cultures de Cellules Animales » (1 to 2 sessions per year + certain stages), Member of the committees M1 et M2 Master “Biologie Intégrative and Physiologie, spécialité Neurosciences”.

7 graduate students were mentored over the period, and 5 already defended get their PhD.

## Assessment of the five-year plan and strategy

This emerging team is interested in the cellular and molecular mechanisms underlying plasticity of the sexual brain to hormonal and environmental stimulations. Besides better understanding of central regulation of female and male fertility, there are practical reasons to elucidate the mechanisms of sexual differentiation and activation in the brain. In recent years, evidence has accumulated to show that various compounds in our environment, either natural (phytoestrogens) or man-made (pesticides, bisphenol A, phtalates) can have endocrine disrupting effects. A potential link between the increased environmental pollution and diseases and dysfunctions related to fertility has been strongly suggested. Their recent studies show that male and female mice exposed to bisphenol A, a widely used compound in food containers, exhibit reduced sexual behavior and delayed puberty, respectively. To understand how BPA or other endocrine disrupters could impact the female and male brain, it is important to progress in the understanding of endogenous hormone effects in physiological conditions and increase the knowledge of the mechanisms underlying their central effects. Indeed, such endocrine disrupters can interfere with hormone actions by binding to or altering the expression of sex steroid receptors.

Two main research objectives are proposed for the upcoming years. The first objective is to analyze the molecular mechanisms underlying the neural regulation of female behavior whereas the second objective involves studies of the molecular mechanisms underlying neural plasticity induced by the first sexual experience in the male brain.

Regarding the first objective, brain-specific ERα and ERß knockout mouse models are proposed to elucidate their respective roles in female behavior. However, it is not explained why these mouse models would be an added value to these studies since there is no real evidence that peripheral ER actions are important in female behavior (which is clearly different from the male, where a complete KO of the AR will lead to a female body type, no penis etc). Another potential problem is that these mouse models lack either ERα or ERß in brain regions important for sexual behavior throughout all life stages and thus that no distinction can be made between developmental and adult actions of estradiol on the brain and behavior. There is strong evidence in the literature that ERα is critical for activating female behavior in adulthood, thus a brain-specific ERα KO will not resolve the role of this receptor in the development of female behavior, simply because their behavior cannot be activated in adulthood.

Regarding the second research objective, it is proposed to study whether a first sexual experience will induce specific changes related to neuroplasticity in the preoptic area of male mice by monitoring gene expression, with a particular attention to the nNOS pathway and free radicals. Then at mid-term proteomic and epigenetic approaches will be used in order to elucidate how a first sexual experience will lead to certain adaptations in the male brain. This objective is rather vague and is not worked out very well. How are they going to determine an epigenetic contribution to this phenomenon? What proteins are they going to be looking for? Also is there a link to endocrine disruptors and their effects on the brain and this particular research line?

Overall, the strategy of the project is not very well described and the link between the research of both staff scientists is not clear as well, and not well defined.

## Conclusion

- Strengths and opportunities:

The association of the 2 groups could be fruitful if their research objectives are more clearly identified. The proteomic platform in the campus represents an important opportunity; however, again, the aim concerning the analysis of the proteome is not clear.

In addition to the common use of the UMR material, the emerging team has its own specific material necessary for the conduction of their projects (ultrasonic vocalization apparatus, two systems of recording and video tracking, nanodrop, systems for DNA, RNA and protein electrophoresis and transfer, PCR machine, gel analysis system, vibratome, cryotome...).

In the context of the emerging team, a first funding involving all team members has been recently obtained (ANR Blanc 2012).

- Weaknesses and threats:

The team has been formed recently and the objectives are not clearly identified. Reorientations are needed and priorities must be defined.

The team members need to be geographically grouped in the same laboratory. This is planned in 2013 or 2014 depending on the progress of the A3 renovation (UPMC-Nerf program).

Their projects require a functional animal house facility where all parameters (temperature, noise...) are controlled. Since April 2012, many of their behavioural studies did not work or stopped due to the noise generated by the renovation of A and B buildings where the animal house facilities and phenotyping and experimental houses are housed.

- Recommendations:

To be successful the merger of these 2 partners is very important, and needs to define a clear common project with clear objectives. The role of each PI needs to be clarified and better defined. Stronger collaborations with the other groups in the unit will likely be also beneficial.

# 4 • Team-by-team analysis

**Team 12 :** Axonal Growth and Regeneration

Name of team leader: Ms Fatiha NOTHIAS

## 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 | 2 | 3 | 3 |
| **N3**: Other permanent staff (without research duties) | | | |
| **N4**: Other professors (PREM, ECC, etc.) | | | |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | 1 | 2 | 1 |
| **N6**: Other contractual staff (without research duties) | | | |
| **TOTAL N1 to N6** | 4 | 6 | 5 |

| Team workforce | Number as at 30/06/2012 | Number as at 01/01/2014 |
|---|---|---|
| Doctoral students | 1 | |
| Theses defended | 4 | |
| Postdoctoral students having spent at least 12 months in the unit | 1 | |
| Number of Research Supervisor Qualifications (HDR) taken | 0 | |
| Qualified research supervisors (with an HDR) or similar positions | 1 | 3 |

# • Detailed assessments

## Assessment of scientific quality and outputs

The overall research goal of the team addresses the molecular and cellular mechanisms underlying axon regeneration, with the final aim of contributing to the development of repair strategies for traumatic injury to the nervous system. The team's research efforts are divided into three main research aims; two address, essentially, the fundamental functions of two (rather large) proteins - MAP1B and Ahnak. The research on MAP1B included investigation into the signaling system controlling phosphorylation and function of this MAP during cytoskeletal remodelling required for axon growth. Ahnak, on the other hand, was identified by the team in a differential screen that studied genes up-regulated after spinal cord injury, and subsequent work demonstrated an involvement of Ahnak in Schwann cell morphology and function, as well as the maintenance of proper integrity of peripheral nerves. The third branch of research undertaken in the team is concerned with the generation of novel biomaterial designed for tissue engineering. This part of the team's activity is very original and has generated interactions with national and international groups. Given the relatively small size of the group and the known difficulty of working with proteins that are of high molecular weight, the committee identified a weakness in the project as these appear too broad. The group has had a good scientific output with 12 identified papers, 6 of those appear to have been published with members of the group as first and/or last author. It is noticeable, however, that the highest impact publications resulted from collaborations of the team at national or at international level. This is a good production, the highest impact paper being J. Neuroscience.

At least three additional papers are being prepared. Making priorities amongst these three stories would certainly help finish one or may be more of these.

During the creation of the UMR 7224, one staff scientist joined the team, as her research topic was identified as being closely related to that of the team; however, she will now head her own 'emerging team' in the new structure of the Department of Neuroscience.

## Assessment of the team's academic reputation and appeal

A number of national and international collaborations have been established, providing the team with mutant mice and different cDNA sequences for functional analyses. These include groups at University of Vienna, Institute. Cochin, Paris, Massachusetts University, University of Cambridge, UK, Institute of Neurosciences, Grenoble.. Almost all of these collaborations have resulted in publications. It is, however, noticeable that the team has a low international visibility: there are currently few foreign post-docs working in the lab and the members of the team receive relatively few invitation to present their work at international level.

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

The team has attracted funding in the past, but its current budget is not particularly large. The leader identified also in the SWOT analyses that there is a continuing reduction in the basic budget over the last years, which has been difficult to compensate though third party grants and allocations.

The collaboration with a team in Lyon (IMP, UMR CNRS 5223, Univ. Lyon1) led to the registration of a patent with equal contribution in 2012. A scientific agreement contract has also been signed with Bioforce Nanosciences Inc. (Ames, USA) in 2008.

## Assessment of the team's organisation and life

The team is currently of small to medium size. It seems that several postdocs have left the team during the course of the last period. In addition to the research director, the team consists of only one additional Researcher (first class), two University lecturers (one joined in 2012), one technician and one PhD student. Out of the three proposed research directions, two will be jointly directed by the team leader and one staff scientist (Aims 1 and 3), whilst one will be under the direction of the other Researcher. The team may well experience a problem with manpower, especially given that salary support of scientists (at PhD and postdoc level) who have been indicated as working on specific research aims has not yet been attracted. However, the recent addition of an assistant professor with strong expertise in cellular neurobiology, is likely to alleviate some of these constraints, especially with respect to the experimental work described in Aim 1.

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

Five Master students and six PhD students have trained with the team leader; thus the group is very actively involved in the education and training of junior scientist. In addition to this, the team leader continues to provide workshops in Neurosciences and cellular and molecular aspects in Neurobiology at Master level, as well as serves on a number of different university boards at PhD level (i.e. PhD admision and PhD jury). These involvements indicate a genuine interest of the team in student training, and the development of administrative and managerial skills associated with this task.

## Assessment of the five-year plan and strategy

For the period, the team plans to build upon the recent work published by the group. The three aims focus on questions regarding, in Aim 1, the detailed assessment of regulatory kinase inputs onto the microtubule associated protein MAP1B. Specifically, the team will test the physiological significance of different proline directed kinases (including CDK5, GSK-3 and JNK) in the control of MAP1B function in different cell types. They propose to use MAP1B deficient Cos-7 cell as an initial functional screening platform, which will be complimented by testing rescue of MAP1B deficient DRG neurons using phosphorylation mutants. One continuing problem that is encountered in numerous labs working in the MAP1B field is the large size of the protein, with the consequential labour-intensive generation of cDNA vectors and associated difficulties in cellular manipulation. However, they seem to tackle this problem in collaboration with team E7. Another branch within the MAP1B work will focus on aspects related to the control of intracellular trafficking responses, which will entail epistasis experiments in combination with defined extracellular signals. Overall, the proposed experiments seem less hypothesis-driven, but given the preliminary nature of the underlying rationale for the proposed work, its feasibility is difficult to assess at this stage. In Aim 2, they propose work that is aimed at analysing Ahnak, another very large protein, in Schwann cell function. The group has generated in vivo lentiviral shRNA knockdown conditions in sciatic nerves of mice, which will complement the characterisation of Ahnak-ko mice, and undoubtedly produce interesting results of this rather understudied protein in Schwann cells. The experiments are all planned ambitiously; they encompass detailed structural, functional, as well as proteomics analyses of protein-protein interactions using mass spec analyses. Finally, in the Aim 3, the team proposes to continue the generation of bio-scaffolds that are applicable to promoting axon regeneration following traumatic lesion to the nervous system. Within this aim, the team hopes to work towards testing bio-scaffold in preclinical settings. It is reasonable to expect that future work in the team will consolidate the position of this approach as highly competitive in the field of regenerative medicine. The goals are well thought out, with clear lines of investigations and sets of feasible experiments.

During the site visit, the committee recognised that the nature of the planned work may benefit from focussing the work on a smaller number of aims; i.e. it was recommended that the two work plans associated with the work on MAP1B could well be reduced to one. Whilst the Ahnak work as laid out in the proposal seemed rather preliminary, discussions with group members during the site visit raised the expectations into the feasibility of the proposed experiments. This notwithstanding, a strong recommendation was to focus specific projects undertaken by the team in order to be able to consolidate the position of the team within this fast moving and competitive area of research.

## Conclusion

- Strengths and opportunities:

The team members appear to possess a wide array of expertise, including experimental work in animal models in vivo, cell biology approaches for functional analysis (micro contact printing) and extensive biochemistry.

- Weaknesses and threats:

One immediate weakness may be seen in the potential limitations of the team’s access to high-end time-lapse microscopy systems, which are absolutely necessary for a number of proposed projects.

- Recommendations:

The committee noticed that the team has several manuscripts in preparation and the results of this work appear to provide the basis for several of the proposed Aims. In order to remain competitive in this particular area of research the team urgently needs to finalise those manuscripts for submission, which will also be essential to attract essential grant support that will warrant progression of the team’s work.

# 4 • Team-by-team analysis

**Team 13 :** Navigation, Memory and Aging

Name of team leader: Ms Laure RONDI-REIG

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

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

# • Detailed assessments

## Assessment of scientific quality and outputs

The scientific quality and output of the team is excellent and very promising for the near future.

The team was created only recently in 2007 with the help of two grants (ANR, FRM) obtained by the team leader. The main research focus is on the analysis of the neural processes related to memory as well as how aging affects these processes using both mouse models and human subject. They recently challenged one of the key theories in neuroscience about the implication of long term depression (LTD) occuring in the cerebellum during motor learning. They found that cerebellar LTD is not required for motor learning, but instead, it is important in the mental construction of the representation of space which suggests that the cerebellum is anatomically and functionally connected to the hippocampus. This led to an important publication in Science in 2011. In addition, they have developed a behavioral device making it possible to detect memory loss related to aging in the mouse as well as in humans.

Over the last three years, some very high quality papers have been produced (2 in Journal of Neuroscience, 1 in PNAS, 1 in Science); a total of 13 publications (9 research papers and 4 reviews) have been produced as a research team in last 5 years. The team has been quite successful in obtaining research funding, although the PI did not obtain ERC funding, but she will try again in the next call.

## Assessment of the team's academic reputation and appeal

The team seems to be well-established and has several collaborations at the national and international level. The leader received the bronze medal from the CNRS in 2010 given to “young CNRS researchers recognized as talented specialists of their domain of expertise” as well as a prize from the FRM for her research on aging in 2012. Furthermore, she has been invited five times to give a talk at international conferences. However, two staff scientists have not been invited regularly to give a talk at international conferences (albeit giving poster presentations of their work). So this should be improved over the years. The team is part of the Laboratory of Excellence BioPsy.

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

Their research has been highlighted in a documentary made by Swiss TV Romande. Several video and radio performances have been performed as well. Two interviews were done via the internet (New Scientist). Their research has been diffused mostly at the local (UPMC) and national (CNRS) level. No patents have been deposed by the team. Perhaps they should have done so regarding the development of the behavioral device used for detecting memory loss in mice and humans?

## Assessment of the unit's organisation and life

Overall the team is well-organized. It consists of the leader, 1 CNRS CR1 scientist and 2 assisant professors UPMC who have both quite a heavy teaching load. In 2013 one will leave the team to start his own team, but a new CR1 researcher will join the team who will be mostly involved in the neuroimaging studies of the human brain. One scientist will retire in 2014. There is no mention of her being remplaced. Four PhD students have joined the team over the last 5 years, one defended in 2011, and two new postdoctoral fellows arrived in late 2012, so there seems to be a good dynamic in the team. Furthermore the team is supported by 2 engineers. So the team consists of a total of 9 people, an average size team within the Neuroscience Unit.

The lab space and facilities seem to be adequate to conduct their research. They have a behavioral facility of three independent rooms that can be controlled for noise, temperature and light, as well as that they are equipped with a video tracking system, so all the necessary equipment is present for the behavioral analyses. However,they might face some potential problems later regarding the mouse facility.

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

The team is involved in training through research. A total of 8 masters' students and 7 PhD students have been supervised by either of the staff scientists. Four of the 7 graduate students have now defended their PhD (within 4 years) and have found a job. This is a good score.

Furthermore, the assistant professors have teaching duties in Masters' 1st and 2nd years. Scientists from the teams also give courses related to Neuroscience.

## Assessment of the five-year plan and strategy

The main research question concerns the analysis of the role of the cerebellum in acquiring, organizing, and employing spatial knowledge in goal-directed navigation. They recently challenged one of the key theories in neuroscience about the implication of long term depression (LTD) occuring in the cerebellum during motor learning. They actually found that cerebellar LTD is not required for motor learning, but instead, it is important in the mental construction of the representation of the space which suggests that the cerebellum is anatomically and functionally connected to the hippocampus. So the focus of their research seems to move away from studies on aging to the role of the cerebellum in spatial representations and in navigation. The five-year plan is basically built on their latest publication in Science. Studies in both mice and humans are proposed. Briefly, using mouse models, they will determine 1) whether the integration of external and self-motion information required for spatial representation in the hippocampal and parahippocampal system relay on mechanisms of plasticity in the cerebellum, and 2) which regions of the cerebellar cortex are anatomically and functionally interconnected with the cortical and hippocampal areas involved in navigation and spatial representation.

One could ask whether objective 2 and in particularly subtask 2.1 should not preceed objective 1? It seems to be important to first determine whether there is any anatomical and functional connection between the hippocampus and the cerebellum before analyzing the role of cerebellar plasticity in hippocampal functioning. Another potential problem is that the postdoc involved with subtask 2.2 (synchronized activity between the cerebellum and navigation forebrain areas) starts around the same time (october 2012) as the postdoc involved with subtask 2.1 (organization of the anatomo-functional connections between the cerebellum and navigation forebrain areas) whereas subtask 2.2 clearly depends on the outcome of subtask 2.1. It needs to be determined first which cerebellar regions are anatomically connected to the forebrain navigation areas to know where one should implant recording electrodes in the cerebellar cortical areas. At present, this information is still lacking so how can one try to disrupt or rescue the PKC-dependent LTD occuring at PF-PC synapses in specific subregions of the adult cerebellum if these regions have yet to be determined (as described under subtask 1.2)?

Regarding the human studies, they will analyze the role of the cerebellum in spatial representations during navigation in humans using fMRI. Few details are provided on the subjects (Men versus Women, Young versus Old, Patients versus Non-Patients). As stated, the human studies might ultimately provide new tools to analyze deficits in spatial representations due to sensori-motor dysfunctions. However, it is not clear in which context and how these studies might help design new cognitive therapy for memory disorders.

## Conclusion

- Strengths and opportunities:

The team is built on several permanent (5) and non-permanent members (PhD students, postdoctoral fellows). The team is dynamic. Excellent quality of scientific publications (2x Journal of Neuroscience, 1x PNAS, 1x Science), good funding, translational approach of their research question, i.e. using both transgenic mouse and human studies. Use of cutting-edge techniques combining behavior and electrophysiological recording with anatomical and functional techniques such as track tracing and cellular imaging.

- Weaknesses and threats:

Although the team has several very high quality papers as mentioned above, the overall scientific production is a bit on the low side considering the size of the team and the number of permanent members. The h-indexes are rather low for each permanent member regarding their age/experience (from 14 to 6). Perhaps not enough international visibility? The assistant professors have no international invitations so far. Furthermore, the bioinformatician does not hold a permanent contract. This could be a potential threat to the group.

- Recommendations:

Improve the international visibility of the team by attracting more foreigners (post-docs, visiting professors, sabbaticals etc).

Obtain European funding to increase the visibility of the team at the European level.

# 4 • Team-by-team analysis

**Team 14 :** Development and Plasticity of Neural Networks

Name of team leader: Mr Alain TREMBLEAU

## 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 | | 2 | |
| **N3**: Other permanent staff (without research duties) | | | |
| **N4**: Other professors (PREM, ECC, etc.) | | | |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | 2 | 2 | 1 |
| **N6**: Other contractual staff (without research duties) | | | |
| **TOTAL N1 to N6** | 5 | 7 | 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 | 2 | |
| 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

The team was created in April 2007 as an Avenir/INSERM group with a completely new lab. The scientific quality of the team is very good. During the first 5 years of its life, the group has set the basis for investigations on the development and plasticity of the mouse olfactory system and was the main promoter team. The PI of the DPRN team is however the scientific advisor of the EM facility and the viral vector facilities. Two main biological questions were addressed: 1) The role of local synthesis of Odorant Receptors (ORs) in axons in the sorting of sensory neuron axons; 2) The role of dendritic local translation in the morphological and functional integration of granule cells into the adult Olfactory Bulb network. The group was the first to show that OR mRNAs are translated in sensory neuron axons, and that their transport and translation in this compartment is developmentally-regulated. They identified Fragile X Mental Retardation Protein as a regulator of morphological differentiation and functional insertion of neoneurons into the adult olfactory bulb and demonstrated that dendritic translation of CaMKII mRNA is critical for olfactor learning.

The associated group Neuronal and Glial Differentiation (DNG) covers two fields: secondary injury after traumatic lesion in spinal cord, and axon regeneration in cerebellum. They demonstrated that JNK inhibition has neuroprotective effects and results in an increased sparing of white matter at the lesion site. They also found that thyroid hormone T3 acts through the Klf9 transcription factor to determine the end of the critical period during which Purkinje cells have the ability to regenerate their axon. From these results the DNG group proposed the concept of Purkinje cell metamorphosis as part of a general program triggered by T3 in concert with body maturation.

Both teams have a very good scientific production. The DPRN team published 9 peer reviewed papers and 2 review articles of which 3 have high IF, 1 is in a top journal (PNAS); the DGN team also has 9 peer reviewed papers and 2 review articles, 3 have high IF, 1 is in a top journal (PNAS). Members of the combined teams have other 17 publications obtained outside the team.

## Assessment of the team's academic reputation and appeal

The team leader is an established scientist with several high level national and international collaborations. Attractiveness of the group is very good and is witnessed by the presence of international students and two visiting professors from the USA. These collaborations led to 2 published papers and one NIH grant, and organization of an international Symposium. A collaboration with a group in Prague was supported by a grant for the salary of a co-supervised PhD student. The group has strong academic connections with the main institutions in the area of Paris and with other good labs in the country. The growing international reputation and scientific visibility of the PI is also shared by the other permanent staff and by the PI of the associated DNG team. Although the number of publications is not particularly high, likely due to the initial start-up phase of the lab, the PI has published in well reputed and highly visible journals. The number of citations of the recent papers stemming from the new research projects of the DPRN team indicates the interest of the scientific community for the original research topics of the group. The scientific production of the DNG team is of comparable level and the future collaboration with the DPRN is predicted to be highly beneficial for both groups reputation and visibility.

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

The dissemination activities have been carried out at very good level, but the group relies entirely upon the efforts of one staff scientist who has been coordinator of the Brain-Awareness Week (Semaine du Cerveau) for Paris in 2010 and 2011. Due to the number of events and various research centres involved, this is certainly a remarkable work with high impact on the social and cultural life of the city. The team, does not seem to consider the possibility to interact with economical entities and has presently, no programmes for technology transfer towards industrial exploitation of the research results. The group participates to a network with clinicians (Labex) but, at present, no collaboration has started.

## Assessment of the team's organisation and life

The teams' organization is very good. The units comprises 1 Prof., 2 Lecturers, with high teaching duties plus 1 technician, 2 postdocs, 2 Ph.D. students and 1 masters student. The DGN team, created in 2002 as an ATIP/CNRS team, currently comprises 1 PI, 1 lecturer (2 having full research tenure positions at CNRS and INSERM, respectively) and 2 technicians. The fact that the DNG team will join the DPRN team, is a smart decision and it is expected that the presence of two full-time researchers will re-inforce both the organization of the team, and the development of ongoing projects.

The impressive involvement of the PI and the other permanent staff members in the organization of Neuroscience Schools (PhD and Master) and technical core facilities in collaboration with various institutions in Paris is certainly a major contribution of the unit to the scientific life in Paris and may have an important return for the group. The team's benefits stemming for the affiliation to the Paris School of Neuroscience (ENP), the BioPsy Labex network and other many local scientific initiatives are in terms of scientific exchanges and access to core facilities. Apparently, collaborations with clinicians through the Labex project have not yet initiated.

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

Training of young scientists is excellent and is a major strength of the combined team: 8 post-docs (5 DPRN + 3 DGN), 5 PhDs (4 DPRN + 1 DGN) and several Master students.

The team leader is the current Director of the Masters of Neurosci. program at UPMC (130 students each year), and will become Director of the Neurosci. Ph.D. program ED3C "Brain, Cognition, Behavior" (350 PhD students) in Jan. 2013. He has created, with another scientist, a multidisciplinary Bachelor program "Life Science and Social Sciences", between UPMC and IEP Sciences-Po Paris and is co-Director since this creation of the Pasteur Course "Development and Plasticity of the Nervous System" (a 5 week-long international workshop held every Fall for Masters, PhD and post-PhD trainees).

One staff scientist is the current head of the Neuroscience program of the European Masters in Genetics of Univ. Paris-Diderot. PhD students and post-doc had publications in the last years and do seem to have continued their career in science.

## Assessment of the five-year plan and strategy

The research plan for the next five years has been designed with very good strategy and appears feasible as it is based upon consolidated expertise. The team aims at understanding the mechanisms by which the local translation of mRNAs in developing axons and dendrites regulates the development and plasticity of the olfactory bulb neural network, characterized by an adult neurogenesis. The project builds on important previous studies which identified a novel role of translation of ORs mRNAs in axons in sorting sensory axons through a combined in vivo analysis of olfactory neurons development with trafficking and translation of axonal mRNAs. The project has the following aims:

- (Aim 1) To understand the molecular mechanisms regulating the synthesis of ORs in axons and the OR-dependent axonal sorting,

- (Aim 2) to characterize the molecular and cellular mechanisms regulating the functional insertion and structural plasticity of neoneurons into adult networks in response to learning with a focus on activity-dependent functions of FMRP and its target mRNAs in regulating the remodelling of the adult brain circuits.

In Aim 1, the team will identify the cis-acting elements (sequences of the OR mRNAs) and trans-acting factors (RNA-binding proteins) involved in OR mRNA transport and translation using transfection of reporters in OSNs in culture. In addition, they will study the expression of OR mRNA variants in the ofactory bulb, by qPCR, in situ hybridization and will determine their translational status in polysomes preparations. Similarly to the strategy used for CaMKII, the team plans to generate with collaborators transgenic mice that lack the trafficking elements of one or more ORs to seek further support to their hypothesis that the role of axonal targeting of OR mRNA is to favor homotypic fasciculation of axons through the local translation of these receptors.

In addition, they will further characterize the localization of the translational machinery by immunohistological techniques at electron and confocal microscopes in OB axons in vivo. The sites of active translation will be identified by analysis of incorporation of fluorescent AHA aminoacids. Within the same collaboration (supported by an NIH grant). Using an ex vivo explant culture of the olfactory system and mice expressing the M72 OR and GFP in a majority of immature OSNs, they plan to study fasciculation of axons with or without local translation of OR mRNAs. Additional experiments will be done on cultures of OSN explants in microfluidic chambers allowing the physical separation of OSN axons from their cell bodies. Using the microfluidic system, homotypic fasciculation and sorting of OSN axons will be further studied to create matematical models and investigate signaling pathways.

In the Aim 2, the team will investigate if olfactory learning induces morphological changes of OB neoneurons using labeling of neoGCs with a GFP-expressing lentivirus. They will compare the learning-induced morphological modifications of neonate-born versus adult-born neurons and will study the involvement of FMRP by using genetically engineered mice (Nestin::CreERT2 X FMR1flox/flox), in which it is possible to induce the mutation of Fmr1 in all newborn neurons. Using biochemical tools, they plan to analyze the local translation of several FMRP target mRNAs encoding plasticity genes such as CamKII, Arc, Map1B, PSD95, Shank1, SAPAP3/4, profilin, rac1, PP2Ac. Moreover, they will analyze the local translation of Kaede-CamKII3'UTR reporter in wt or FMR1 mutated spines by live imaging on OB slices coupled to electrophysiology. Finally, antagonists of group I metabotropic receptor (previously used in clinical trials for Fragile-X) will be tested for their ability to rescue the phenotype observed in FMR1-ko olfactory neurons.

The plan involves the strategic combination of two groups in 2014: the DPRN team who started the project and has established important international collaborations and strong local academic connections which warrants continuous recruitment of students; and the DNG with full research committed personnel and complementary expertise. Of note, an INSERM researcher will join the DGN team at the end of 2014 to Paris to bring in the group his experience in RNA/protein interactions and olfactory bulb development. This "merge" appears as a smart planning as the two groups have complementary expertise to tackle dynamics of olfactory sensory axon growth, sorting and differentiation.

## Conclusion

● Strengths and opportunities:

- Very good planning and organization,

- High national and international visibility of the team,

- Specialization of the group on a single model of plasticity in vivo (olfactory system),

- Association with a strong research group (DNG) with complementary expertise and converging interests,

- Uniqueness of the topic: mRNA trafficking and translation in axons of olfactory and analysis of olfactory neurons growth and integration in response to learning,

- Wide range of well integrated approaches applied to a specific biological problem: from cellular to behavioral analysis,

-Full accessibility to core facilities essential for the group,

- Selective and highly relevant international and national collaborations with leading labs in the field,

- Very good fundings,

- Affiliation to local networks of excellence,

- Excellent capacity for training new generations of scientists.

● Weaknesses and threats:

While the DNG and DPRN groups have clear converging interests (e.g.integration of neurons within a preexisting network, axonal navigation), they use different models (e.g. olfactory system vs. cerebellum) and still have different biological questions which appear not yet integrated and may disperse the focus.

The part of the project which falls within the DPRN group expertise is very well described however, the part of the project on the identification of RBPs and cis-acting sequences that will require the expertise of the DNG group lacks of several details on the research strategy.

Although certainly appropriate from a scientific point of view, the clinical relevance of the studies in olfactory bulb for Fragile-X patients may not be so high to attract interest of funding bodies.

In addition to teaching duties, the group leader and the other two permanent staff are involved in the direction of additional courses and schools, which is likely to determine a heavy administrative workload.

The involvement in several local networks may also represent a threat, if they will not have a clear return for the team.

- Recommendations:

The team as a whole will have to consider carefully how to keep the focus and allocate efforts and resources coherently in order to avoid non-integrated projects between the DNG and the DPRN groups.

A relatively novel project on identification of the molecular mechanisms of OR mRNA transport and translation will be started. To be successfull, this project will likely need to absorb a significant part of the group's efforts and resources and therefore, a careful planning is recommended.

The publication output should be improved (but the group has already some new papers submitted).

Evaluation of alternative options with repect to Fragile-X syndrome (through Labex or other networks) to find other (genetic) diseases in which defects in olfactory bulb are highly relevant for the patients' life should be considered in view of future search for funding and possible clinical applications.

Accurate management of the team is fundamental. In particular, a definition on the internal responsabilities and leadership should be made at the time of the "merge" between the DNG and DPRN groups.

The PI should seek support by a secretary assistant for the administrative work (it seems to be possible, at least for the PhD School).

The relationship with the other institutions, networks of excellence and multiple affiliations in Paris should be managed appropriately in order to avoid time investments without a return for the group.

# 4 • Team-by-team analysis

**Team 15 :** Gene Regulation and Adaptive Behaviors

Name of team leader: Mr François TRONCHE

## 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 | 5 | 4 | 3 |
| **N3**: Other permanent staff (without research duties) | | | |
| **N4**: Other professors (PREM, ECC, etc.) | | | |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | 3 | 3 | 2 |
| **N6**: Other contractual staff<br>**N6**: Other contractual staff (without research duties) | 2 | | |
| **TOTAL N1 to N6** | 11 | 8 | 6 |

| Unit workforce | Number as at 30/06/2012 | Number as at 01/01/2014 |
|---|---|---|
| Doctoral students | 6 | |
| Theses defended | 7 | |
| Postdoctoral students having spent at least 12 months in the unit* | 3 | |
| Number of Research Supervisor Qualifications (HDR) taken | 2 | |
| Qualified research supervisors (with an HDR) or similar positions | 5 | 4 |

# • Detailed assessments

## Assessment of scientific quality and outputs

The overall research objective of the team is to characterize cellular and molecular mechanisms by which emotional life experiences and stress may lead to physiological and behavioral changes that could result in pathological brain defects associated with psychiatric disorders. To address this problem, the team focuses on the functional and behavioral analysis of glucocorticoid (GR) and androgen receptors (AR) modulation in specific monoaminergic neuronal populations through the development of numerous mice models that carry AR and GR gene mutations in dopaminergic and serotonergic neurons.

The scientific output of this team has been outstanding during the past four years. The members of the future team have published a total of 32 peer-reviewed papers (including one in Science). In addition a group that will join the team in 2014 has published 41 papers. Five more papers have been published outside the group in collaboration with other teams in France or elsewhere. In general, the manuscripts were published in journals with very good to excellent impact factors, including 3 J Neurosci, 1 Science, 1 Nature Neuroscience, 1 PNAS, 1 Brain, 1 Biol Psychiatry. In addition to a strong publication record, the team has also been able to get solid external funding from ANR and other federal and private sources, including ANR Blanche, until 2014. The addition of new members to the team in 2014 is a major strenght that should help them move forward successfully in 2014-2018 funding year.

## Assessment of the team's academic reputation and appeal

The national and international reputation of the team is outstanding. Both leaders have excellent reputation in their field which benefits the Unit's reputation and appeal at the national and international levels. In total, both of them and some members of their team have been invited 32 times to give talks at international meetings. Team leaders have organized numerous meetings and workshops at the national and international level (11 in total), sit on two editorial boards, participate in grant and paper reviews for top journals (Nature, J Neurosci, etc.). One staff scientist received a prize from the European College of Neuropsychopharmacology in 2009. Another scientist is also a strong leader who should help strengthen the reputation and appeal of the Unit. Three contracts have been secured with industry.

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

The teams' interaction with social, economic and cultural environment is excellent. Team members have given conferences to the general public (n=8) and professional associations (n=9). Both leaders also have had some collaboration with the industry (3 contracts + 5 strains of mice distribution by EMMA). One patent has been filed and five strains of mice distributed by the EMMA Consortium.

## Assessment of the team's organisation and life

The teams' organization and life is very good to excellent, though nothing overly special is mentioned in the report about the general organization. Both groups offer complementary expertise and seem to work well together based on the very good productivity of trainees in both groups. They hold weekly lab meetings to review data and progress.

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

The team involvement in training through research is excellent. A total of five M1, seven M2 and one student from an engineer school, as well as three postdocs have been trained since 2007 in one group, while one M1, three M2 and one postdoc went through the other group during the same period. Currently three PhD students are part of the team. Many students and postdocs who were trained in this team succeeded to get good academic/industry positions (engineering, postdoc position in US or Europe). In addition to mentoring duties, both team leaders give lectures to M1 and M2 students (40 hrs/year). The team leader also gave a lecture to students in Croatia during the past funding period.

## Assessment of the five-year plan and strategy

The proposed plan and strategy for the next five years is outstanding. The proposed research programs are strong, well integrated and complementary to each other. The arrival of a new group will help make this even stronger. The emphasis on GR and AR genes, stress and related pathogenesis of stress-related brain disorders is excellent and has been very successful during the previous period. It is an exciting and highly valuable area of research to be further explored because of the critical role stress plays in various neurological and psychiatric brain disorders. The translational significance of the proposed work towards the understanding of human disorders and the development of new therapeutics is important. The techniques being used are at the cutting edge and suitable to address the main goals of the proposed studies. The excellent network of national and international collaborations the team leaders have established will help them achieve the proposed goals of their studies.

## Conclusion

●Strengths and opportunities:

- Outstanding leaders with national and international recognition,

- Solid team of strong investigators with excellent productivity and complementary technical expertise,

- Excellent funding from external sources in past five years,

- Recruitment of new highly promising investigators,

- Research strategy is well designed and scientific issues under study are highly relevant for human disorders,

- Translational aspect of research is very strong and the scientific collaborations are put in place to make sure they flourish,

- Team provides a suitable environment for training PhDs and postdocs who can get strong positions,

- Possible collaborations with clinical field through Labex is well developed and perfectly suited for the work done in this team.

●Weaknesses and threats:

Uncertainty about building renovation and expansion of animal facilities may impact productivity, if not achieved in coming years because of reduced capabilities for mice breeding. This issue is particularly relevant for this team because of their interest in stress-related disorders. The team should pay closer attention to compensatory developmental changes in gene regulation in their various strains of mice.

●Recommendations:

The unit and University must ensure that scientists in this team and others have access to upgraded infrastructure for animal breeding and expansion.

The program in place is very strong and has been very successful in past years. The leaders and team members are encouraged to build up on this strong foundation and continue along the same path.

# 5 • Conduct of the visit

Visit dates:

Start: Wednesday, 5, december, 2012", at 8:00 am

End: Friday, 7, december, 2012", at 5:00 pm

Visit site(s): Barre bat. B, 5h floor

Institution: UMPC

Address : quai St Bernard, Paris

Specific premises visited: no laboratory or platform visit could be organized, due to a lack of time

## Conduct or programme of visit:

The visit took place within the B building, Quai St Bernard, on the main UPMC campus, during three full days, from 8am to 7pm, on the 5-7 December 2012. After a general introduction by the AERES representative and the chairman, a 30 min general presentation of the unit by the future director was given in the presence of most of the group leaders and some additional personnel of the unit, followed by 30 min discussion. Each group leader presented the past activities and projects for 25 min followed by 20 min discussion in the presence of the team members and the director. The director and team members left the room 5 min before the end to allow a "private" discussion between the AERES committee members and each group leader. Then 10 minutes discussion was allowed between the AERES experts to discuss and evaluate the quality of the team on the 6 different aspects requested by the AERES. At the end of the first two days, a door-closed meeting of 1-2 hours was conducted to qualify each team being evaluated during the day. The committee was split into three groups each having one hour discussion with i) the students and post-doctoral fellows, ii) the researchers with permanent position, excluding the team leaders, and iii) the technicians and engineer staff. Half an hour exchange with the representatives of the university Pierre et Marie Curie (UPMC), the research organization (CNRS and INSERM), the hospital (CHU) took place the last day, before the final door closed meeting.

Two technician representatives of INSERM (CSS6) and CNRS (section 25) were present on site during the visit. They attended the presentation and discussion of most teams, but did not participate in the discussion, nor remain in the room during the 5 min "private" discussion with the team leader. They organized a general discussion with the Engineers and technicians, in preparation of the one with the AERES committee representatives. They did not participate in the discussion with the AERES committee representative with the technical staff.

## Specific points to be mentioned:

The president want to thank all experts from the committee for their very active participation during the discussion, their constructive questions and remarks to the team leaders, bringing about a very nice humane and scientific atmosphere, optimal for such a unit evaluation.

The committee regrets to not have had the possibility to visit the laboratory and the platforms during the 3 days of the visit (in particularly the animal facility).

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

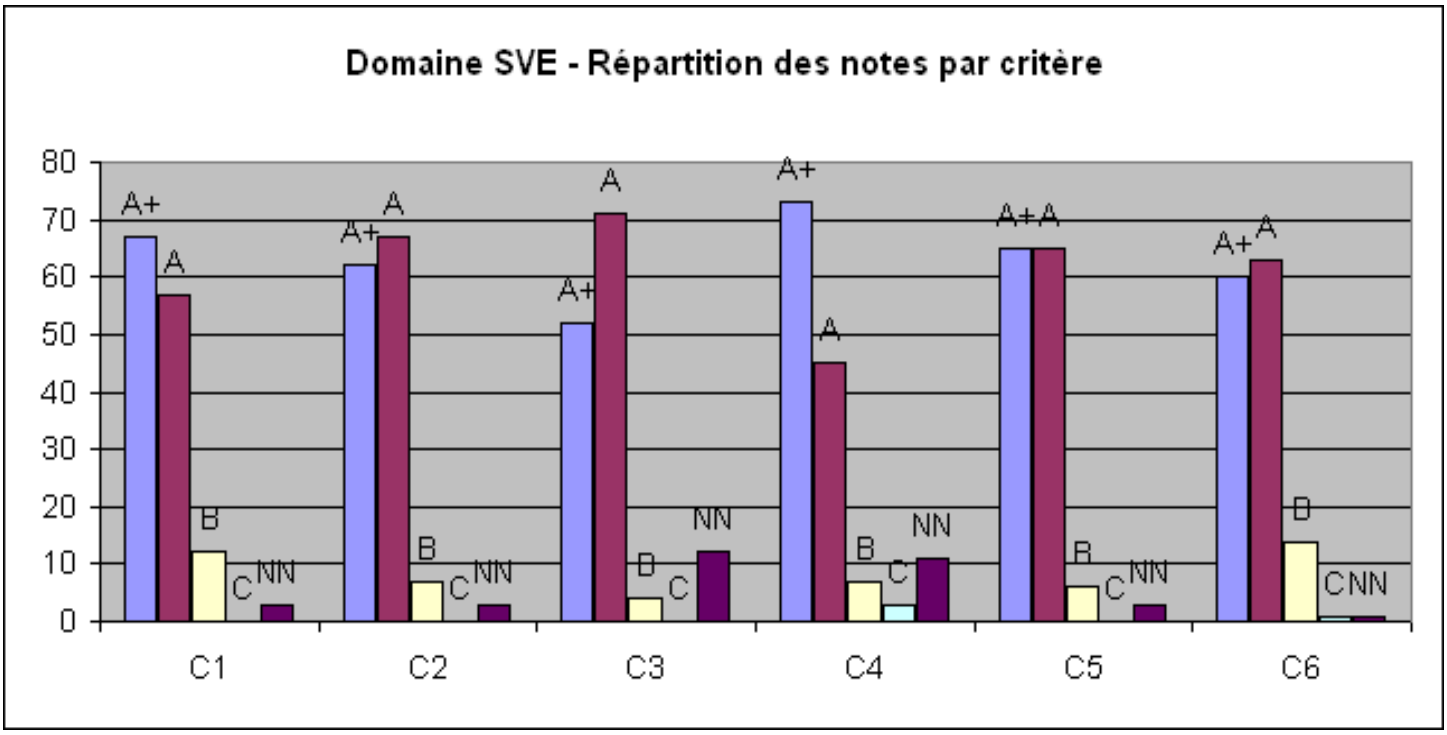
## Grades

| 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 23 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 Neurosciences Paris Seine, porté par M. Chneiweiss. 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
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# Answers to the AERES Report concerning Neuroscience Paris Seine Unit

## *NPS general introduction*

We regret the high heterogeneity of the reports for each team, a minimal skeleton of common criterias should have been more fair.

## *1. Team 1 Catalina Betancur*

### 1. Assessment of the unit's academic reputation and appeal: the "10 presentations at international conferences"

Include an invitation to speak at a Gordon Research Conference in 2012.

### 2. Assessment of the unit's involvement in training through research

*"Despite her long-standing academic activity (>10 years), the team leader has a relatively limited research training experience (4 master students, 3 PhD students, 2 technicians, 2 psychologists), that clearly reflects the small size of her research group through these years."*



Until she became the leader of an emerging team in 2009, C. Betancur was part of teams led by M. Leboyer and then B. Giros; during this period she was actively involved in the training of several PhD students even though she was not the official supervisor. It was only in 2009, when she became independent, that she started to receive directly requests from students wanting to work with her. Being the only researcher with a permanent position in the team, the number of PhD students she currently supervises (2) is the maximum allowed by the doctoral school at UPMC.

### 3. Assessment of the unit's involvement in training through research

*“Team E1 did not show attractiveness for foreign postdocs; her documented training activity is limited to few French PhD students during several years of activity."*

One of the M2 students in Team 1 was a medical doctor from Colombia who came to work with Dr. Betancur for 18 months, before starting his residency training in the USA.

4. **Weaknesses and threats**

*"The very limited experience in academic teaching by the Team leader is also seen as a weakness, potentially reducing attractiveness of the group."*

C. Betancur has a position a director of Research at the INSERM, and as such, she is not required to teach at the University. This clearly does not reduce the attractiveness of the team, since every year since she became independent she receives numerous requests of M2 or PhD students wanting to work with her. Being the only researcher in the team, the number of students that she accepts is the maximum allowed by the doctoral school.

## *2. Team 2 Jocelyne Caboche Peter Vanhoutte*

1. **Recommendation:**

*"A strategy for obtaining sufficient funding should beconsidered. Owing to the collaborative network already established, EU fundingcould be considered. Strengthening links with a biotechnology company seems to bea real opportunity to fund, at least partly, the research program"*

As mentioned during the audition in order to maximize the chances to obtain funding, the team leaders of team 2 already concentrated their efforts and submitted applications that are under consideration:



-1 ANR-BLANC (acronym CYPHUNT)

-1 ANR-call SAMENTA (acronym SIGNADDICT)

-1 PEPS CNRS on Math-Bioinformatic call

-1 european call : Joined program for Neurodegenerative Disease Research PROTECTEG

-Before the end of 2013, team members will pursue their effort and will apply to call from the american "Tourette Sydrome Association".

2. **Senior researchers of team 2 trained currently 4 PhD students.**

Five students have defended their Ph.D. thesis over the five-year period. Several members of the team 2 are involved in training courses in a permanent or occasional manner. Team leaders participate in master classes, in jury of thesis viva and hold academic responsibilities, further illustrating the very good training activity of the team.

Team 2 belongs to the "Ecole des Neurosciences de Paris" Network, during the lastfive years a PhD student elected by the highly competitive ENP has join the group and already found a post-doc position in a laboratory of renown in England. The training of our Master 2 students very often led to PhD funding from the ministry of research or the "région Ile de France", which is dedicated to top master candidates. For the last five years, all PhD students trained

in team 2 obtained post-doctoral positions in prestigious laboratories and published in international journal with high impact factors. Importantly, after their post-doctoral training, most (if not all) people trained in the group obtained permanent positions either in academic laboratories or private companies.

## 3. Team 3 Bruno Cauli Bertrand Lambolez

No specific comment

## 4. Team 4 Glial Plasticity H. Chneiweiss and M.P. Junier

### 1. 2014 – 2018 Number of project producers

All the scientists that will belong to the team are actively working, however our post-doc Elias El-Habr, in the team since October 2011 has not yet published but will be first author on the first paper reporting on the variation of metabolism between gliomas stem cells and these cell taken out of stemness after expression of miR302-367 that we are presently writing.



### 2. Assessment of scientific quality and outputs

*“Good funding although excessively fragmented”.*

Since we are considered as working in the field of cancer we were strongly encouraged to apply only to INCa and charities and not to ANR. This resulted in funding from INCa (2 grants), ARC and Ligue (Teal with a label 2007-9). For the next 3 years (2013-15) we’ll have only 3 major grants: INCa, Ligue and ARC (only 2013-14)

### 3. Assesment of the unit's organisation and life:

*“Furthermore, the group also has 5 engineers/technicians that take responsabilities in the different technical facilities and platforms of the unit*.”

The group has only one full-time technician. During the last five years we had 2 CDD for 2y, one technician and one assistant ingeneer. In addition two technicians of the neuropathological department of Saint Anne hospital dedicated 10% of their time to our work.

4. **Weaknesses and threats:**

"*The spreading of the research facilities is negatively impacting the work of the group. This situation might not be easy to solve due to present economical constraints. Funding from local sources probably compromises to much time in paperwork with little benefit for the research.*"

This situation will greatly improve when the team, currently located at Sainte-Anne hospital, will join the Cassan building.

5. **Recommendations:**

*"The group is strongly encouraged to increase the international networking, especially within the EU and to gain access to additional funding sources*."

We are already reinforcing our international networking in the EU. HC will chair with Rossella Galli a symposium for the next FENS meeting (Milan, Italy, 2014), and MPJ was invited to give a lecture at the Eurogenesis meeting (Bordeaux, June 2013). In addition, MPJ is co-editing with Steven G Kernie (a specialist of neurogenesis in the hippocampus from Columbia University College, New York) a book for Springer Eds entitled "Endogenous stem-cell based brain remodelling in mammals".

## *5. Team 5 Salah El-Mestikawy*

**No additional comment**



## *6. Team 6 Philippe Faure*

No additional comment

## *7. Team 7 Pathophysiology of Psychiatric Disorders B. Giros*

1- **Assessment of scientific quality and outputs**

*A weakness is the lack of significant external funding from ANR or other foundations in France or Europe. Small external fundings and awards were gained by some team members. In order to help solve that problem, the team leader mentions that he will aim at the publication of a lower number of papers in higher impact journals during the next funding period. One the main problems that could jeopardize the team's effort in achieving the goal of getting external funding is the poor animal housing condition this Unit has to deal with in their institution.*

In addition to one ANR (2012-2015), the group obtained one ERA-NET-Neuron grant; WM2NA: *White Matter Imaging, microstructure, and negative affects: translational study in humans and mice*, Budget (for our team): 116,000€/3 years (2013-2016).

**2- Assessment of the unit's interaction with the social, economic and cultural environment N/A**

Bruno Giros and Eléni Tzavara are creators of the society “MELKIOR Pharmaceutical” with Jocelyne Caboche, Peter Vanhoutte and Fabrice Trovero. This society will develop new compounds for depression, based on an established patent (TAT DEF Elk 1 peptide as novel antidepressant drug. 10/2008. European Patent: EP 08305636 Inventors : B. Giros, J. Caboche, E. Tzavara, P. Vanhoutte). The patent has now been licensed to INSERM Transfer, and the society is under negotiations with INSERM Transfer Initiative for fundings.

## *8- Team 8 Jamilé Hazan*

### 1. Assessment of the unit's organisation and life

*"Team 8 is an ‘emerging team’ within the proposed Department of Neuroscience. The leader becomes a group leader for the first time..."*

Whereas the leader of team 8 had been a group leader as a human geneticist from Jan 1995 till Nov 1999 in Jean Weissenbach's research unit (Genethon and Genoscope/CNS, Evry, France). During these five years, she headed a team of 5 people including one postdoctoral fellow, two PhD students and two technicians.



*"87K is the amount available over a 3-year period to support research in the team",*

while this amount of money will be used to fund consumables and small equipment for this group until mid 2014. Other pending grant applications have been submitted to support the team after June 2014.

### 9- TEAM 09 Nathalie Leresche régis Lambert

No additional comment

## *10- Team 10 Pascal Legendre*

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

*There is relatively little evidence that the team has made a significant contribution in this area. One of the co-leader has served on INSERM Scientific Councils over an extended period.*

In this item the referee did not take into account the fact that one member of the team (A CZARNECKi) participated to a social event named the « semaine du cerveau ».

He also forgot to take into account the past and present participations of one of the team leaders (P. Legendre) to several scientific councils listen bellow:

***National or international expert evaluation and research direction.***

- IR INSERM, 2008.
- ASI Université Paris VII, 2009.
- Telethon Italy (2008-2010).
- ANR, AFM, FRM, NERF, ville de Paris, Fondation motrice.
- AERS 2009 : INSERM U573.
- AERS 2009 : Institut Magendie (Bordeaux).
- AERS 2010 ; coordinator INMED (Marseille).
- Selection comity: Professor position Université Aix-Marseille INMED, 2010.
- Selection comity: associate professor position, Aix-Marseille INMED, 2012.
- Selection comity: associate professor position, UPMC, Paris, 2012.

-Thesis comity: 16 since 2007.

***Scientific comity.***

- INSERM Contrats d'interface, since 2009
- Postes d'accueil INSERM, since 2009
- Scientific comity Animal Physiology, INRA, 2007-2014 (nominated).



### 2- • Weaknesses and threats:

*The team is included in the Vertical Axis that relates to both Mental Illness and Neurological Disease. However, there is no indication in the team's plans* ***that the research will be applied at a more disease-focused level. Instead, the concentration appears to be solely on the fundamental biological mechanisms. While is not a weakness per se, it is perhaps a current limitation of the team's research program and vision.*** *In order to*

*deliver on the research agenda, it seems likely that additional grants would need to be achieved, and there is a risk to the program if this is not forthcoming…..*

*AND*

*Recommendations:*

*Additional collaborations, particularly clinical, should be established to provide a more translational outlet for the group's research…….*

We agree with the referee that interactions with clinicians will increase the team's research vision. But we must mention that we already collaborated with a clinical institute through "a contrat d'interface" (2008-2012 P. Legendre) and that we are collaborating on a projectabout autism with C Betancur (P. Legendre and H. Le Corronc), thus indicating that we currently have clinical collaborations.

## *11- Team 11 Sakina Lhaouty-Kodja .*

*Regarding the first objective, brain-specific ERα and ERβ knockout mouse models are proposed to elucidate their respective roles in female behavior. However, it is not explained why these mouse models would be an added value to these studies since there is no real evidence that peripheral ER actions are important in female behavior (which is clearly different from the male, where a complete KO of the AR will lead to a female body type, no penis etc).*



Although estrogens are not required for differentiation and initial development of the female reproductive tract, females ubiquitously lacking ERα or ERβ exhibit several phenotypes including a lack of sexual maturation of the gonadal ducts, severe ovarian and uterine dysfunctions (reviewed byCouse et al. J. Steroid Biochem Mol. Biol 2000; Dupont S et al., Dev Dyn. 2003). Estrogen receptors are also expressed in other non-reproductive tissues and play a key role in cardiovascular functions, cell proliferation in breast, osteoblast regulation… For all these reasons, the use of models with conditional mutations for ERα or ERβ is pertinent.

*Another potential problem is that these mouse models lack either ERα or ERβ in brain regions important for sexual behavior throughout all life stages and thus that no distinction can be made between developmental and adult actions of estradiol on the brain and behavior. There is strong evidence in the literature that ERα is critical for activating female behavior in adulthood, thus a brainspecific ERα KO will not resolve the role of this receptor in the development of female behavior, simply because their behavior cannot be activated in adulthood*

First, a non-activated behavior of ERα KO females in adulthood is exactly the phenotype we are expecting. This won't hamper our studies, which will be performed in postnatal and prepubere females in order to determine the neural targets of ERα in the developmental regulation of sexual behavior by estradiol. Furthermore, we also aim to evaluate the role of neural ERα in pubertal onset induced by ovarian estradiol and this can be assessed only in these conditional mutant females.

Second, the expert did not mention that the second genetic model is also of great interest since the role of ERβ in estradiol effects still remains to be precised. Our very recent studies on females lacking Erβ in the nervous system assign a new role to this receptor (Naulé et al., paper in preparation). Third, in both models, the comparison of the proteome of the interesting brain areas (punches) between control and mutant females will help to determine the molecular targets, either known (oxytocin, NOS) or not, of each of these receptors. This project is conducted by S. Mhaouty-Kodja and a PhD student.

*Regarding the second research objective, it is proposed to study whether a first sexual experience will induce specific changes related to neuroplasticity in the preoptic area of male mice by monitoring gene expression, with a particular attention to the nNOS pathway and free radicals. Then at mid-term proteomic and epigenetic approaches will be used in order to elucidate how a first sexual experience will lead to certain adaptations in the male brain. This objective is rather vague and is not worked out very well. How are they going to determine an epigenetic contribution to this phenomenon? What proteins are they going to be looking for? Also is there a link to endocrine disruptors and their effects on the brain and this particular research line?*



We precised at the oral presentation that we are interested in the role of the androgen receptor (AR) in the adult regulation of male sexual behavior by testosterone and how this signaling pathway could be affected by exposure to endocrine disrupters. Thanks to their expertise, the two other senior scientists of our team (H. Hardin-Pouzet and V. Grange-Messent), with two Master 2 students, have started addressing this question in the hypothalamic preoptic area. Two models exhibiting a similar sexual alteration are used: mice lacking AR in the nervous system (Raskin et al. 2009, 2012) and mice exposed to bisphenol A during adulthood (Picot et al. in revision). They will first check known signaling pathways potentially involved in the expression of sexual behavior (NOS and free radicals, dopamine, oxytocin). Then, they will perform a proteome analysis in both models in order to identify and compare between the two models the other altered targets either expected or not. This will allow, in one hand, to precise for the first time the targets of AR in the regulation of sexual behavior. On the other hand, this will permit to confirm or not our hypothesis that some endocrine disrupters largely known for their estrogenic activity like bisphenol A can act as anti-androgens in the adult male brain (Picot et al. in revision). In the case of irreversible modifications induced by adult exposure to endocrine disrupters at specific targets, epigenetic studies will be planned at long term in collaboration with groups that posses a good expertise in this area. This project is based on our studies showing that the AR seems to be required in the adult activation rather than perinatal organization of male behaviors by testosterone (Picot et al. in revision; Marie- Luce et al. in revision). These data, which

indirectly assign a more important role for estrogen receptors during the perinatal period, are in line with studies performed by other groups with international recognition in this field (Simerly et al., PNAS 1997; Ogawa et al., PNAS 1997; Kudwa et al., PNAS 2005; Hisasue et al., J Sex Med 2010; Juntti et al., Neuron 2010). They contrast with the hypothesis of the expert member of the AERES committee J. Bakker (Bakker et al., Horm Behav 2004; Pierman et al., Horm Behav 2008), suggesting a potential conflict of interest.

Finally, we would like to emphasize that:

- The concerns, listed in the present report, about our projects have not been raised by the expert in this field during the 20 min of discussion! This would allow us to directly answer these questions in front of all members of the AERES committee.

- The two projects were reviewed by experts and granted by two main public fundings: the "ANR Blanc" (2013-2016) for the first project and the "Agence nationale de la sécurité des aliments" (2013-2017) for the second one.

## *12- Team 12 F. Nothias.*

### 1- Assesment of the unit's organisation and life

*"Given the relatively small size of the group and the known difficulty of working with proteins that are of high molecular weight, the committee identified a weakness in the project as these appear too broad."*



Our team is currently, and will be in the future, composed of 5 permanent EPST (2 CNRS, 2 MCU-UPMC, and 1 AI-UPMC); thus, the team may rather be considered as being of medium size (and see below).

### 2- Assessment of the unit's academic reputation and appeal

*"A number of national and international collaborations have been established, providing the team with mutant mice and different cDNA sequences for functional analyses."*

This sentence is not clear to us, as it could be interpreted in a way as if our collaborations were only based on exchange of material, while in fact they have been, and continue to be based on strong scientific interactions, as can also be verified from the author order in the respective common publications. To cite juste one example, our long lasting collaboration with F Propst was awarded two travel grants (Egide), allowing for an exchange of our respective PhD students (3 from our, and 3 from Propst's lab), and has given rise to 5 common publications. Moreover, as noted in the *Nat. Cell Biol.* paper, F. Nothias was involved in planning the project, and has also received the first two co-authors of this publication in her lab, where they realized part of their experiments.

### *3-* Assesment of the unit's organisation and life:

*« It seems that several postdocs have left the team during the course of the last period. »*

We do not know how to interprete this sentence. To avoid any confusion, during the last period there have been 3 post-doc researchers in the team :

**Sophie Féréol** (salary from CNRS-grant for a period of 2 years), under F. Nothias supervision. The work accomplished by S Féréol has been published (Féréol et al., 2011). She now has a permanent position (MCU-Univ. Créteil), and she will join our team again in september 2013, for a period of 2 years.

**Coralie Fassier** (FRM salary), from the beginning under supervsion by J. Hazan, publication Fassier et al., 2011. C. Fassier now has an INSERM-permanent position, and is currently part of the J Hazan team.

**Divya Unni** (from India; one year NeRF salary non renewable, attributed to F. Nothias team from july 2011-June 2012). For a familial reason, D. Unni has stopped her academic research activity in April 2012. The work started by D. Unni is now pursued by L. Vincensini, recently recruted on a MCU position attributed to our team.

### 4- Assessment of the unit's involvement in training through research

*« team leader continues to provide workshops in Neurosciences and cellular and molecular aspects in Neurobiology at Master level »*

Rather than the team leader, this assessment in fact concerns Sylvia Soares (MCU-UPMC), who has educational responsibilities and is also involved in coordination of teaching at UPMC. At the UPMC, F. Nothias is member of the Thesis and HDR commission, as she is also a member of the CNRS commision-25.



### 5- Assessment of the five-year plan and strategy

*Aim 1, the detailed assessment of regulatory kinase inputs onto the microtubule associated protein MAP1B. Specifically, the team will test the physiological significance of different proline directed kinases (including CDK5, GSK-3 and JNK) in the control of MAP1B function in different cell types.*

We would like to precise the following: 1) regarding JNK, we have already published our data demonstrating the function of this signalling pathway in axon regeneration, which depends on MAP1B as a downstream effector, and have also shown the differential involvement of the 3 JNK isoforms in axon initiation and elongation (Barnat et al., J Neurosci 2010; and thesis). 2) We also have investigated the function of GSK3 in axon regeneration, which again depends on MAP1B for the regulation of the stability of microtubule pools (Barnat, thesis; and manuscript under writing). Since we have found that inhibition of CDK5, known to phosphorylate MAP1B in developing neurons, does not affect MAP1B phosphorylation nor axon regeneration in adult neurons, this part of our project on MAP1B will particularly investigate the cross-talk between JNK and GSK3 pathways in regulating MAP1B phosphorylation during axon regeneration.

*''Aim 2, they proposes work that is aimed at analysing Ahnak, another very large protein, in Schwann cell function.[…] and undoubtedly produce interesting results of this rather understudied protein in Schwann cells…"*

This statement seems in contradiction with the next comment *: "Whilst the Ahnak work as laid out in the proposal seemed rather preliminary, …"*

Although AHNAK is indeed a very large protein, we are the first team who demonstrated its role in Schwann cells, and our first *in vitro* analysis of its function has been published (Salim et al, 2009). The recent strong, and definitive (rather than preliminary) results further confirm our hypothesis of AHNAK being involved in Schwann cell-basal lamina interaction and its consequence on morphology and motility of these cells. It should be noted that several pathologies of peripheral nervous system are due to the dysfunction of Schwann cell interaction with basal lamina components. Nevertheless, we would like to mention that this project will be pursued only if the team gets a positive response from at least one of 2 pending grant applications (ANR and AFM) that should also provide a salary for a post-doc, and cover the expenses for the required manpower of the two ongoing collaborations: one with Nicolas Tricaud (Montpellier, Inserm équipe Avenir) whose main project concerns the physio-pathology of myelination in peripheral nervous system, and who thus is very interested in our work on AHNAK; the other one with Sophie Féréol and Redouane Fodil (Créteil University), specialists in the use of AFM (atomic force microscopy) who recently confirmed our hypothesis that lack of AHNAK in Schwann cell affects the stiffness of these cells, rendering them more rigid. This corroborates our data on ahnak-ko mice, showing defects in Schwann cell migration, axon sorting and myelination in the peripheral nerve. In addition, we were able to coIP this very large protein with beta-dystroglycan (major Schwann cell laminin receptor). All these data are included in a ms that will be submitted this month (april; see below).



## 6- Updates

**Publications**

*Submitted*

• Milbreta U, von Boxberg Y, Mailly P, Nothias F and Soares S. Astrocytic and vascular remodeling in the adult rat spinal cord injury after Chondroitinase ABC treatment.

Finalized and under reading by coauthors before submission

• Ysander von Boxberg, Sylvia Soares, Sophie Féréol, Redouane Fodil, Jacques Taxi, Michiyoshi Kouno, Nicolas Tricaud, and Fatiha Nothias. AHNAK1 deficiency affects axon sorting and myelination in peripheral nervous system.

**New grants :**

• **AAP 10 SDV-SDM-STIC**, call « Maturation de projets innovants » 2013, Université de Lyon-Claude Bernard ; Nothias CoPI with Laurent David as coordinator ; this includes one year salary for a PhD student under Nothias' direction.

• **FRM**, **Aide aux projets innovants,** ChitoSpin, Biomatériaux à base de Chitosane pour la régénération axonale après lésion traumatique de la moelle épinière (2013-2014), Nothias CoPI with Laurent David.

**Pending grant applications :**

ANR-Blanc-SVE4, S Soares as coordinator (applied in January 2013)

ANR- Blanc- SVE1, Nothias as coordinator (applied in January 2013)

AFM, Nothias as coordinator (applied in March 2013)

ANR-PRTS- TranSpiRe, Nothias as coordinator (April 2013)

## *13- TEAM 13 Laure Rondi-Reig*

**Comments**

- *The 1st paragraph mention: « although the PI did not obtain ERC funding, but she will try again next year"*

It is puzzling to read that the successful selection to the step 2 of the ERC consolidator is here mentioned negatively.



- Concerning the main conclusion, it is also puzzling that assistant professors with heavy duty of teaching (as mentioned in the report) are criticized for their h factor and their international invitations. In particular, concerning one of this assistant professor, there is no mention of her first authorship in Science (2011) obtained only three years after her arrival in the team (2008).

## *14- Equipe DPRN (A. Trembleau)*

1) As is clearly written in the document, and was clearly explained during the presentation/discussion with the AERES members, the DGN team members who join the DPRN team will drop the cerebellum as a model, and join the DPRN team projects on the olfactory system. Therefore, since the team will work on a single model, as highlighted as a strength in the "Strengths and opportunities" section of the report, it is unfair and contradictory to write, in the "Weaknesses and threats" section that the DPRN and DGN groups "use different models and still have different biological questions which appear not yet integrated and may disperse the focus".

2) We apologize if the strategy for the identification of cis- and trans-acting elements was not clear enough in the document, mainly because of the lack of space. Should the committee members have asked the question during the visit, we would have been pleased to explain our strategy in details. We mention here that this part of the work will not be done by the former DGN team members, but by the INSERM researcher currently in sabatical in the US. The part dedicated to the former DNG members (1 PI and one technician) will be devoted more specifically to the study of the fasciculation of axons, by developping in vivo and ex vivo models.



3) Our team mainly focuses its projects on the local translation of mRNAs as a molecular mechanisms of development and plasticity of neural networks, and not on diseases affecting the olfactory function. The purpose of studying the functions of FMRP in the olfactory bulb is thus to decipher the functions of this RNA-binding protein, known to play a critical role in local translation of mRNA in neurons, in new contexts such as adult neurogenesis, dendritogenesis, and functional insertion of neoneurons into an adult network. Actually, this project obtained significant financial support from the Lejeune Foundation, the interest of which is focused on mental diseases including Fragile X Syndrome. Therefore, we do not fully agree with the suggestion of finding other genetic diseases in which defects in olfactory bulb are highly relevant for the patients' life.

4) The return from the local networks (i.e. the Labex Bio Psy) may arise in the near future. This Labex is new, and we will participate to the next meetings aiming at developing scientific interactions with other scientists and clinicians of the network. Of particular interest, other team leaders having strong interactions with clinicians, and working in the field of autism spectrum disorders, are highly interested in local translation of mRNAs, and discussions with them are planned in the next future.

5) The management of the team has been made very clear : the PI of the current DPRN team will still be the PI of the future DPRN team once the two members of the current DGN team, plus the INSERM researcher, will join the DPRN team.

## 15. Team 15 (François Tronche)

**Comments on « Non-publishing » scientists.**

Considering the AERES criterias we listed two but can argue that both are highly productive if we consider the recent dynamic.

The first one is Sheela Vyas, senior author in a 2011 paper in PNAS and also senior author in 2 papers presently submitted, one already in revision in a very good journal, (Carrillo de Sauvage MA, Pasco M, Arnoux I, Diez AS, Maatouk L, Delahaye M, Newman T, Calvo CF, Herrero MT, Audinat E, Tronche F, Vyas S. Potent and multiple anti-inflammatory actions of microglial glucocorticoid receptors during inflammation, *In favorable revision in Cell Death and Differentiation (IF 8.8).) the other one with a pending decision (*Carrillo de Sauvage MA, Guerreiro S, Barcia C, Parnaudeau S, de Pablos V, Fernandez-Villalba E, Hirsch EC, Tronche F, Michel PP, Herrero MT *, Vyas S*. * co-corresponding, Rescue of Midbrain Dopamine Neurons through a Direct Action of Glucocorticoids. *Submitted to Nature Communications (IF7.4)).

The second « non-publishing » is a post-doctoral fellow Samah Karaki that joined the team only a year ago and will not stay after the 1st january 2014.

Of note Sébastien Parnaudeau, presently in a post-doctoral period but that we hope will get back to the lab next year just had a paper published as first author in Neuron with an editorial comment for this paper (plus echos in Nature and Science)



La composition de l'équipe indiquée dans le rapport que nous avons rendu à l'AERES est :

Jacques Barik (MCU UPMC)

Arndt Benecke (CR1, CNRS)

Jean-Pol Tassin (DR1 INSERM emeritus)

François Tronche (DR2 CNRS)

Sheela Vyas (CR1 INSERM)

Samah Karaki (Postdoc, ANR TIMMS)

Christophe Lanteri (Postdoc, ARN)

Sébastien Parnaudeau (Postdoc, return planned in 2013)

Layal Maatouk (PhD Student)

Camille Baranovsky (PhD Student)

Ana Clara Bobadilla (PhD Student)