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

Section des Unités de recherche

AERES report on the research unit

Physiologie et Physio-pathologie du Système Nerveux Somato-Moteur et Neurovégétatif (PPSN)

From the

University of Aix-Marseille 3

March 2011

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From the

University of Aix-Marseille 3

Le Président de l'AERES

Didier Houssin

Section des unités de recherche

Le Directeur

Pierre Glorieux

March 2011

Research Unit

Name of the research unit : Physiologie et Physio-pathologie du Système Nerveux Somato-Moteur et Neurovégétatif (PPSN)

Requested label : USC INRA and UMR CNRS

Name of the director : Mr. Jérôme TROUSLARD

Members of the review committee

Committee chairman

Mr. Laurent FAGNI, University of Montpellier, France

Other committee members

Mrs. Daniela COTA, University of Bordeaux, France

Mr. Maurice FALEMPIN, University of Lille 1, Villeneuve d'Ascq, au titre du CNU

Mr. Daniel LÉVESQUE, University of Montreal, Canada

Mr. Charles-Henri MALBERT, INRA Center, Saint-Gilles, France

Mr. Martial RUAT, UPR CNRS, Gif-sur-Yvette, au titre du CoNRS

Observers

AERES scientific advisor

Mr. Bruno BONTEMPI

University, School and Research Organization representatives

Mr. Jean-Marc PONS (University Paul Cézanne Aix-Marseille 3)

Mr. Driss BOUSSAOUD (CNRS)

Report

1 • Introduction

- Date and execution of the visit

The visit took place March 25th 2011 in the building of the candidate unit, at the University campus of Saint-Jérome (Marseille). Following a general presentation of the structure of the unit by the candidate director, Jérôme TROUSLARD, the Committee listened to each team during 45 minutes and asked questions. The Committee also visited the infrastructure of the candidate unit. Three separate meetings allowed free discussions with students and post-docs, technicians, and researchers, in the absence of the candidate director of the unit and team leaders. Finally, the Committee had also an exchange with the representatives of CNRS and University to which the candidate unit wishes to be affiliated.

The application is for the creation of a University Research Unit/Unité de Recherche Universitaire (UR) entitled: "Physiology and Patho-physiology of the somato-motor and neurovegetative nervous system"/ "Physiologie et Physio-pathologie du Système Nerveux somato-moteur et neurovégétatif" (PPSN). This application is combined to the request for a renewal of an USC-INRA contract and obtainment of a CNRS label. Following discussions with University and CNRS representatives, the Committee noted that CNRS will take the request of PPSN into consideraton. The University representative clearly stated that the University fully supports the application of creation of PPSN, and that it will carefully evaluate the possible obtainment of a CNRS label.

- History and geographical localization of the research unit, and brief presentation of its field and scientific activities

The project will be carried out by the teams of J. TROUSLARD (Team 1) and Jacques FANTINI (Team 2). Presently, these teams belong to the department of Neurovegetative Physiology/Physiologie Neurovégétative (PNV) of the Centre de Recherche en Neurobiologie-Neurophysiologie de Marseille (CRN2M). They are located on the scientific campus of Saint-Jérôme (Faculty of Sciences and Technologies of the University of Aix-Marseille 3), whereas the CRN2M is located at the medical school of North-Marseille. These two campuses are quite distant from each other. Team 1 focuses on the vegetative nervous system and control of food intake. Team 2 is specialized in molecular interactions between proteins and membrane lipids, in a context of neurodegenerative diseases (Alzheimer's, Parkinson's and Creutzfeldt-Jacob diseases).

The PPSN displays a strong potential of researchers with teaching duties (professors and assistant-professors) who are strongly involved in the Biochemistry/Physiology/Neuroscience Licence, Professional Licence and Master of the University of Aix-Marseille 3. The different locations of CRN2M and PPSN units generate a dispersion of their activities on the two different sites. In addition, the teaching activities of PPSN members are on 2 other sites (cities of Aix and Marseille). Such a spreading of activities weakens both research work and teaching activity of the teams, thus negatively affecting their visibility. The unification of the 2 teams into a single unit and single site is therefore essential for their visibility. The creation of the PPSN unit is also important for guarantying the presence of research/teaching activity in biology on the campus of Saint-Jérome.

- Management team

The candidate director of PPSN, J. TROUSLARD, will have his own team (Team 1) and Jacques FANTINI will lead the second team (Team 2). Management of PPSN will be based on collegial rules. The Executive Committee/Comité de Direction will consist of the director of the unit, with representatives of each team and representatives of technicians/ITA/IATOS. Each team will be financially independent, with however a participation of 30% of their budget to the global budget of the unit. This global budget will cover hygiene and security costs, as well as professional formation and training costs of the personel of the unit.

The Committee recommends a more in depth description and establishment of management rules. Namely hygiene and security rules need to be clearly defined. The same applies to quality-control of experiments, external communication (i.e. a website for the unit) and relationships with the general public.

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	14	16
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	1
N3: Number of other researchers including postdoctoral fellows (Forms 2.2, 2.4 and 2.7 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	7
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.8 of the application file)	6	
N7: Number of staff members with a HDR or a similar grade	7	6

2 • Overall appreciation on the research unit

- Summary

The PPSN is a combination of two existing research groups, which share interests and expertise in the nervous control of food intake, from physiology to pathology (obesity, cachexia and anorexia), and from molecular to integrative level of analysis. Team 1 has made important contributions in the functional and neurochemical properties of the dorsal vagal complex (DVC) network, a structure involved in food intake. The team has identified new cellular signaling properties of various factors such as BDNF and endocannabinoids in the DVC, and characterized a novel form of plasticity of the brainstem network that involves neurogenesis and gliogenesis. Team 2 activity complements this integrated level of analysis by investigating molecular and structural aspects of lipid-lipid and lipid-protein interactions. Namely, Team 2 has characterized a new type of protein domain (SBD), which interacts with sphingolipids and that appears to be involved in the association of amyloid proteins such as prion protein, gp120, beta-amyloid peptides and alpha-synuclein, with lipid rafts. Team 1 provides a highly respected professor and internationally recognized scientist in the field. The new director of PPSN and new leader of Team 1, Jérôme TROUSLARD, benefited from this professor experience. He is a brilliant scientist, but with lower international recognition. The leader of the Team 2 has a long-standing experience and knowledge in the mechanisms underlying lipid-protein interactions. His expertise is also well established at international level. Persistent collaborative work and sharing experience between these two teams has been beneficial for successful accomplishment of some of their projects. The Committee believes the association of these two teams into a unique unit (UR-PPSN) will be a positive step that should allow further improving their visibility in terms of research and teaching activities on the University sites of North Marseille and Aix-en-Provence.

- Strengths and opportunities

The Committee has observed the following strengths and opportunities of the candidate PPSN unit.

1. Optimal convergence of research activities of the teams
2. Complementary expertise of the 2 teams (biochemistry, immunohistofhemistry, electrophysiology, feeding behavior analysis, quantitative imaging of cell signalling) from living animals to in vitro preparations
3. A thematic of high priority in public health (mechanisms of food intake regulation) and development of a niche of research in the field of neurovegetative physiology that is relevant both at local and national level.
4. Important involvement of both teams in the organisation and execution of high-grade university teaching (Licence, Master and Professional Master)
5. A large majority of young scientists composes the candidate unit
6. Strong interactions with INRA Department of human nutrition combined to several national (Nice, Paris) and international (Marocco, Argentina) collaborations
7. Hosting of a start-up (Biomeostasis) that was created by two former researchers of the teams. Biomeostasis develops protocols for pharmacological studies in animals, applied to food intake and metabolic disorders.

- Weaknesses and threats

A few weaknesses have been identified by the Committee.:

- The teams are composed almost exclusively of researchers with teaching duties (Professors and MCs). This may create difficulties for accomplishing competitive research work, as only part of the time can be dedicated to the research activity.

- Financial support is mainly obtained from institutions (CNRS, University, INRA) and associations of patients, but not from competitive calls such as both National and European Programmes.

- The recruitment of full-time researchers (with no teaching duty) and post-docs is very limited.

- Recommendations

The Committee recommends the following:

- It is critical that the candidate unit seeks for post-doctoral fellows and full-time researchers, and not only at a national, but also international level. To this end, the Committee strongly recommends the obtainment of a CNRS label.

- The PPSN teams have proven their ability in collecting sufficient budget to finance their research activities. However, in order to improve their visibility, the Committee recommends to increase the performance of the unit in submitting and obtaining grants from national and international calls. The presence of a start-up (Biomeostasis) in the unit should be taken into consideration, as this should help the unit in carrying out this task.

- The Committee appreciated the continuous support of the University in the renovation of the laboratory and animal facilities space, personnel recruitment and appropriate maintenance of the animal facilities. The Committee recommends to maintain this support until the team obtains enough grant-operating money. The animal experimental facilities must be linked to a local ethical committee. We recommend that all projects involving animals are approved by such a committee.

- The Committee also appreciated the regular occurence of seminars in the unit and encourages more frequent invitations of external speakers.

- Project leaders are encouraged to emerge in the next few years.

- Production results

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	16
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	1
A3: Ratio of members who are active in research among staff members [(A1 + A2)/(N1 + N2)]	1
A4: Number of HDR granted during the past 4 years (Form 2.10 of the application file)	2
A5: Number of PhD granted during the past 4 years (Form 2.9 of the application file)	6

3 • Specific comments

- Appreciation on the results

Both PPSN teams provide long experience in their field of research. For instance, Team 1 has discovered major roles of secreted peptides, neurotrophic factors, endocannabinoids and prostaglandins in the nervous control of food intake. Team 2 has identified a new structural domain of interaction between amyloid and synuclein proteins and lipids that could contribute to the devastating action of these proteins in neurodegenerative diseases. These results open a large panel of potential therapeutic targets for the treatment of pathologies of major impact in public health, such as food intake disorders, Parkinson's, Alzheimer's and Creutzfeld-Jacob diseases.

From 2006 to 2010 the members of PPSN have published 100 original articles, including 33 that have been generated outside of the unit. Six publications appeared in very good journals, among which 3 were obtained in the unit (EMBO J., PNAS, J. Cell Biol.) and 3 (FASEB J, J. Neurosci., Nat. Rev. Neurosci) from outside of the unit by members that recently joined or will join PPSN in 2012. The PPSN members also published 65 abstracts in national and international meetings, among which 17 were invited communications. Considering that all the researchers of the unit have important teaching duties, this scientific production is very good. During the last 5 years, 6 Ph.D. students defended their thesis and 2 researchers obtained their HDR. Also, 2 Assitant-Professors/MCs became Professors.

The PPSN teams have stable contracts with national institutions (University, CNRS, INCA and INRA) and associations of patients. They obtained 2 ANRs. The total budget of the unit from 2006 up to now is of 518 kEuro.

- Appreciation on the impact, the attractiveness of the research unit and of the quality of its links with international, national and local partners

Members of PPSN have been invited to 17 international conferences, among which a Gordon Conference in 2011. The PPSN unit recruited 1 CR2, 3 MC and 1 post-doc during the last 5 years. They have also recruited 8 Ph.D. students whose fellowships were supported by national or international grants.

The unit is an associate member of the 7th PCRD NEUROMED network, member of the France-Marocco GDRI Neuroscience CNRS program and holds an USC-INRA contract. It holds an industrial collaborative contract (CIFRE) for transfer of technology on nanoparticles and a patent has been recently deposited for this new technology.

Two former researchers of PPSN created a start-up (BIOMEOSTASIS) that develops protocols for pharmacological studies in animals, applied to food intake and metabolic disorders. Two members of the unit participated to the national socio-cultural event « la semaine du cerveau » by giving 3 public conferences.

- Appreciation on the management and life of the research unit

The candidate director of PPSN is a well known scientist. He displays high capacity to obtain grants, to supervise groups of research and clearly has the energy, drive and capacity to head PPSN and lead its further improvement. The management organization of PPSN described above appears efficient and well accepted by all members of the unit. A very good dynamic exists between the researchers and students within the unit. Lab meetings are organized every week. The technical personnel provide adequate assistance to the researchers, and senior researchers provide very good training to the students joining the unit. Thus, the unit supports the animal experimental training of the students, which is greatly appreciated by the local Ecole Doctorale. Students of the unit are also encouraged to participate in academic teaching and training activities of the university. They are also encouraged to attend meetings and the unit supports their participation. Thus far, all the students of the unit have found a post-doctoral employment. The Committee considers this success as promising for the recruitment of future students. The technicians support the idea of staying in the unit and all the researchers experienced very good interactions in their research work as well as in their teaching activities.

There are solid scientific objectives. However, a limited number of cutting edge projects should be identified and both manpower and financial resources should be dedicated to these tasks. Projects with lower visibility/priority should stop. Organization of the unit appears to be structurally sound and well balanced between experienced scientists and students. The unit also benefits from well-trained technicians. As mentioned above, the Committee noticed that PPSN needs to recruit full-time researchers and post-docs.

Most of PPSN researchers are highly implicated in teaching organization, from Licence to Master level. This attests to the recognition of their expertise.

- Appreciation on the scientific strategy and the project

The PPSN teams have long experience in physiology of food intake. Their project is in the continuity of their previous work, that is to understand integration of nervous, hormonal and paracrine informations that lead to food intake regulation. Team 1 will develop physiological studies in more integrated systems, and Team 2 will shift from studies in artificial membranes towards living cells. PPSN provides a large panel of methodologies and techniques, applied to molecular and integrated systems, thus covering a large multidisciplinary expertise.

The general theme of their project is not only physiologically relevant, but also essential to understand the pathological aspects of neurovegetative and brain functions (food intake disorders and neurodegenerative diseases). Their project is fully feasible, first because the different objectives are precisely addressed and fit with the expertise of the teams. Namely, a good balance exists between risk-taking and well-validated working hypotheses. Secondly, the two teams expertise is complementary (i.e. electrophysiological and biochemical approach of the capacity of alpha-synuclein to form ion channels). Thirdly, PPSN provides sufficient technical and human resources. None the less, the expansion of animal facilities might require an additional technical staff. Finally, preliminary results are encouraging and support the technical feasibility of the research hypotheses.

The objectives of the project are original, particularly those focusing on the possible role of glia and cerebrospinal fluid contacting neurons in food intake and related disorders. Also the question of the role of lipid-proteins interactions in amyloid protein aggregation is certainly an exciting topic. Thus, the Committee has a positive appreciation of the overall scientific project of PPSN.

4 • Appreciation team by team

Intitulé de l'équipe 1 : NEUROBIOLOGY OF FOOD INTAKE AND DORSAL VAGAL COMPLEX

Nom du responsable : Mr. Jérôme TROUSLARD

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	7	10
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	1
N3: Number of other researchers including postdoctoral fellows (Forms 2.2, 2.4 and 2.7 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	1
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.8 of the application file)	6	
N7: Number of staff members with a HDR or a similar grade	5	4

- Appreciation on the results

The research activity of Team 1 focuses on determining the role of the dorsal vagal complex (DVC) in the regulation of food intake and on its implication in eating-associated disorders, such as anorexia and obesity. In particular, in the period 2006-2010, the team has investigated the mechanisms underlying BDNF action in the DVC, the role of endocannabinoid signalling in this brain area, the role of PGES-1 in inflammatory anorexia, the presence and potential role of neurogenesis and the identification of a new glial cell subpopulation in the DVC. The research carried out so far is original and the recognized expertise of the team in the study of the DVC represents an important contribution, since only few laboratories in France work on this brain structure. Nevertheless, the committee has noticed a dispersion of themes and sub-projects carried out during the past 4 years, which might have in part overshadowed the ability of the team to highlight their most original findings. Consequently, this dispersion has not favoured the international visibility of the team.

In the period 2006-2010 the team has obtained 32 publications in good quality, specialized journals. However, the team should use in the future a more ambitious publication strategy by increasing research efforts on specific findings that are particularly novel and original, thus targeting higher impact factor journals. During the same period, 6 Ph.D. theses were completed.

The team members have participated mainly to national conferences. Their presence and participation to international conferences is generally low and should be increased.

Team 1 has mainly national collaborations and is an associate member of the 7th PCRDT NEUROMED network, which has allowed hosting students from foreigner countries (mainly Morocco).

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

In the period 2006-2010, the team received a total of 17 invitations to national or international conferences. These invitations were addressed to team members that are highly respected professors and internationally recognized scientists in the field. A Ph.D. student has received a Prix Servier for the studies carried out on inflammatory anorexia.

All the personnel recruited in the period 2006-2010 are French, which attests for a good visibility of the team at National level. The team recruited 1 CNRS CR in 2006, who however has now left the unit. The team has also hosted for different periods of time (from 7 months to 1 year and half) 4 ATER and recruited 3 MCs and 1IE. The team has also hosted 8 Ph.D. students, with 1 student coming from Morocco.

The committee appreciates the effort made in finding funds, although further attempts should be made in obtaining more substantial research contracts at both National and European level. The team currently does not have any industrial contract. This aspect should however be improved by the recent creation of a start-up company (BIOMEOSTASIS), whose R&D activity should attract the interest of the industry. The creation of this start-up is part of a valorisation strategy, which has strengthened the socio-economic value of the research activity carried out by team 1 so far. The current partnership of the team with the NEUROMED European network (7th PCRD) should help exchanging students among partner laboratories, as well as favour the hosting of foreigner Ph.D. students.

- Appreciation on the scientific strategy and the project

The project proposed by team 1 is in line with the previous research activity carried out by the team. The technical and human resources of the team as well as the integrative approach and use of state-of-the-art models, such as specific transgenic and conditional knockout mice, guarantee its feasibility. The project and in particular the studies dedicated to the characterization of the role of glia and cerebrospinal fluid contacting neurons (CSF-CNs) in the DVC physiology are particularly original and innovative. Nevertheless, there are also parts of the project that result less focused and structured. In particular, the studies on the visceral sensory afferents in the section dedicated to the BDNF need to be more deeply processed. The general impression is that, although potentially very interesting, the project in its current form is dispersive and at times not sufficiently developed. Specific leaders should be identified for each research line illustrated in the project.

A specific funding strategy to support the most innovative aspects of the project should be developed by the team. At the same time, the ability of the team to identify and favour high-priority research lines and produce preliminary data should ease the obtainment of funding.

- Conclusion

  - Summary

During the past 4 years, Team 1 has discovered major roles of secreted peptides, neurotrophic factors, endocannabinoids and prostaglandins in affecting food intake, by modulating specific neuronal circuits in the DVC. The research activity of the team is original and its expertise in the study of the DVC is remarkable, particularly taking into account that few other laboratories in France work on this structure. The research project of the team is original and feasible and is in line with the research activity carried out so far. The teaching personnel have important academic organizational duties and guarantee several teaching courses.

  - Strengths and opportunities

The team was able to set up an efficient recruitment strategy, which allowed replacing the permanent personnel that left the team. Importantly, most of the personnel are young (in their late thirties and forties), which represents an opportunity for the scientific growth of the team. Furthermore, their expertise is complementary and clearly bolsters the feasibility of the team's research project. There have been 6 PhD theses completed in the period 2006-2010 with most of the students able to find a professional position. The participation of the team to the NEUROMED programme and the scientific exchange with Morocco are good opportunities for hosting students from a foreigner country.

- Weaknesses and threats

The Committee noticed the following weaknesses:

- The project seems at times dispersive and needs to have specific subprojects. Specific staff carrying out these studies needs to be clearly identified.

- The team has good national, but limited international visibility. The international visibility of the team director is also limited.

- There are currently no post-docs recruited in the team.

- The funding is limited to research agencies at national level.

- Recommendations

The team should identify the most original aspects of their research project and invest more in them so to guarantee a better visibility in the medium-long term. This strategy should also allow improving the visibility of the director of the team.

The ability of the team to obtain funding should be strengthened. Thus permanent researchers, in particular MCs, should make more efforts in applying for grants at both National and European level. This would allow recruiting post-docs, thus guarantying the presence of personnel exclusively dedicated to research.

Intitulé de l'équipe 2 : Molecular Interactions And Membrane Systems

Nom du responsable : M. Jacques FANTINI

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	7	6
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Forms 2.2, 2.4 and 2.7 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.8 of the application file)	0	
N7: Number of staff members with a HDR or a similar grade	2	2

- Appreciation on the results

The main focus of this team is the characterization of the molecular mechanisms controlling lipid-lipid and lipid-protein interactions in biological membranes and the consequences of these interactions for membrane-mediated cellular functions. They identified and characterized a specific recognition motif for sphingolipids (sphingolipid binding domain, SBD), which appears to be involved in the association of cellular and pathogen-associated proteins and membrane microdomains enriched in cholesterol and/or sphingolipids, especially gangliosides. This particular domain has been identified in a wide range of proteins, including prion proteins, HIV-1 surface envelop glycoprotein, and Alzheimer's beta-amyloid and Parkinson's alpha-synuclein peptides. This discovery (SBD) is highly original and had an important impact in this field of research.

This team has published 37 publications in peer-reviewed journals and 4 reviews between 2006 and 2010. The average levels of the journals range from good to very good (J. Biol. Chem., Biochemistry J., Mol. Biol., BBA, Plos One), with also high impact journals such as J. Cell. Biol, and PNAS. During this period, the team presented its work in 4 local and national conferences, and 1 communication in an international meeting. Amongst their publications, the work showing a modulation of glycosphingolipid membrane composition on Notch ligand activity, published in J. Cell. Biol. in 2010 (impact factor: 9.58), is of particular importance. They identified and characterized the *a1, 4-N-acetylgalactosaminyltransferase1* (*a4GT1*) gene as a gain of function suppressor of *mib1* in *Drosophila*. Using genetic and biochemical analysis of *a4GT1* function, they observed that specific changes in glycosphingolipid (GSL) composition can rescue the defects in Dl and Ser trafficking and signaling seen upon inhibition of *mib1* activity, thereby establishing a new functional link between GSLs and Notch signaling. This study has made the cover of the issue of the journal. The team has submitted a patent for the development of cholesterol nanoparticles able to trap and measure contents of the main endocannabinoid, anandamide.

Two other papers published in 2010 in Plos One (impact factor: 4.35) and J. Mol. Biol. (impact factor: 3.87) have significant impacts for two major human neurodegenerative diseases: Alzheimer's and Parkinson's diseases. In the second paper, they described the interaction between the alpha-synuclein, a peptide associated with familial forms of Parkinson's disease, and ganglioside GM3. They studied the role of GM3 (enriched in astroglial cells) in the formation of membrane ion channels composed of alpha-synuclein oligomers, which might participate in the toxicity of this protein.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

Because of the uniqueness of the team discovery (identification of a sphingolipid binding domain in proteins), a number of national and foreign laboratories have established collaborative works with the team. So, the project leader has developed a good network of national (Paris, Nice, Avignon) and international (Argentina, Israel) collaborators. For instance, in collaboration with a group from Argentina, they have identified potential cholesterol recognition sites in the human nicotinic acetylcholine receptor, and a manuscript is in revision in PNAS (impact factor: 9.43). Despite the important impact of his work, the team leader has been invited in only one international meeting (Gordon conference, 2011)

The team obtained national contracts with ANR (71.4 kEuro, 2009-2011), INCA (90 kEuro, 2008-2011) and INRA (5.5 kEuro, 2010), but no European or international fund resources.

A MCU has been recruited in 2006 and another MCU obtained a PR2 promotion in 2009. A post-doctoral fellow is actually supported by an ANR contract. However, there is no Ph.D. student in this team at the present time.

- Appreciation on the scientific strategy and the project

The project proposed for the next 4 years is perfectly in line with previous work done by the team. Four themes will be developed.

- Interaction of amyloid proteins with lipids in reconstituted membranes (lipid bilayers and Langmuir mono- and bi-layers). These studies are in continuation with previous ones.

- Modulation of cholesterol/sphingolipid contents in brain-derived cells in vitro. Here the objective is to identify if spingolipid/cholesterol contents alters amyloid functions. Modulation of lipid contents will be achieved using pharmacological, metabolic and silencing RNA approaches.

- Mechanistic studies of the toxicity of amyloidoidergic proteins. The main goal of these studies is to evaluate the effect of lipid contents on binding and internalization of amyloid and synuclein proteins, as well as on plasma and mitochondrial membrane functions. Studies will be performed in primary cultures of dopaminergic neurons.

- Effect of environmental contaminants. The team will evaluate the effect of pesticides, such as rotenone, known to be risk factors for the development Parkinson's disease, on fibrillation of alpha-synuclein and formation of alpha-synuclein-based channels that have been shown to destabilize membranes. They will also investigate alpha-synuclein mutants that have been genetically associated with familial forms of Parkinson's disease. Deciphering this complex network of lipid-protein interactions related to alpha-synuclein and beta-amyloid proteins should help to understand how alteration of the function of these proteins induces neuronal cell toxicity and may lead to new conceptual approach for therapeutic intervention in neurodegenerative disorders.

The feasibility of the first two objectives is high. For the two other objectives, more intensive collaborations with team 1 (that should be facilitated by the fusion of the two teams), as well as collaborations with external groups expert in the study of cellular and animal models of Parkinson's and Alzheimer's disease, are highly recommended.

• Conclusion

▪ Summary

This is a good research program, presented by a good research team. The feasibility of the project is very good overall and is addressing an important subject at the fundamental research level. Translation of the results in applied science has already been demonstrated (submitted patent) and there is a potential for application in pre-clinical research as well.

▪ Strengths and opportunities

The Committee has observed the following strengths:

- Excellent recognition of their work in the scientific community.

- Very good publication record, both in quantity and quality.

- Very good diversity and complementary of experimental approaches (from in silico modelisation, biophysical approaches, reconstitute membrane bilayers, cell cultures, electrophysiology).

- Good network of collaborators.

▪ Weaknesses and threats

There are a few weaknesses that have been identified by the Committee:

1. The number of full-time researchers (with no teaching duty) and PhD students is actually insufficient (low attractivity)

2. Low participation to international meetings (low visibility)

▪ Recommendations

The Committee recommends the following points:

- The team should make big efforts to increase its international visibility, for instance by participations to international meetings.

- Collaborations with external groups' expert in the study of cellular and animal models of Parkinson's and Alzheimer's disease are highly recommended.

- Applications to competitive European and other international calls are strongly recommended to increase the team research budget and visibility.

- The ability of the team to attract full-time researchers and PhD needs to be improved.

- Thematic Interactions between teams 1 and team 2 should be better demonstrated.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
PPSN - PHYSIOLOGIE ET PHYSIO-PATHOLOGIE DU SYSTÈME NERVEUX SOMATO-MOTEUR ET NEUROVÉGÉTATIF	A	A	A	A	A
INTERACTIONS MOLÉCULAIRES ET SYSTÈMES MEMBRANAIRES [TROUSLARD-FANTINI]	A	A	Non noté	A	A
NEUROBIOLOGIE DE LA PRISE ALIMENTAIRE ET DU COMPLEXE VAGAL DORSAL [TROUSLARD-TROUSLARD]	B	A	Non noté	A	A

C1 Qualité scientifique et production

C2 Rayonnement et attractivité, intégration dans l'environnement

C3 Gouvernance et vie du laboratoire

C4 Stratégie et projet scientifique

Statistiques de notes globales par domaines scientifiques

(État au 06/05/2011)

Sciences du Vivant et Environnement

Note globale	SVE1_LS1_LS2	SVE1_LS3	SVE1_LS4	SVE1_LS5	SVE1_LS6	SVE1_LS7	SVE2 _LS3 *	SVE2_LS8 *	SVE2_LS9 *	Total
A+	7	3	1	4	7	6		2		30
A	27	1	13	20	21	26	2	12	23	145
B	6	1	6	2	8	23	3	3	6	58
C	1					4				5
Non noté	1									1
Total	**42**	**5**	**20**	**26**	**36**	**59**	**5**	**17**	**29**	**239**
A+	16,7%	60,0%	5,0%	15,4%	19,4%	10,2%		11,8%		12,6%
A	64,3%	20,0%	65,0%	76,9%	58,3%	44,1%	40,0%	70,6%	79,3%	60,7%
B	14,3%	20,0%	30,0%	7,7%	22,2%	39,0%	60,0%	17,6%	20,7%	24,3%
C	2,4%					6,8%				2,1%
Non noté	2,4%									0,4%
Total	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

*** les résultats SVE2 ne sont pas définitifs au 06/05/2011.**

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

• SVE1 Biologie, santé
- **SVE1_LS1 Biologie moléculaire, Biologie structurale, Biochimie**
- **SVE1_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes**
- **SVE1_LS3 Biologie cellulaire, Biologie du développement animal**
- **SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie**
- **SVE1_LS5 Neurosciences**
- **SVE1_LS6 Immunologie, Infectiologie**
- **SVE1_LS7 Recherche clinique, Santé publique**

• SVE2 Ecologie, environnement
- **SVE2_LS8 Evolution, Ecologie, Biologie de l'environnement**
- **SVE2_LS9 Sciences et technologies du vivant, Biotechnologie**
- **SVE2_LS3 Biologie cellulaire, Biologie du développement végétal**

APPENDICE

S2UR120003653 - PPSN
Physiologie et Physio-pathologie du Système Nerveux somato-moteur et neurovégétatif - 0132364Z

Réponse du directeur d'unité : Jérôme TROUSLARD

❖ **Team 1** : Neurobiology of food intake and dorsal vagal complex (DVC) ; team leader : **Jérôme Trouslard**

The committee points out that specific leaders within the team should be identified.This apparent absence of leaders results from a voluntary choice in the presentation of the team rather from a real absence of leaders. As perfectly sound by the committee, we put forward three main research lines: role of glia cell, cerebrospinal fluid contacting neurons, and BDNF in the physiology of DVC and hypothalamus. These three lines are actually supervised by three identified leaders. One professor and two assistant professors coming outside of PPSN will join us at the time PPSN will be created. They will conduct their research in one of these themes.

I recall that this team faced the departure in 2008 of its previous team leader and of his associated full-time researcher in 2011. Since then, we developed a two-fold strategy. First, we identified these three themes and funded them. In our mind, that was the first obligatory step before finding more substantial research contracts (ANR and European grants). Second, we support the development of the start-up Biomeostasis (created by two of our previous PhD students) that should allow us to get industrial contracts.

❖ **Team2** : Molecular interactions and membrane systems ; team leader : **Jacques Fantini**

No specific comment.