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

Section des Unités de recherche

AERES report on the research unit

Unité de Neurobiologie des canaux Ioniques et de la Synapse

From the

Université Aix-Marseille 2

INSERM

March 2011

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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 : Unité de Neurobiologie des canaux Ioniques et de la Synapse

Requested label: UMR INSERM

N° in the case of renewal: UMR 641_S

Name of the director: Mr. Dominique DEBANNE

Members of the review committee

President

Mr. Christophe MULLE, University Bordeaux Segalen, Bordeaux

Other members

Mr. Jean-Louis BESSEREAU, Institut de Biologie de l'Ecole Normale Supérieure, Paris
Mr. Thierry GALLI, Université Paris Diderot, Paris
Mr. Enrico CHERUBINI, International School for Advanced Studies, Trieste, Italy
Mr. Maurice FALEMPIN, Université Lille Nord de France, Lille CNU representative

Observers

AERES scientific advisor :

Mr. Christian GIAUME

University, School and Research Organisation representatives:

Mrs. Catherine LABBE-JULLIE, INSERM
Mr. Pierre CHIAPPETTA, Université Aix-Marseille 2

Report

1 • Introduction

- Date and execution of the visit

The visit began at 9h Am on March 1st and ended the same day at 5h45PM. The agenda included the presentation of the unit past activities and project by the head of the unit, presentation of axis 1,2, and 3 successive meetings with staff members, engineers and techniciants, students and post-doc and University of representatives.

The INSERM UMR 641 was created in 2002. It is located on the campus of the Faculté de Médecine Marseille Nord, and has been a member of the IFR Jean Roche. The research field is cellular neurobiology of ion channels and synapses. It is currently composed of 4 teams, three of which are part of the current proposal. One of the teams is an Avenir team, which started in 2007. The teams work on mechanisms regulating synaptic vesicle release, on sodium and potassium channel trafficking and on the plasticity of intrinsic properties of neurons.

- Management team

The head of the unit is M. Dominique DEBANNE.

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	12	10
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	4	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	13	11
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	3	
N6: Number of Ph.D. students (Form 2.7 of the application file)	5	
N7: Number of staff members with a HDR or a similar grade	10	7

2 • Overall appreciation on the research unit

- Summary

This is a very good and productive research unit with strong expertise and a clear focus in the neurobiology of ion channels and synapses. The previous management and life of the unit was highly appreciated. The unit should strengthen its international position and attractiveness, and make sure that the development of translational projects and services does not hinder basic research activities.

- Strengths and opportunities

The research themes are coherent, complementary and well focused on ion channels in neuronal excitability and synaptic release process. The committee was highly positive about the originality of the previous findings and the hypotheses. Overall the production is very good and rather equivalent between the groups. Team leaders have a good international visibility. Finally, the scientific environment and on site core facilities are of high quality.

- Weaknesses and threats

Despite the scientific quality of the unit, the committee was concerned with the rather low attractiveness for PhD students and post-docs, especially from abroad, and in the modest implication in international networks and in international grants. The committee also felt that the loss of a team with expertise in cell biology was unfortunate. The integration of the clinical project within the basic research activities is not optimal, and there is an unclear distinction between service activities and basic research. Finally some projects may appear somewhat over ambitious.

- Recommendations

The committee members recommend increasing the number of students and post-docs by a clear policy of external communication and international networking. It would also be sensible to recruit a new team with expertise in cell biology, and to continue the efforts towards further interactions between teams.

To be successful, the proposed translational project would require the future emergence of a dedicated team on miRNA, exosomes and prenatal brain hypoxia with a critical mass. Diagnostic activities and services would benefit from being separated from research activities with a clearly identified manager.

- Production results

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	3
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	9
A3: Ratio of members who are active in research among staff members [(A1 + A2)/(N1 + N2)]	0,93
A4: Number of HDR granted during the past 4 years	0
A5: Number of PhD granted during the past 4 years	11

3 • Specific comments

- Appreciation on the results

The unit was established in 2004. It is currently composed of three established groups of around 10 scientists each and one Avenir group created in 2007, with a common interest in the neurobiology of ion channels.

During the past 4-year term, the unit has addressed central questions in neuroscience in a very competitive international environment. The teams have recently made major discoveries and proposed original ideas and concepts, among which the link between SNAREs and V-ATPAse (Neuron, 2010), the role of CDK2 and CDK5 kinases in the the accumulation of ion channels at the axonal initial segment (J Cell Biol, 2008) and the importance of release probability of glutamate in synaptic delay (Neuron 2007).

During the past 4-year term, the research themes were coherent, complementary and well focused on ion channels in neuronal excitability and synaptic release process, with two main levels of approaches, molecular and cell biological studies for teams 1 and 3, and neurophysiology for the teams 2 and 4. The head of the unit rightly points to the fact that this complementarity of approaches is a real asset for the unit, as illustrated by the study published in Neuron by team 1, with the collaboration of team 2. This is a promising example, although rather isolated, and this cross-interaction should have been more prominent.

In total, the unit has published 44 original scientific articles in international peer reviewed journals. Team 4 has had an excellent publication record from his previous post-doc period, but has not yet published a major research article as an Avenir group (2 papers have been submitted). Apart from the major publications cited above (2 Neuron, J Cell Biol), the unit has published in a few very good journals (2 PNAS, 2 J Neuroscience) and other very solid and respected more specialized journals (Traffic, JBC, J Physiol, Mol Pharmacol). Overall the production is very good and rather equivalent between the groups.

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

Individually, several scientists of the unit are well recognized in their field at the international level, as illustrated by the invitation to publish in major review journals such as Phys Rev, and by some invitations as speakers to international conferences. In addition, the participation in international editorial boards and international committees should be noted. The unit has hosted as visiting scientist a prominent leader in the field.

The unit has been attractive by recruiting a French post-doc to establish an Avenir team, and locally, by recruiting 3 professor/clinicians and a CR1 INSERM to develop disease-oriented research topics. However, the unit has not demonstrated a great capacity in attracting foreign young scientists as students or post-docs.

Teams of the unit have established a few productive collaborations at the national and international level (leading to very good joint publications, i.e in PNAS and Neuron). There is however limited participation in structured and well funded international networks, apart from an FP6 project which ended in 2007. Members of the unit should make more efforts in organizing international conferences or workshops.

One of the clear current weaknesses, noted in the document, is the relatively low number of PhD students and post-docs. Overall the balance between students/post-docs (8) and staff scientists (12) is low.

In general, funding from national research grants has been very good until 2010. A sizeable part of external resources was provided by the leaving team. Future funding depends on the success of several pending grants (ANR and FRM team).

In terms of valorization, one of the research team has developed a test for pharmaceutical use of a peptide derived from the V-ATPase (patent in 2009) for autoimmune diseases (see team#1).

- Appreciation on the management and life of the research unit

The unit has a strong activity of internal scientific events, and is well prepared to develop interactions between the groups. Students and researchers are very positive about the scientific environment and communication between the teams, within and outside the unit. Regular seminars organized by the IFR were highly appreciated, and should be continued despite the end of the IFR program, funded and organized through a "convention" between the neuroscience units on site.

All groups are involved in teaching activities.

Locally, the unit has participated in the activities of Marseille Nord (IFR etc….), and shares core facilities with the other two neuroscience units of the campus. Given the small size of the unit as compared with more common large Research Centers, the committee considers that a stronger integration at the level of Marseille Nord (that goes well beyond the present proposed "convention" may be pertinent and should be re-discussed in the context of the future Neuroscience Research building planned within the next 5 years.

- Appreciation on the scientific strategy and the project

The document denotes a well-thought scientific strategy for the future unit. This is a small unit with a clear scientific focus, shared technical expertise, and a real will to strengthen interactions between the groups. The departure of a team with an excellent expertise in cell biology of ion channels may appear unfortunate given the common general interest in the neurobiology of ion channels. However, the director points to the fact that all the expertise remains in the laboratory. Nevertheless, the committee considers that the field of cellular biology is crucial for several projects and may require recruiting an additional team.

There is a clear effort to develop interactions with clinicians of the CHU by recruiting clinicians in the unit, and to promote research training of medical doctors. The committee was not fully convinced by the proposed translational project, and has expressed some doubts about its integration with the current activities of the unit, particularly team #1. The diagnostic/service activity should continue. However it should be separated from basic research activities. Both these activities may greatly benefit from being grouped into an additional team placed under the responsibility of a scientific manager (the previous head of the unit is potentially a very good candidate for taking such a responsibility).

4 • Appreciation team by team

Team E01 : Molecular mechanisms of neurotransmitter release

- Name of the team leader: Oussama EL FAR
- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	4
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 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)	3	3
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	0
N7: Number of staff members with a HDR or a similar grade	3	4

- Appreciation on the results

The previous team leader has contributed regularly with a few excellent (Neuron) and very good publications (PNAS, JBC, etc) and is a recognized expert in calcium regulation of neurosecretion. The group is strong on studying the molecular mechanisms of neurosecretion with particular emphasis on calcium-calmodulin, V-ATPase and SNAREs. The work on calmodulin and V-ATPase are original contributions in a very competitive field. These contributions place this group at a high level in the international competition.

The team has also important diagnostics activity for several autoimmune diseases with anti- ion channels autoantibodies and the detection of botulinum neurotoxins using innovative and patented assays.

The scientific output of the group is good with 13 publications in the last 5 years out which there are 8 first or last author publications. They include 3 papers in prestigious journals such as PNAS and Neuron (a most prominent contribution to the field) and very good ones like Traffic and JBC. The group was invited to present their results at a few international meetings. In particular, work on the V-ATPase and calmodulin are very innovative and this team is tackling interesting problems with a high level of experimental expertise and regularly offers new ideas.The group has difficulty in recruiting post-docs and students. The ratio between permanent scientists and PhD students/post-docs is low.

The previous team leader has obtained a grant from ANR (as a PI) in the previous contract, and a main grant from AFM. In addition he has established a very fruitful industrial partnership with several companies (Ipsen, Veolia) and hospitals throughout France regarding diagnostics.

The team has developed fruitful collaborations with leaders in the field (JE Rothman, and S Mochida).

The previous team leader will retire within a few years and one scientist has emerged as new team leader. The previous team leader was the head of the unit and his management was highly appreciated.

- Appreciation on the project

The group will continue to study V-ATPase, calmodulin, and SNAREs and to have a diagnostics activity. The project is devided in three subprojects which all are run, under the supervision of the team leader. Detailed organization (who works on which project?) was not provided in detail.

The research is original and on a very high level of expertise. The project on V-ATPase is risky in its hypothesis (potential role as a fusion pore) and approaches (in vitro reconstitution, CALI).

- Conclusions
  - Summary

The committee considers that this is very good group with good level of international recognition, with an original project and hypotheses. It is with however moderately succesful in obtaining substantial grant support, and has had difficulty in attracting PhD students and post-docs, particularly from abroad.

  - Strengths and opportunities

The group has an excellent biochemical expertise that should be further combined with electrophysiological expertise of the two other teams. The group made very original contributions on V-ATPase and calmodulin in the competitive field of neurosecretion.

  - Weaknesses and threats:

The group lacks of students and postdocs, although this may be conjonctural. The groups shows suboptimal funding capacity (ie to attract post-docs…). The V-ATPase project is challenging and may require in vivo data in genetically modified mutants (use of invertebrate model?) or more cell biological expertise unless the team concentrates on biochemistry and biophysics only. Finally there is a potential scientific divergence between the diagnostics activity and the research project.

  - Recommendations:

The group should consider separating the diagnostics activity in a distinct team of service. In addition, it should be more ambitious in attempting to secure national or international grants. Finally, from a scientific point of view, it may be interesting to consider all possible functions of V-ATPase.

Team E02 : Dynamics of neuronal excitability

- Name of the team leader: Dominique DEBANNE
- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	5	5
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	
N7: Number of staff members with a HDR or a similar grade	4	3

- Appreciation on the results

In the last five years the main research goal of the group has been to characterize changes in intrinsic neuronal excitability associated with functional plasticity processes in the brain. Along this line of research, one of the major achievements is the finding that, after induction of non maximal LTP, dendritic integration by back propagating synaptic potentials is facilitated by local down-regulation of the hyperpolarization activated current Ih, mediated by HCN channels. Of particular interest is the discovery that the regulation of voltage-dependent channels in principal cells and interneurons via the activation of metabotropic glutamate receptors constitutes a new mechanism for homeostatic regulation of cell firing. This mechanism may be particularly relevant in pathological processes such as epilepsy. It is worth mentioning that this group has developed neuron-computer hybrid tools such as the dynamic clamp technique and the hybrid feed-forward network which have been instrumental for studying how synaptic or voltage-dependent conductance regulate synaptic plasticity processes at single cell and at the network level.

The study aimed at investigating the mechanisms which regulate changes in synaptic latency is particularly innovative. This stems from the original observation that the temporal regulation of neuronal activity is critical for information processing. Using pair recordings from monosynaptically connected neurons, the group has found that the synaptic delay is regulated by the probability of transmitter release and by the waveform of the action potential.

Finally an important achievement concerns the role of intrinsic membrane voltage-dependent and ligand-gated channels on spike timing and network synchronization.

The research activity of this group is of high level as documented by the productive track records of publications in first class international journals including Neuron and J Neurosci and in very good more specialized publications such a J Physiol, Frontiers Syn Neurosci, Nature Protocols, etc. The planned collaborative work with team#1 (which has led to a joint paper on Neuron) fits very well with one of the main research goal of the group. This collaboration is still limited and should be further encouraged.

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

The international reputation of the team leader and members of the group is documented by a few invitations to give lectures at national and international conferences including the Gordon conferences and by the Editorial activity of the group leader as Senior Editor of J Physiol and Reviewing Editor of EJN. The invitation to write a review article for Physiol Reviews and a perspective in Science Signaling further highlights the relevance of the team leader's work for the international research community.

- Appreciation on the scientific strategy and the project

Along the same lines of research pursued over the years, the group intends to use a variety of approaches to clarify the mechanisms regulating intrinsic plasticity in dendrites and axonal compartments in physiological and pathological conditions. Particularly innovative is the idea to measure intrinsic plasticity in the axonal compartment of principal cells and interneurons, using double patch recordings.

Overall, this project is quite ambitious, but on the basis of previous achievements the committee is confident that the group has the expertise, leadership, and motivation to successfully carry out the proposed experiments in five years time.

The arrival of a group of expert neonatologists, to develop markers for the neurological status of fetal brain in prenatal anoxia-hypoxia, will certainly be an added value, which may contribute to boost the interaction between basic and clinical research. However, the integration of these complementary activities may not be easy, as the team does not have strong expertise in brain development.

- Conclusion :
  - Summary

This is a highly competitive, outstanding project aimed at clarifying the mechanisms regulating intrinsic plasticity in dendrites and axonal compartments of principal cells and interneurons in both physiological and pathological conditions, using a variety of experimental approaches. The committee considers that the molecular and cellular aspects of these mechanisms in collaboration with team #1 are not fully developed. The integration of the translational clinical activity does not appear optimal and may need refocusing.

  - Strengths and opportunities

This group has all the expertise, leadership, and motivation to successfully carry out the proposed experiments in the next five-year term. The committee was particularly positive about the originality of the project. The group shows very good productivity, and the group leader has a very good international visibility.

  - Weaknesses and threats

The committee considered potential difficulties in integrating new members. The molecular and cellular biology tools are not optimally developped. Finally, despite the visibility of the work at an international level, there is a rather modest international attractivity for post-docs, and participation in international networks.

  - Recommendations

The group should further implement collaboration with group #1 in order to clarify the molecular and cellular mechanisms regulating intrinsic plasticity in dendrites and axonal compartments.

In addition, it should better integrate the translational and the basic research projects by expanding the existing knowledge on intrinsic plasticity in prenatal and early postnatal brain.

Team E03 : Homeostasis and neuronal excitability and neuromodulation

- Name of the team leader: Jean-Marc GOAILLARD
- Staff members

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

- Appreciation on the results

This team is a young team launched in 2007 with the support of the INSERM Avenir program. Its leader has a very strong track record of excellent publications from the work conducted during his post-doctoral stay at the Volen Institute (Brandeis University). Specifically, he is now building on the work conducted in invertebrates to investigate the mechanisms underlying the homeostasis of excitability in rat dopaminergic neurons of the substantia nigra.

Equipment and experiments are now up to speed and the results already obtained are very promising—some of them being submitted for publication.

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

The team leader has already acquired some visibility based on invitations to international meetings and contribution of reviews in good journals. It should be stressed that apart from the team leader, who recently obtained a permanent position at the INSERM, the project managed to attract two post-docs and a PhD student.

Funding was sufficient in the last years, largely benefiting from the AVENIR program. One of the post-doc was awarded a post-doctoral fellowship from FRM. However, the committee was concerned by future funding, which is not yet secured. An ANR grant is pending, written in collaboration with an ENS team expert in theoretical modeling.

- Appreciation on the scientific strategy and the project

The scientific project is original and ambitious, trying to decipher the mechanisms underlying the homeostasis of neuronal excitability. It addresses several questions including the co-regulation of potassium channels among individual cells and in response to acute or chronic perturbation of cellular homeostasis, the analysis of signaling pathways underlying such regulations, and the role of calcium binding proteins in the acquisition of specific electrophysiological phenotypes.

Although most proposed experiments are based on strong evidence, the rationale for investing time and energy on the role of calcium-binding proteins was not totally convincing. In addition, the project appeared a bit oversized with respect of the human power of the existing team and it will be necessary to rank the priorities of the different aims. The project will undoubtedly generate a set of very interesting data, but it remains unclear whether the proposed strategy will be able to solve the complexity of the system and address its physiological relevance.

- Conclusion:
  - Summary

This is an ambitious and original project proposing to decipher the mechanisms underlying the robustness of electro-physiological phenotypes among a well defined class of neurons. The team is young but already obtained promising results, some of them being currently submitted for publication. If successful, this work might provide important new concepts to understand neuronal homeostasis. However, the experimental strategies are complex, and some of the proposed aims might be too ambitious and difficult to address experimentally. There is yet some uncertainties with future funding.

  - Strengths and opportunities

The project is original and addresses important questions. It will benefit from the local environment and potential interactions with team 2. Results might be relevant to understand new modes of neuronal dysfunction in brain diseases.

  - Weaknesses and threats

There is some discrepancy between the ambition of the project and the relatively small size of the team. The questions are extremely complex and experimentally challenging. It will be a constant challenge to address the complexity of the system and generate physiologically relevant results.

  - Recommendations

The team needs to grow and attract additional researchers with expertise in molecular and cellular biology. It will also be important to focus on a more limited number of achievable aims. Publications are now needed to ensure the visibility and future funding of the team.

Team E04 : Neuronal polarity and ion channels

- Name of the team leader: Bénedicte DARGENT

Past activities only, the team will not be part of the next Unit project

- Effectifs de l'équipe ou affectés au projet (sur la base du dossier déposé à l'AERES) :

	Dans le bilan	Not involved
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)	2	
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	3	
N3 : Nombre d'autres enseignants-chercheurs et chercheurs y compris chercheurs post-doctorants (cf. Formulaires 2.2, 2.4 et 2.7 du dossier de l'unité)	2	
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	3,5	
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)	1	
N6 : Nombre de doctorants (cf. Formulaire 2.8 du dossier de l'unité)	2	
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées	4	

- Appreciation on the results

The group has been a world leader since a seminal paper in Science (2003) in the mechanisms involved in the polarized expression of proteins at the axonal initial segment. The activity of the group on this aspect was clearly focused, and highly recognized. During the 2006-2010 period, the group has provided evidence for the dynamic regulation of the localization of ion channels and ankyrin G at the AIS by the protein kinases CK2, CDK2 and CDK5. This cell biology work performed in dissociated cell cultures and cell lines, made use of innovative tools such as single particle tracking and surface plasmon resonance. The impact of the work is indicated by the qualitatively high level of publication (2 articles in J Cell Biol).

Another aim of the group was to understand the function of the striatin family members. This work has accumulated additional information on the traffic of multimodular scaffolding proteins, with publications in good/very good journals of the field (J Neurochem, Traffic, J Comp Neurol), with 2 as first/last author from the group. This project will be discontinued at the end of 2011. A final aim of the group is to link sodium channels and neurodegenerative diseases, using motor end plate disease mice as a model. This project correlates with the recruitment of a professor/clinician in the group in 2008 (with one publication in 2006), and no subsequent publication.

Members of the group have been invited as speakers at a few national (1) or international (2) conferences.

The group has been extremely efficient in obtaining research grants and fellowships for PhD students and post-docs, including an Equipe-FRM grant. There are however few (or none) foreign students of post-docs: although the scientific quality of the group is well recognized at an international level, this has not led to a clear participation in international networks or to the attraction of young foreign students/post-docs.

The group leader has been implicated in high level responsibilities at a national level, and was awarded the silver medal of the CNRS.

In parallel to the research activities, a professor/clinician is involved in clinical and valorization activities in a distinct field.

- Conclusion :
  - Summary

The group has a very strong focus on the cell biology of the AIS for which it has an excellent scientific recognition. The group has managed to publish in excellent journals. There are two other scientific projects of less high impact. The group leader has been very efficiency in securing grants during the last term. The group leader has a good international visibility. The group did not attract any foreign PhD students/post-docs.

  - Strengths and opportunities

The group has an excellent scientific recognition at national and international level, in cell biology of the neuron, and has managed to publish in excellent journals. The group leader has been very efficient in securing grants during the last term.

  - Weaknesses and threats

The group did not attract any foreign PhD students/post-docs. There are two aspects of the scientific activities which were not of the same caliber as the AIS project, and will apparently not be continued.

  - Recommendations

The group will not be part of the unit project for the next term. This may appear unfortunate as the group project on the cell biology of ion channels appears to fit very well with the main themes of the unit.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
UNIS - UNITÉ DE NEUROBIOLOGIE DES CANAUX IONIQUES ET DE LA SYNAPSE	A+	A	A	A	A
DYNAMICS OF NEURONAL EXCITABILITY [DEBANNE-DEBANNE]	A+	A	Non noté	A+	A+
MOLECULAR MECHANISMS OF TRANSMITTER RELEASE [DEBANNE-EL FAR]	A+	A	Non noté	A	A
HOMEOSTASIS AND NEURONAL EXCITABILITY AND NEUROMODULATION [DEBANNE-GOAILLARD]	Non noté	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**

UMR-S-641
Neurobiologie des Canaux Ioniques

Dominique Debanne, porteur de projet de l'UNIS

à

Comité AERES,
Conseil Scientifique de l'Université de la Méditerranée,
Département Evaluation et Suivi des Programmes de l'INSERM

Premier volet de la réponse au rapport AERES

Nous remercions vivement le comité AERES pour ses suggestions et commentaires. En particulier, la suggestion portant sur la séparation des volets fondamentaux et appliqués (tests diagnostiques) développés à l'intérieur de l'équipe 1 sera rapidement mise en oeuvre. Nous développerons une structure opérationnelle organisée sur le plan d'une plateforme translationnelle qui sera dirigée par le chef d'équipe / directeur d'Unité sortant (M. Seagar). Ce dispositif serait conforme à la stratégie de l'INSERM et de l'Université de la Méditerranée et pourra évoluer dans le temps vers une équipe autonome à l'interface entre l'UNIS et le CHU-Nord. Ainsi, le volet fondamental du projet portant sur les mécanismes moléculaires de la neurotransmission pourra être développé de manière plus focalisée par le nouveau chef de l'équipe 1.

Appréciation générale de l'unité

Nous souhaitons apporter des précisions à propos des remarques portant sur l'attractivité de l'UNIS en termes d'étudiants et post-docs au niveau international. Nous tenons à préciser qu'au cours du dernier quadriennal, les 3 équipes de l'UNIS ont attiré 5 post-docs (1 Américain, 1 Australienne, 1 Indien et 2 Français) formés dans des laboratoires étrangers réputés (Brandeis University, USA; RIKEN, Japan ; Menzies Institute of Tasmania, Australia) et 3 post-docs français formés en France. Au total, la force post-doctorale des 3 équipes de l'UNIS de 2006 à 2011 est importante et représente plus de 140 homme-mois. D'autre part, nous tenons à souligner notre visibilité en termes d'échange de post-docs. Six de nos étudiants et post-docs ont été recrutés par les meilleurs laboratoires étrangers (FMI Basel, Freiburg University, UCL, Hebrew University Jerusalem, NIH Washington, Johns Hopkins Baltimore). Outre les 5 étudiants rattachés à l'UNIS, nous accueillons actuellement 3 étudiants étrangers pour des stages de moyenne durée (3 mois/an sur 3 ans). Enfin, nous souhaitons mentionner que notre capacité d'accueil de doctorants est plafonnée par les directives de l'Ecole Doctorale des Sciences de la Vie et de la Santé qui impose l'adéquation entre le nombre d'étudiants et le nombre de chercheurs habilités à diriger les recherches. Selon cette analyse, nous sommes proches de notre maximum. Nous comptons néanmoins augmenter la capacité d'encadrement par les soutenances de 3 HDR programmées en 2011.

Une des recommandations est de développer notre participation à des réseaux internationaux. Comme cela a été souligné lors de la visite sur site, nos liens avec des laboratoires étrangers de premier plan sont nombreux et structurés. Ceux-ci se font au travers de participations à des réseaux européens, d'échange de doctorants, de collaborations scientifiques récentes avec les Universités de Tokyo, Yale, Berkeley et New York, et par l'accueil d'un éminent neurobiologiste, membre de l'Académie des Sciences des Etats Unis. Ces interactions internationales sont très efficaces et ont déjà donné lieu à 4 publications conjointes dans *Neuron*, *PNAS* et *Frontiers in Syn Neurosci* au cours des 2 dernières années. Cependant, nous tiendrons compte des recommandations faites par le comité, en nous impliquant encore d'avantage dans les réseaux européens et extra-européens.

Nous souhaitons dissiper la crainte du comité concernant l'affaiblissement de l'unité dans le domaine de la biologie cellulaire après le départ de l'équipe 4. L'expertise reste dans l'UNIS et en particulier dans l'équipe 1. L'équipe 4 s'est montrée peu ouverte aux collaborations an sein de l'unité au cours

des dernières années et de ce fait son départ ne constitue pas une perte réelle en termes de valeur scientifique ajoutée. Par contre ce départ engendre une structure beaucoup plus cohésive. Nous avons néanmoins parfaitement conscience qu'une solide expertise en biologie cellulaire est profitable à l'épanouissement de certains projets proposés par les équipes 2 et 3. Cette expertise sera apportée en interne par l'équipe 1, en externe par des collaborations (exemple : collaboration établie depuis janvier 2011 entre l'équipe 2 et une équipe du Centre de Biologie Moléculaire de Madrid,) et comme le recommande le comité, par le recrutement d'un chercheur spécialisé dans ce domaine pour renforcer l'équipe 3 et l'attraction d'une jeune équipe. Nous tenons à rappeler que plusieurs contacts ont été établis avec de jeunes biologistes cellulaires ayant le profil de chefs d'équipe et désirant rejoindre notre unité. Nous estimons qu'au moins un de ces contacts se concrétisera dans les prochains mois et s'accompagnera d'une demande d'équipe Avenir/ATIPE.

Nous souhaitons également dissiper toute crainte concernant l'intégration des nouveaux chercheurs et enseignants-chercheurs (cliniciens et universitaires). Ce processus a déjà débuté : accueil des nouveaux membres au sein de l'unité et premiers résultats expérimentaux concluants depuis l'automne 2010. Enfin, nous attirons l'attention du comité sur le fait que les relations solides nouées depuis longtemps avec ces nouveaux arrivants garantissent leur intégration.

Remarques spécifiques des équipes

Equipe 1

Suivant les recommandations du comité, une nouvelle organisation du projet translationnel sera mise en place. Une structure pilotée par l'ancien directeur du laboratoire, Michael SEAGAR, prendra en charge le transfert de technologie, le nouveau projet translationnel ainsi que les dosages d'auto-anticorps anti-canaux ioniques.
Le comité aurait souhaité plus de clarté sur l'organisation détaillée « qui fait quoi » du projet écrit. Nous avons cependant donné ces détails dans notre présentation orale lors de la visite du comité. Nous tenons à disposition du comité une liste complète des intervenants par projet.
Le comité a souligné les risques associés au projet V-ATPase et aux approches expérimentales associées (reconstitution *in vitro*). Nous souhaitons apporter la précision suivante: nos résultats sur la reconstitution *in vitro* des composants de la V-ATPase vont dans le sens de notre hypothèse de travail.
D'autre part, nous suivrons les recommandations du comité concernant l'intérêt que représente l'utilisation d'organismes modèles. En effet, nous venons d'obtenir un accord de principe pour une collaboration internationale avec un laboratoire leader dans le domaine de la V-ATPase et utilisant la levure comme modèle génétique. D'autres contacts sont en cours afin d'établir des collaborations internationales sur des modèles de transmission synaptique chez la drosophile.
En ce qui concerne les financements, 2 contrats ANR sont en cours d'évaluation. Dans le cas favorable, ils permettront d'embaucher 1 ou 2 post-doctorants étrangers.

Equipe 2

Nous suivrons l'ensemble des recommandations faites par le comité. Nous développerons la collaboration déjà établie avec l'équipe 1 pour comprendre les mécanismes moléculaires de la plasticité intrinsèque des dendrites et de l'axone et cerner le rôle de certains facteurs développementaux dans ces plasticités.

Equipe 3

Les recommandations faites par le comité correspondent totalement aux préoccupations actuelles du chef d'équipe. Comme cela a été affiché lors de la visite par le chef d'équipe et le porteur de projet de l'UNIS, la priorité de l'équipe est de recruter un statutaire (ingénieur ou chercheur) pour ancrer les compétences en biologie cellulaire et moléculaire nécessaires à la poursuite des projets envisagés. Nous veillerons à rester pragmatiques pour éviter toute dispersion dans les projets. En ce qui concerne les financements à venir, un contrat ANR est en cours d'évaluation et une demande d'ERC sera déposée à l'automne 2011 pour permettre le renouvellement des forces vives de l'équipe.

Fait à Marseille, le 7 Avril 2011

Dominique Debanne

UNIVERSITÉ DE LA MÉDITERRANÉE
AIX-MARSEILLE II

Objet : Réponse au rapport d'évaluation - **S2UR120001643 - UNIS - Unité de Neurobiologie des canaux Ioniques et de la Synapse - 0131843H** - de l'unité UNIS - Unité de Neurobiologie des canaux Ioniques et de la Synapse

Observations d'Aix-Marseille Université

Appréciation générale de l'unité

Concernant l'attractivité de l'UNIS en termes d'étudiants et post-docs au niveau international, au cours du dernier quadriennal, les 3 équipes de l'UNIS ont attiré 5 post-docs (1 Américain, 1 Australienne, 1 Indien et 2 Français) formés dans des laboratoires étrangers réputés (Brandeis University, USA; RIKEN, Japan ; Menzies Institute of Tasmania, Australia) et 3 post-docs français formés en France.
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Concernant l'affaiblissement de l'unité dans le domaine de la biologie cellulaire après le départ de l'équipe 4, l'expertise reste dans l'UNIS et en particulier dans l'équipe 1. Le départ de cette équipe ne constitue pas une perte réelle en termes de valeur scientifique ajoutée.

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Par contre ce départ engendre une structure beaucoup plus cohésive. Nous avons néanmoins parfaitement conscience qu'une solide expertise en biologie cellulaire est profitable à l'épanouissement de certains projets proposés par les équipes 2 et 3. Cette expertise sera apportée en interne par l'équipe 1, en externe par des collaborations (exemple : collaboration établie depuis janvier 2011 entre l'équipe 2 et une équipe du Centre de Biologie Moléculaire de Madrid,) et comme le recommande le comité, par le recrutement d'un chercheur spécialisé dans ce domaine pour renforcer l'équipe 3 et l'attraction d'une jeune équipe. Nous tenons à rappeler que plusieurs contacts ont été établis avec de jeunes biologistes cellulaires ayant le profil de chefs d'équipe et désirant rejoindre notre unité. Nous estimons qu'au moins un de ces contacts se concrétisera dans les prochains mois et s'accompagnera d'une demande d'équipe Avenir/ATIPE.

- Page 5, 2nd paragraphe. L'article publié dans Neuron en 2007 ne concerne pas le rôle des canaux ioniques dans la fidélité de la décharge mais l'importance de la probabilité de libération de glutamate sur le délai synaptique.
- Page 5, 3ème et 4ème paragraphe. La numérotation des équipes devrait suivre celle du reste du document. Les équipes focalisées sur la biologie moléculaire et cellulaire sont donc les équipes 1 et 4, celles centrées sur la neurophysiologie sont les équipes 2 et 3.
- Page 5, 4ème paragraphe. L'unité a signé en fait 2 articles dans PNAS (Ji et al., 2007 et Karatekin et al., 2010). Cette correction doit s'appliquer également en page 7.
- Page 5, 8ème paragraphe. Le nombre d'étudiants et de post-docs est de 8 et non de 7.
- Page 5, dernier paragraphe. Le brevet déposé par l'équipe 1 porte sur les utilisations pharmaceutiques d'un peptide dérivé de la V-ATPase et non sur un test diagnostique.

Remarques spécifiques des équipes

Equipe 1

La suggestion portant sur la séparation des volets fondamentaux et appliqués (tests diagnostiques) développés à l'intérieur de l'équipe 1 sera rapidement mise en oeuvre. Nous développerons une structure opérationnelle organisée sur le plan d'une plateforme translationnelle qui sera dirigée par le chef d'équipe / directeur d'Unité sortant (M. Seagar). Ce dispositif serait conforme à la stratégie de l'INSERM et de l'Université de la Méditerranée et pourra évoluer dans le temps vers une équipe autonome à l'interface entre l'UNIS et le CHU-Nord. Ainsi, le volet fondamental du projet portant sur les mécanismes moléculaires de la neurotransmission pourra être développé de manière plus focalisée par le nouveau chef de l'équipe 1.

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D'autre part, concernant l'intérêt que représente l'utilisation d'organismes modèles, l'équipe vient d'obtenir un accord de principe pour une collaboration internationale avec un laboratoire leader dans le domaine de la V-ATPase et utilisant la levure comme modèle génétique. D'autres contacts sont en cours afin d'établir des collaborations internationales sur des modèles de transmission synaptique chez la drosophile.

En ce qui concerne les financements, 2 contrats ANR sont en cours d'évaluation. Dans le cas favorable, ils permettront d'embaucher 1 ou 2 post-doctorants étrangers.

Equipe 2

L'équipe 2 développera la collaboration déjà établie avec l'équipe 1 pour comprendre les mécanismes moléculaires de la plasticité intrinsèque des dendrites et de l'axone et cerner le rôle de certains facteurs développementaux dans ces plasticités.

Page 9, « appreciation of the results ». L'article publié dans J Neurosci en 2008 concerne la facilitation de l'intégration dendritique des potentiels synaptiques et non des potentiels d'action rétropropagés.

- Page 10, chapitre « Weaknesses and threats ». Aucun Clinicien ne rejoint l'équipe 2. .

Equipe 3

. Comme cela a été affiché lors de la visite par le chef d'équipe et le porteur de projet de l'UNIS, la priorité de l'équipe est de recruter un statutaire (ingénieur ou chercheur) pour ancrer les compétences en biologie cellulaire et moléculaire nécessaires à la poursuite des projets envisagés.

Nous veillerons à rester pragmatiques pour éviter toute dispersion dans les projets. En ce qui concerne les financements à venir, un contrat ANR est en cours d'évaluation et une demande d'ERC sera déposée à l'automne 2011 pour permettre le renouvellement des forces vives de l'équipe.

En accord avec les deux autres établissements d'Aix-Marseille

Le Président
de l'Université de la Méditerranée

Yvon BERLAND

Le Vice-président du Conseil Scientifique
de l'Université de la Méditerranée

Pierre CHIAPPETTA