

Adaptations neurovasculaires et métaboliques aux environnements

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Adaptations Neurovasculaires et métaboliques aux
environnements

From the

University of Lyon 1

CNRS

May 2010



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From the

University of Lyon 1

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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

May 2010



Research Unit

Name of the research unit : Adaptations Neurovasculaires et métaboliques aux environnements

Requested label: UMR CNRS

N° in the case of renewal

Name of the director : M. Jean-Louis SAUMET

Members of the review committee

Chairperson :

Mr. Eric VICAUT, Université Paris 7

Other committee members

M. Axel PRIES, Charité University medicine, Berlin

M. Angela SHORE, Universities Exeter and Plymouth

M. Jean-Jacques MOURAD, Université Paris 13

M. Rémi NEVIERE, Université Lille 2

M. Jean Sebastien SYLVESTRE, Université Paris 6

Committee members nominated by staff evaluation committees (CNU, CoNRS, INSERM and INRA CSS...)

M. Claude DELCAYRE, CoNRS member

M. Jean-Claude WILLER, CNU member

Observers

AERES scientific advisor

M. Pierre BEDOSSA

University or School representatives

M. Jean- François MORNEX

Research Organization representatives

M. Alain DOUCET représentant du Dir. Scientifique Adjoint de l'INSV du CNRS

Mme Anne-Marie HELLE, le délégué régional du CNRS,



Report

1 • Introduction

- Date and execution of the visit

The visit took place on the 21th of January. Almost all members involved in the project were present for the presentation. The presentation was made by the head of team and each of the member of the management team commented and answered the questions of the committee.

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

The project is based on the grouping of 4 previous units (FRE CNRS 3705 EA 4220, INSERM U820, UMRCNRS 5123 and EA 4170) that were involved in the study of neurovascular regulations and on metabolic adaptations to environment. They decided to group their strength in order to propose an integrated project in this field. At the present time they are localized in different laboratories but have the opportunities to be localized together in a common place at the Domaine Rockfeller. The team insisted on the benefit to share the experience and skills of the different units that merged in the present project. They insisted on the complementarity of the different technics that were developed in the laboratories that are involved in the project.

- Management team

The management team insisted on their common vision of a management on the group based on the consensus between the different managers of the previous teams.

- Staff members

| | Past | Future |
|--|------|--------|
| N1: Number of researchers with teaching duties (Form 2.1 of the application file) | 15 | 14 |
| N2: Number of full time researchers from research organizations (Form 2.3 of the application file) | 10 | 9 |
| N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file) | 7 | 7 |
| N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file) | 16 | 16 |
| N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file) | 4 | 0 |
| N6: Number of Ph.D. students (Form 2.7 of the application file) | 16 | 4 |
| N7: Number of staff members with a HDR or a similar grade | 18 | 16 |



2 • Overall appreciation on the research unit

- Overall opinion

The project is based on the grouping of four teams. All these teams have different research topics and a good level of publication in their research field. The aim of the research unit proposal is to create the conditions for a development of synergies between researchers allowing them to investigate neurovascular dysfunction in more depth.

The project director has previously described the existence of a pressure induced vasodilation (PIV) in skin microcirculation. This PIV is altered in different pathologies and thus can be considered as a marker that can explore neurovascular dysfunction in an integrated way. This approach is interesting because it might provide a tool to explore neurovascular dysfunction that is a highly relevant problem in several pathologies (such as diabetes for instance) and might potentially be a predictor of diabetes complication. However, this approach would have been more powerful if the researchers had put this observation of PIV in a more detailed perspective of physiological or pathophysiological meaning. This would also have provided opportunities for a more in depth presentation of the two main parts of the research project that were presented and would have explained the exact involvement of each team of researcher in the research project. The new research unit would certainly benefit from the addition of the techniques of each previous individual team, but, as the project has been presented, the synergy between the different teams in the scientific approach to define the new research project was not very cohesive. Considering that several researchers including the project director will retire in few years, it would have been useful to propose a more formal organization of the governance of the new unit which would facilitate both the management of the researchers and technicians and the stability of the unit in the future.

- Strengths and opportunities

For several aspects of the project, the researchers have been pioneers in their fields and have a good level of publication. Young researchers are present in a good proportion and show great dynamisms. An important number of technicians are enrolled in the project, which is important for the feasibility of planned experiments. All participants have a strong will to collaborate within each team and with other teams. Note also the good success in PhD thesis. The University supports the project and has facilitated the grouping by providing, in the near future, adequate space for new laboratories in a university building.

- Weaknesses and threats

- Before the present project there is no history of collaboration between the four teams.
- Several key members of the teams will retire in the next few years. This is also the case for important technicians.
- The internal organization of the unit is not clear. The benefit of the new structure for the researchers outside the previous directors research team was not clear were presentes.
- The scope of the project appeared too broad and in some aspects, fields of research, rather than a real common research project were presented.

- Recommendations to the head of the research unit

- The project would gain by focusing on some precise topics but giving for each topic a larger emphasis on the mechanistic questions.
- Governance and internal organization could be stated more precisely.
- The transmission of knowledge and skills from those technicians who will retire in a few years to the younger ones should be organized on the basis of the definition of the priorities of the research project.
- Clinical aspects of the proposed research are very important and should be developed further.



- Data on the work produced :

(cf. http://www.aeres-evaluation.fr/IMG/pdf/Criteres_Identification_Ensgts-Chercheurs.pdf)

| | |
|--|-----|
| A1: Number of permanent researchers with or without teaching duties (recorded in N1 and N2) who are active in research | 24 |
| A2: Number of other researchers (recorded in N3, N4 and N5) who are active in research | 5 |
| A3: Ratio of members who are active in research among permanent researchers [(A1)/(N1 + N2)] | 96% |
| A4: Number of HDR granted during the past 4 years | 3 |
| A5: Number of PhD granted during the past 4 years | 20 |
| A6: Any other relevant item in the field | |

3 • Specific comments on the research unit

- Appreciation on the results

The research project is original and largely based on an exploration of neurovascular dysfunction based on a vasomotor phenomenon originally described by the project director. The topic is highly relevant and might provide additional tools to explore patients (such as diabetic) in order to predict the risk of complications. Of note, very few tests exist which explore neurovascular function in an integrated way. The quality of results was good, but would certainly be increased by additional efforts to go further into their physiological meaning.

Altogether, publications were at a good level. Number of publication is very high, highly related to the previous history and the mixing of 4 different groups. Nevertheless, several articles have been published as leading author in good speciality journals (Circulation, J Hypertens, Ann Surg, J Invest Dermatol) or specialized journal of lesser quality (Toxic Applied Pharmacol, Malaria, Diabetologia). Publication in best impact factor journals appears as collaborations (Nat Immunol, Brain, Circul res). However, there was a rather large heterogeneity between researchers and groups.

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

A large degree of heterogeneity among the different members of the team also exists regarding the number of invitations to speak.

The attractiveness for top-level scientists or Post-Doc from abroad appears is rather limited but the number of PhD students is high.

There is a good ability to raise funds even in the context of competitive grants such as ANR.

The international collaborations appear rather limited.

They have four patents and good collaborations with pharmaceutical industry.



- **Appreciation on the strategy, governance and life of the research unit**

It appears very interesting to group 4 small sized teams in a larger unit, thus giving the possibility to create synergies. The project would, however, benefit from a more precise presentation of the governance (steering committee, rules for budget or resources allocation, teaching and personal development project...). This would also allow a better scientific coordination allowing a better prioritization of the different topics potentially feasible by the team.

- **Appreciation on the project**

The project aims to explore neurovascular dysfunction, which is a highly relevant topic. However, the committee feels that a general overview is lacking. It is unclear for example what are the benefits of the project to those researchers who were not previously working in the team leader group.

A major weakness is that the project presented a very large scope without real prioritization rather than taking the decision to analyze the cellular or molecular mechanisms of a more focused part of the described neurovascular dysfunction.

The committee also regrets that some working hypotheses have not been more explicitly defined.

The committee appreciates the potential interactions regarding the techniques used by the different teams but failed to identify clearly how they will interact in the scientific project.

The project is original and not risk taking.

| Note de l'unité | Qualité scientifique et production | Rayonnement et attractivité, intégration dans l'environnement | Stratégie, gouvernance et vie du laboratoire | Appréciation du projet |
|-----------------|------------------------------------|---|--|------------------------|
| B | A | B | B | B |

Villeurbanne, le 20 Avril 2010

M. Pierre GLORIEUX
Directeur de la section des unités de l'AERES
20 rue Vivienne

75002 PARIS

Monsieur le Directeur,

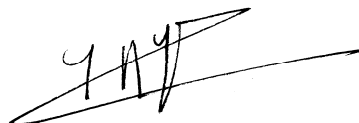
Je vous remercie pour l'envoi du rapport du comité de visite concernant l'unité de recherche :

«Adaptations NeuroVasculaires et Métaboliques aux Environnements » rattachée à mon établissement.

Ce rapport n'appelle pas de commentaire particulier de la part de l'université.

Je vous prie de croire, Monsieur le Directeur, à l'expression de ma meilleure considération.

Le Président de l'Université



Lionel Collet



Département de physiologie et pharmacologie clinique

Université Claude Bernard Lyon 1
Institut des Sciences Pharmaceutiques et Biologiques
FRE CNRS 3075 « Interactions neurovasculaires :
Modifications en fonction du vieillissement, du métabolisme et de la pression artérielle »

Jean-Louis SAUMET, Professeur
Directeur

«Courrier Officiel»

In its report, the Visiting Committee reported positive and negative indisputable points, claims of accuracy and an appreciation of the level of publications with some indisputable errors. This should be corrected to obtain a report as objective as possible and consistent with international criteria for evaluating research. The overall assessment of the project is generally good but on some points at least it should have been classified as excellent from objective criteria.

1 □ Positive points

Members of the unit thank the guests for having taken into account:

The successful merger of the four teams with unanimous consensus of the members of the unit and an early realization of joint work despite the geographical distance and thematic former teams.

The originality of the research theme. The mechanical sensitivity is studied by many teams and is the subject of publications at the highest level. Often it is discovered at the cellular or sub cellular level. Ours is a high level of integration. If many cells (bone, vascular, coclear ...) organelles or ion channels are mechanosensitive, our approach demonstrates a level of integration that involves not only the vascular and nerve cells but also the local central nervous system. This discovery, made in humans, followed by the development of relevant animal models, shows that research in integrative physiology can be successful if only one leaves him the means. Of course, as suggested by the preliminary report, cellular and molecular approach should complement this experimental and clinical research. That's what we did thanks to collaborations such as the role of TREK1 channels in our model. This work has been published in EMBO Rep. (we are the first and last authors) that was quoted in a recent review published in Nature showing the figure of our article.

This leads to talk of publications qualified by AERES evaluators of Good and not Excellent, while they are in journals of the series Nature or Circulation. We return to this issue below.

2 □ Negative points

Some are questionable.

About « *the exact involvement of each team of researcher in the research project* » and « *the synergy between the different teams in the scientific approach to define the new research project was not very cohesive* ». The remarks concerning the involvement of former teams did not have to be because **there is now only one team**. Each researcher or senior lecturer acts as an individual and brings its expertise and technical knowledge to the common project, while the skills are in neuroscience, vascular physiology or metabolism. Maintaining the status of former teams would expose us to immobility. For this reason it is urgent retrouper physically very quickly most of the researchers in one place to consolidate a new dynamic.

No common past but as recently demonstrated during the oral presentation of our project through the **presentation of preliminary shared results**. This was the starting point on which we had to build. Our success of a merger under these conditions is quite exceptional and deserves to be recognized.

Some of us are close to the end of occupation. It is indeed important, although we have many young researchers to pursue the recruitment of researchers, senior lecturers and technical staff to ensure continuity of skills. We have demonstrated our ability to recruit and attractiveness in the previous four (2 research scientists and 2 senior lecturers).

The theme of research is considered too broad. It may indeed appear in the document that we sent to the authorities although there is already a major effort to focus on the theme from the neurovascular model we have described. We were very far from the thematic diversity of the four former teams. In the oral presentation, we clearly stated our priorities, neurovascular and metabolism, especially on the work that has started on implementing a joint. This openness to the metabolism had already been initiated in the previous four-year period with publications in Diabetes. It will be enhanced and will develop the expertise of researchers who are not from the team of the project leader. Developing our research in various fields of pathology is quite broad and could be limited but our University and the CNRS encourage us to develop our business (3 ANR, four patents, industrial contracts and European publications and in excellent journals arising from this development!)

“The transmission of knowledge and skills from those technicians who will retire in a few years to the younger ones should be organized on the basis of the definition of the priorities of the research project.”

That's what we intend to do: put resources on the priorities identified by the Steering Committee and presented to the Visiting Committee of AERES during the oral presentation.

3 □ Requests for clarification and recommendations

“The internal organization of the unit is not clear”

The governance of the future research unit has started in practice throughout the preparation of the project: consensus as much as possible and frankly speak. The project manager was surrounded by a group of colleagues (mostly forties) that actually constitute the steering committee of the future research unit and fairly representing all areas of expertise. The choice of projects or subprojects to defend is based on the originality of the research, the level for hoped publications (our university wants a minimum of 5 IF!) and the potential for development (the research unit should find a part their operating funds).

To ensure the perenity, the research unit should designate at the mid-term an assistant director who will be co-opted members of the laboratory and accepted by our university and CNRS. It is a very important point. We should not work in emergency and give ourself time to reflect and observe the operation of the research unit in its new premises, the involvement of everyone in the thematic priority of the laboratory to appoint the Assistant Director. During the visit the researchers mentioned their agreement to choose an assistant director at midterm. This procedure is validated by the university president whose support neither the establishment of the REF or transfer to Lyon's lab director would have been possible.

“The benefit of the new structure for the researchers outside the previous directors research team was not clear were presents”

The benefit for researchers is global. Some bring an original model, others their expertise in the study of metabolism. We have focused on joint work so that everyone can find his account in the new project by developing its skills.

“Clinical aspects of the proposed research are very important and should be developed further.”

In the past, our clinical studies in healthy subjects or patients allow us to published in Circulation, Nature Immunol, Diabetes ... We intend to continue along this path, this will be facilitated by the fact that we have several leaders of hospital unit or responsible of Medical University Hospital among the members of our laboratory.

4 □ Misjudgements

Overall the project is considered good, this is the word that comes up most often about the originality of the research project, funding ... and publications. This "devaluation" of our project is difficult to understand and must be corrected.

In short, take the example of publications:

In the preliminary report it is written: *“Altogether, publications were at a good level. Number of publication is very high, highly related to the previous history and the mixing of 4 different groups. Nevertheless, several articles have been published as leading author in good speciality journals (Circulation, J Hypertens, Ann Surg, J Invest Dermatol) or specialized journal of lesser quality (Toxic Applied Pharmacol, Malaria, Diabetologia). Publication in best impact factor journals appears as collaborations (Nat Immunol, Brain, Circul res). However, there was a rather large heterogeneity between researchers and groups.”*

Qualifier good speciality journals as Circulation, Ann Surg, J Invest Dermatol and Diabetes (which is forgotten) is surprising. Every time, this is the best global journal of the speciality. An IF of 14 for Circulation can not be simply described as good. In any case if this ruling is that the AERES (everyone is free to criteria) must be identical for all teams evaluated. If these reviews are described as excellent in other respects it completely disqualifies AERES assessments that could be accused of working with an elastic yardstick.

Second point : “specialized journal of lesser quality”.

While Diabetologia (IF 6.7) is the second international journal in diabetes. The turn of phrase suggests that we go down very low on the readability of our publications. Now Diabetologia (IF 6.7) (to quote the example) is very close to the best review of diabetes (Diabetes IF 8.8). The delegate or chairman of the Visiting Committee could take advice from a diabetologist when the reputation of the journals in this field.

“Publication in best impact factor journals appears as collaborations (Nat Immunol, Brain, Circul res).”

This is false regarding impact factors. Circ Res is an excellent review but the second when the reputation and impact factor on the international level in the cardiovascular field. The top one is **Circulation ... called « good »** (see above).

The report noted « *The international collaborations appear rather limited.* »

In all cases, they exist and are based on a collaboration of quality (not quantity) that we did not spot a role. Examples include publications in Brain ... But most important publications are putting in Nat Immunol, Nat Rev Microbiol, certainly made in collaboration, but where the first author is either the student or an collaborator of a member of our research unity. Again in the report our role appears minimized.

In conclusion we urge that our comments are taken into account and that the preliminary report be amended accordingly. It is primarily the reclassification of good to excellent based on:

1 our scientific production (publications and patents)

2 our attractiveness: FRE CNRS - EA UCBL1 allowed the federation of four teams including many young researchers. As indicated in our oral presentation, a team from Toronto wishes to join us. The recruitment of young researchers (2 research scientists and 2 senior lecturers in the last four-year period).

3 our governance based on consensus with the creation of a steering committee open to all unit members who wish to get involved, adopting a strategy that has proven at the CNRS with the appointment of an assistant director midterm.

4 a federative project that the visiting Committee has recognized the originality and usefulness.