LPCM - Laboratoire de physiologie cellulaire et moléculaire

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Physiologie Cellulaire et Moléculaire

From the

Université de Picardie

February 2011

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Le Président de l'AERES

Didier Houssin

Section des unités de recherche

Le Directeur

Pierre Glorieux

February 2011

Research Unit

Name of the research unit : Laboratoire de Physiologie Cellulaire et Moléculaire (LPCM)

Requested label: EA

N° in the case of renewal

Name of the director : Ms Halima OUADID-AHIDOUCH

Members of the review committee

Committee chairman

M. David TULASNE, Université Lille 1, Lille

Other committee members

Mrs Elizabeth MACINTYRE, Université Descartes, Paris 5

Mrs Hélène COPPIN, Université Paul Sabatier, Toulouse

M. François-Loïc COSSET, Université Claude Bernard Lyon 1, Lyon

M. Patrice CACOUB, Université Pierre et Marie Curie, Paris 13

M. Jean SOULIER, Université Diderot, Paris

M. Jean-Pierre SAVINEAU, Université Bordeaux 2, Bordeaux, CNU representative

Observers

AERES scientific advisor :

M. David DOMBROWICZ

University, School and Research Organization representatives :

M. Georges FAURÉ, Université de Picardie

Report

1 • Introduction

- **Date and execution of the visit**

Visit took place on February 9th, 2011. The proposed director made a general introduction on the team and the future projects that were more extensively presented by senior researchers from the team. Some posters were presented by PhD students. After close-doors meeting with the University representatives, the committee met researchers, students and technicians in the absence of the proposed director. Evaluation ended with a closed-doors meeting of the jury.

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

This young team was created in 2008-2012 and it is located in Amiens. The team studies the involvement of potassium and calcium channels in breast cancer.

- **Management team**

The head of the lab is Mrs Halima OUADID-AHIDOUCH.

- **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)	9	10
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	2	
N6: Number of Ph.D. students (Form 2.7 of the application file)	7	
N7: Number of staff members with a HDR or a similar grade	5	5

2 • Overall appreciation on the research unit

• Summary

The alterations in the expression of ion channels are involved in the regulation of proliferation, survival, migration, invasion and oncogenesis. Deregulation of ion channels activity, disrupt cell physiology and lead to clinical onset of channelopathies. However, the involvement of ion homeostasis in breast cancer is poorly investigated.

The members of the team demonstrated that K+ (i.e. hEag1) and Ca2+ (i.e. TRPM7, TRPV6) channels are involved in the proliferation and the migration of breast cancer cells. In parallel, close collaboration with clinicians allowed the demonstration of the clinical significance of the over-expression of these channels in breast cancer.

The projects of the team are in continuity with the results previously obtained. First, they will search to further characterize the involvement of ion channels in proliferation, migration or survival in breast cancer cells and in animal models. Second, the expression of ion channels will be evaluated in samples of breast tumors in correlation with clinical parameters.

• Strengths and opportunities

- Originality of the project based on the research of the ion channels involvement in breast cancers, which is poorly investigated while deregulation of ion homeostasis is well known in other cancers.

- The studies of the team are based on complementary competences in electrophysiology, cellular and molecular biology and anatomopathology.

- Strong links between fundamental and clinical research, with translational work involving clinicians of the hospital of Amiens (Service d'Anatomie et de Cytologie pathologiques, service de Gynécologie Obstrétrique et de la tumorothèque de Picardie).

- Recent recruitment of young "maitre de conference" who bring new technical skills in the team (molecular biology, animal model of tumorigenesis) adapted to the competences required for the project of the team.

- Good management of the team with all the projects centered in a well defined thematic and an efficient strategy of recruitment and collaboration to reinforce the competences of the team.

- Ability to raise funding from local and national institutions.

- The equipments and facilities necessary for the project are available in the team with an effort to or in technical platforms (Plateforme d'Ingénierie Cellulaire et d'Analyses des Protéines, Plateforme de Biologie Moléculaire).

- Opportunity: The expression of the calcium channel Orai3 in breast cancer cells is associated to the expression of c-myc a well known oncogene. The study of their function link could be a good opportunity to reveal downstream molecular mechanisms induced by ions channels to regulate proliferation or survival.

• Weaknesses and threats

- Although the work of the team is regularly published in various scientific revues, their impact factors do not exceed 4,6. An effort should be done to publish the studies in more general journals. The characterization of the molecular mechanisms by which the ion channels regulate various cellular responses in breast cancer cells is an impotant issue to improve the impact of the studies.

- The team is constituted exclusively by teachers and clinicians who are involved in other activities than research. An effort should be done to recruit full time researchers.

- The members of the team did not obtain competitive funding such as ANR or INCa. The project will require solid grants since animal models and molecular biology are money consuming experiments.

- **Recommendations**

More ambitious experimental settings should allow to further increase the impact of their research. This goal could be achieved (i) by performing experiments with primary cultures in addition to breast cancer cell lines (ii) by developping animal models to confirm involvement of ion channels in experimental tumorigenesis (iii) with the research of downstream molecular mechanisms induced by ions channels to regulate cell cycle, motility or survival. This appears realistic within the comming years considering the scientific leadership of the PI and because this young team is now well settled technically, with a clear link with primary sample (hospital).

- **Production results**

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	6
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	
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	1
A5: Number of PhD granted during the past 4 years	6

3 • Specific comments

- **Appreciation on the results**

Calcium and potassium channels in breast cancer have been poorly investigated to date in France, while their involvement in other types of cancers is well known. This is a potentially very relevant field of research considering the frequency and severity of this cancer and the need for new biomarkers and therapeutic targets. This team has developed dedicated tools to analyze expression and activation of the ion channels genes. In addition, the studies are based on strong interactions with clinicians who are integrated in the research team. Thus, correlative studies between expression and histology, expression and grade and expression and clinical outcome (metastasis) are efficiently performed. In a complementary manner, the cellular models demonstrated involvement of these channels in regulation of cell cycle and motility. More recently, gene silencing was performed that suggests a direct role of Orai3 in survival and cell cycle.

Altogether, these studies strongly suggest a role of the calcium and potassium channels in breast cancer cells. This is a good basis to set up more experimental studies in the future: gene modulation in cell culture, xenografts, genetically modified mice.

These studies led to robust data which have been published in numerous scientific articles. There is a strong and efficient effort to publish regularly by all the members of the team including students, with a trend to increase the IF, from a range 2-3 to 3-4,6.

Several PhD students of this young team should finish the PhD thesis in the next years.

Several scientific collaborations are developped with French (Lille) and foreign laboratories (USA, Belgium, Germany, Spain, Maroc).

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

Six post-docs, most from France, have worked in the team between 2006 and 2010. Two of them have been recruited as MCU. Four young MCU joined the laboratory between 2006 and 2010, demonstrating the dynamism of the team. However, the efforts should be continued to recruit young researchers in the national institutions (CNRS and INSERM).

The team has demonstrated its capacity to raise funds from various local and national institutions (Région, ARC, Ligue contre le cancer). Nevertheless, the members of the team did not obtain more competitive funding such as ANR or INCa.

- **Appreciation on the management and life of the research unit**

The team is headed by a director well internationally recognized in the subject area and builds on a project shared by all staff. The director is regularly invited speaker in national and international meetings. The scientific animation of the team is dynamic, particularly through a weekly meeting and seminars of invited speakers.

All the research unit staff members are deeply involved in teaching biology and physiology at the master and doctoral level in both scientific and medicine faculties of the Amiens University.

- **Appreciation on the scientific strategy and the project**

The scientific project entitled « Rôle des canaux ioniques et du Calcium intracellulaire dans la Physiopathologie de la glande mammaire humaine » is in direct line with the previous studies of the team. Indeed the team demonstrated the correlation between the expression of membrane ion channels and tumor growth. However, the molecular mechanisms involved in regulation of their expression and the downstream signalling pathways are not well known.

More specifically, the objective is to understand the role of potassic signalling involving the hEag1 et hKCa3.1 channels and calcic signalling involving the TRPM7, TRPV6, Orai3 et RIP3 channel in breast cancers. The long term objective is to propose novel diagnostic and therapeutic strategies.

The project is well constructed with original and ambitious goals which are based on solid experience in this field.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
LABORATOIRE DE PHYSIOLOGIE CELLULAIRE ET MOLÉCULAIRE: LPCM	**B**	**B**	**A**	**A**	**B**

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**

UNIVERSITÉ
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Amiens, le 12 avril 2011

Monsieur le Président

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2011.04.045. GF/SD
Objet : réponse officielle évaluation LPCM
V/Référence : S2UR120001850 - Laboratoire de Physiologie Cellulaire et Moléculaire: LPCM - 0801344B

Monsieur le Président,

Je tiens tout d'abord, au nom de l'Université de Picardie Jules Verne et en particulier au nom du directeur et des membres de l'Unité « Laboratoire de Physiologie Cellulaire et Moléculaire » (LPCM) à vous remercier pour la qualité du rapport d'évaluation ainsi que pour les échanges constructifs que nous avons pu avoir avec le comité lors de la visite du 9 février dernier.

A la suite de la transmission du rapport d'évaluation, le Directeur, les membres de l'Unité et moi-même tenons à apporter les précisions suivantes :

1. Recrutement des chercheurs

L'unité est encore assez jeune (reconnaissance en 2008) et composée uniquement d'enseignants-chercheurs. Cependant, avec le soutien de l'établissement, la stratégie consistera à attirer des chercheurs statutaires dans le but de demander, à mi-parcours, la création d'une Unité Mixte Inserm – Université.

2. Amélioration de « l'impact factor » de nos publications

Nous sommes d'accord avec la critique formulée par le comité d'évaluation de l'AERES sur l'amélioration du niveau de l'impact factor de nos publications.

Cependant, la reconnaissance comme « Jeune Equipe » sur une thématique qui n'existait pas auparavant à l'UPJV date de 2008. Il a fallu nous équiper, recruter des enseignants-chercheurs qui possèdent des compétences en biologie cellulaire et moléculaire et publier.

Depuis 2010, notre stratégie a porté ses fruits puisque nous avons commencé à améliorer l'impact factor de nos publications (e.g. Am J Physiol ; Molecular Cancer).

En 2011, nous avons déjà deux publications acceptées à J. Cell Physiol (IF=4.586), BBA Molecular Cell Res (IF=4.374) et nous avons soumis deux articles : un à Cancer Research (IF=7.543) et un autre à Gastroenterology (IF=12.899).

UNIVERSITÉ de Picardie Jules Verne

Comme nous l'avions indiqué dans nos perspectives, nous avons commencé, en collaboration avec Patrick Dumont et Dominique Leprince (Unité UMR 8161, Institut Pasteur de Lille) et avec le Pr Laurent Martigny et Dr. Jérôme Devy (Unité UMR 6237, Université de Reims Champagne Ardennes) à développer des modèles de xénogreffes sur souris.

Nous avons aussi commencé à travailler sur des cultures primaires. Notre objectif principal est bien entendu de réaliser une recherche "state of the art", ce qui nous permettra de publier nos travaux dans des journaux d'excellent impact factor. Nous pensons qu'avec les modèles animaux, la primo-culture et les compétences des membres du LPCM, cet objectif sera atteint.

3. Sources de financement

L'absence de financement de projets de type européens ou de type ANR dans l'unité reste effectivement un point qui demande à être renforcé.

Dans cette optique, nous avons déposé en 2011 un projet Blanc ANR. Nous sommes également engagés dans un processus de recherche de partenaires pour déposer un projet INTERREG avec l'Angleterre.

Je vous prie d'agréer, Monsieur le Président, l'expression de mes sincères salutations.

Le Président de l'Université de Picardie Jules Verne

Georges FAURÉ

UNIVERSITÉ de Picardie Jules Verne