Développement et évolution du système nerveux

Rapport Hcéres

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

Section des Unités de recherche

Evaluation report

Research unit

Développement et Evolution du Système Nerveux

College de France

March 2009

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Evaluation report

Research unit

Développement et Evolution du Système Nerveux

College de France

Le Président de l'AERES	Section des unités de recherche
	Le Directeur
Jean-François Dhainaut	**Pierre Glorieux**

March 2009

Evaluation report

The research unit :

Name of the research unit : Dévelopement et évolution du système nerveux

Requested label : UMR CNRS

N° in case of renewal : UMR 8542

Head of the research unit : M. Alain PROCHIANTZ

University or school :

Collège de France

Other institutions and research organization:

CNRS

Ecole Normale Supérieure

Date of the visit :

21 & 22th January 2009

Members of the visiting committee

Chairman of the commitee :

M. Nils BROSE, Max Planck Institute for Experimental Medicine, Göttingen, Germany

Other committee members :

M. Bertrand BLOCH, Université Bordeaux 2, France

M. Riccardo BRAMBILLA, San Raffaele Foundation and University, Milano, Italy

Ms Monica Di LUCA, University of Milano, Italy

Ms Britta EICKHOLT, MRC Centre for Developmental Neurobiology, King's College London, UK

Ms Marie FILBIN, Hunter College, New York, USA

M. Jean SALAMERO, Institut Curie, Paris, France

M. Miguel SEABRA, National Heart and Lung Institute, Imperial College London, UK

CNU, CoNRS, CSS INSERM, INRA, INRIA, IRD representatives :

M. Eric AGIUS, CoNRS representative, France

M. Jean-Vianney BARNIER, CoNRS representative, France

M. Jean-Philippe PIN, CSS INSERM representative, France

AERES scientific representative:

M. Erwan BEZARD

University or school representative:

M. Yves GULDNER, Ecole Normale Supérieure

Research organization representatives :

M. Bernard BIOULAC, CNRS

M. Jean HOUMARD, ENS

Evaluation report

1 • Short presentation of the research unit

The unit includes 46 members :

- Full time researchers : 8
- Researchers with teaching duties : 6
- Postdoctoral fellows : 13
- PhD students : 7
- Technicians and administrative assistants : 12

Number of HDR : 8, with 7 being PhD student supervisor
Number of PhD defended : 9
Average duration : 49 months (4 years and 1 month)
Number of lab members with PEDR : 2
Number of publishing lab members : 14 out of 14

2 • Preparation and execution of the visit

The visit occurred in the context of the visit of the Institut de Biologie de l'Ecole Normale Supérieure on the 21st and 22nd January 2009. The preparation and execution of the visit was as specified in the Aeres guidelines. The visit went smoothly with all aspects of the evaluation covered satisfactorily. The specifics of this sub-project were covered as detailled below :

Day 1

Time : from 16:50 to 18:15
Presentations Developmental Biology & Neurosciences

16h50-17h00 : Presentation of the future unit moving to College de France
17h00-17h30 : Biologie cellulaire des homéoprotéines
17h30-18h15 : Développement et neuropharmacologie

Day 2

Time : from 14:00 to 18:30
General discussions

14h00-15h00 : Parallel meetings with committee's members
Meeting with engineers, technicians and administrative assistants
Meeting with the PhD students and postdocs
Meeting with researchers with permanent position

15h30-18h30 : Door-closed meeting: Committee members, AERES representatives

3 • Overall appreciation of the activity of the research unit, of its links with local, national and international partners

Remarks set out in the IBENS report apply to this unit. The principal investigator is a world leader in his field and has moved the field forward not speaking of his aside add-ons towards the general public. He is certainly one of the leading figures in French Neurosciences.

4 • Specific appreciation team by team and/or project by project

Team 1 : Biologie cellulaire des homéoprotéines

The work by this group has its origin in the analysis of the mechanisms by which homeoproteins are secreted and internalized through non-conventional pathways. Homeoproteins are a class of transcription factors that share the unusual property of intercellular transfer, involving the secretion of the protein from expressing cells followed by its internalization into adjacent cells. Both events rely on unconventional mechanisms due to the absence of classical secretion signals within homeoproteins and their accumulation in cytosolic and nuclear compartments following internalization. The group has characterized a minimal secretion sequence within the homeodomain of the Engrailed homeoprotein, based on the ability of synthetic peptides to cross an impermeant cellular barrier. This process is highly specific for homeoproteins as it requires both homeodomain internalisation (Penetratin) and secretion (Sec) sequences. For the next four years, the group plans to further analyze the possible link between the nucleus and the unconventional secretion process, and to investigate the role of lipids in unconventional secretion. The role of lipids in unconventional secretion will be further analyzed by modification of the intracellular lipid content in specific sub-cellular compartments and by studying mutant proteins deficient in lipid-binding. The principal investigator team is publishing at a reasonable level and collaborate nationally and internationally. Their projects are nicely focused on the key expertise of the team and adequate to its size. Their research focus is of great interest and should lead to the discovery of unsuspected mechanisms of the molecular transfer of information between cells within tissues. Biotechnological applications are within reach since the crossing of biological membranes remains a limiting step that restricts the use of therapeutic molecules.

The group has developed a non-viral strategy allowing the cellular delivery and intracellular biological action of hydrophilic nucleic acid and peptidic molecules, based on the fusion to small peptide sequences, known as Cell-Penetrating peptides. Although mainly based on ex vivo models, the physiological significance of their studies will be continuously assessed through a close collaboration with the team “Développement et neuropharmacologie”. In particular, the study of homeoprotein paracrine activity in the regionalization of the chick embryonic neuroepithelium provides an ideal context to analyze the functional consequences of quantitative or qualitative variations of homeoprotein secretion. While the team is addressing questions in the field of unconventional mechanisms of cell biology, it should also implement more 'conventional' investigations. Strong expertise exists at the IBENS as well as more generally in the field of cell biology of membrane transport (e.g. live-cell studies or ultrastructural studies employing microscopy techniques) should be taken into account in order to further examine the cell biology of homeoprotein secretion and transport. Also the search for specific molecular partners or machineries involved in homeoproteins pathways should be prioritized. Another concern is the level of independency of this group in the future. Most of its activities, although clearly focused on the cell biology processes of homeoproteins, are related, if not directly linked, to the group “Développement et neuropharmacologie”, with regard to both past studies and future work. In the future, the team should make an effort to establish an independent research profile, while maintaining the strong and fruitful collaboration with the group of origin. They should also consider classical molecular and cell biology approaches, aimed at analyzing the subcellular localization, quantitative aspects of intracellular transport, and biophysics of homeoproteins.

Team 2 : Développement et neuropharmacologie

The principal investigator is world-leader in his area of research. Clearly the highlight is the discovery of a novel mechanism of signal transduction involving the intercellular passage of homeoprotein transcription factors. Also, the subsequent analysis of this process and of its role in brain development has led to important new insights and excellent publications. Together with the IBENS head, the principal investigator is one of the two leading figures within the IBENS.

5 • Appreciation of resources and of the life of the research unit

Remarks set out in the IBENS report apply to this unit.

6 • Recommendations and advice

Remarks set out in the IBENS report apply to this unit.

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

Yves GULDNER
Directeur adjoint

AERES
Section des Unités
20, rue Vivienne
75002 PARIS

Ref : YG/EF 2009.019

Paris, le 17 avril 2009

OBJET : Rapport d'évaluation du Laboratoire Développement et Évolution du Système nerveux - UMR 8542

Je vous prie de bien vouloir trouver ci-joint les observations de Monsieur Alain Prochiantz, Directeur du Laboratoire Développement et Evolution du Système nerveux (UMR 8542)concernant le rapport d'évaluation de son unité, ainsi que ses remarques factuelles.

Avec nos salutations les meilleures.

Yves GULDNER

DÉVELOPPEMENT ET ÉVOLUTION DU SYSTÈME NERVEUX
CNRS UMR 8542
ÉCOLE NORMALE SUPÉRIEURE
COLLEGE DE FRANCE

Alain Prochiantz
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Paris, le 17 Avril 2009

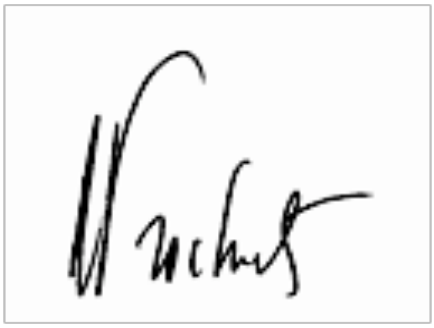
Commentaires généraux

En tout premier lieu, je voudrais remercier le Comité AERES pour son travail d'évaluation.

Je désire aussi attester de la totale indépendance scientifique d'Alain Joliot et rappeler que la signalisation par transfert d'homéoprotéines est une découverte que nous avons faite ensemble. Certes, Alain Joliot était à l'époque étudiant dans mon laboratoire, mais il reste que nous avons travaillé côte à côte à la paillasse pour nous assurer de la réalité de ce phénomène.

Il est donc normal qu'Alain Joliot continue de s'intéresser à cette affaire, comme il est normal que nous collaborions. Cela ne remet pas en cause son indépendance intellectuelle et contribue grandement au avancées de nos deux équipes qui partagent un grand nombre d'outils conceptuels et aussi pratiques et dont les membres ont grand plaisir à travailler ensemble sur un thème qui nous a occupé pendant près de 20 années.

Cordialement,



Alain Prochiantz
Directeur de l'UMR8542