LCRB - Laboratoire de cristallographie & RMN biologiques

Rapport Hcéres

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

Section des Unités de recherche

Evaluation report

Research unit :

Laboratoire de Cristallographie et RMN Biologiques

University Paris 5

February 2009

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

Section des Unités de recherche

Evaluation report

Research unit :

Laboratoire de Cristallographie et RMN Biologiques

University Paris 5

Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

February 2009

Evaluation report

The research unit :

Name of the research unit : UMR 8015

Requested label : UMR CNRS

N° in case of renewal : 8015

Head of the research unit : M. Frédéric DARDEL (past director: M. Arnaud Ducruix)

University

University Paris 5

Other institutions and research organization:

CNRS

Date of the visit :

January, 14th of 2009

Members of the visiting committee

Chairman of the commitee :

M. Gilbert DELEAGE, University of Lyon 1

Other committee members :

M. Walter CHAZIN, Vanderbilt University, USA

M. Stephen MATTHEWS, Imperial College of London, UK

M. Gabriel WAKSMAN, University College of London, UK

M. Bruno Klaholz, University of Strasbourg 1

M. Marc DREYFUS, Ecole Normale Superieure Paris

Mrs. Marie-Christine SLOMIANNY, University of Lille

CNU, CoNRS, CSS INSERM, représentant INRA, INRIA, IRD.....) representatives :

M. Philippe WALTER, CoNRS representative

Observers

AERES scientific representative :

M. Thierry RABILLOUD

University or school representative :

M. Bruno VARET, University representative

Research organization representative :

M. Thierry MEINNEL, CNRS representative

1 • Short presentation of the research unit

- Numbers of lab members : 32
  - Researchers with teaching duties : 13
  - Full time researchers : 7
  - Postdoctoral fellows and invited scientists : 4
  - PhD students : 3, all with a fellowship
  - Engineers, technicians and administrative assistants : 8
- Numbers of HDR : 9
- Numbers of PhD students who have obtained their PhD during the past 4 years : 7
- Average length of a PhD during the past 4 years : 3 years and 5 months
- Numbers of lab members with a PEDR : 5
- Numbers of "publishing" lab members (among permanent researchers with or without teaching duties): 20 out of 20

2 • Preparation and execution of the visit

The one day visit (instead of the two days initially planned) was prepared with the help of the written report provided on time by the laboratory. The evaluation was based on the report, the oral presentations of the future director plus the group leaders and the visit of the teams in the lab. The report appeared well organised, even if the list of publication was globalised for the whole unit hindering the quantitative evaluation team by team. The committee interviewed the present and future directors during 45' (closed door meeting), then the future director made a public complete overview (40') of the unit past activities and perspectives, then each group leader presented the past activities and their projects (20'+10'). In the afternoon, the visit of the teams was performed by committee subgroups thus giving ample time for discussions with young researchers and students. A 15' parallel session of 1) ITA visit by coCNRS representative and 2) laboratory council was organised. Finally, the committtee met the "supporting tutelle" in the absence of the directors for a 30' discussion.

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

The challenge of developing a new structural unit at the center of Paris has been met; the gamble paid off thanks to the enormous energy expended by both directors (current and future). The productivity of the unit is very good although penalized by the important renovation of the lab during past years. Moreover, during the last 2 years, the associate director had responsibilities at the highest level of CNRS scientific direction. The current director is now involved in the management at the top of University. Despite this, the unit continued to work and publish and it is now recognized as a very good center of RNA/protein structure-function analyses. The orientation towards RNA/proteins interactions is encouraged and approved by the evaluation committee. The opportunity has been taken of pushing young researchers in the front of the lab as new group leaders. As a consequence, all group leaders have been changed and this constitutes the next challenge of the Unit. Two of them result from internal appointments, and the two others are external recruits.

The unit is very well connected with other laboratories as inferred by the numerous collaborations and is an important piece of IMTCE (Institute of Medical drugs, Toxicology, Chemistry, Environment) which will be a new transversal organization of University Paris Descartes federating 15-20 research units on two sites. The meeting with tutelle of the laboratories emphasized the important support provided by CNRS (technician/engineer staff + 1 ATIP) and University (opening of at least 2 PR positions).

The unit exhibits good indicators as 93 peer-reviewed publications, 53 deposited PDB files, 12 invited conferences (5 international), 2 book chapters, 1 popular science book, 3 patents. The unit has a lot of collaborations and grants at both national and international levels.

Both directors can be commended for the work done since the creation of the Unit in 1999.

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

Team 1 "Lentivirus translation"

The research team working on lentivirus translation recently joined the research unit as a new, independent group (ATIP CNRS program). It is lead by a promising young scientist who is very enthusiastic and embarks on a series of challenging projects covering different aspects of eukaryotic translation regulation in viral RNAs, in particular internal ribosome entry in messenger RNAs from HIV. The future projects concern functional studies on the translation of lentiviral mRNAs, which requires the production of viral RNAs and eukaryotic translation initiation factors for the characterisation and in vitro reconstitution of minimal initiation complexes. Structural studies on lentivirus IRES are also considered: beside enzymatic and chemical probing, more precise approaches (notably NMR spectroscopy) are envisaged. These experiments could be performed onsite to a significant extend, thus providing opportunities for internal collaborations that would further increase the consistency of research topics within the research unit (RNA and structural biology).

A recommendation would be to focus on some leading projects within the broad research area envisaged. The team is supported by appropriate grants and it can be expected that the team size will increase soon, which will be required for tackling its challenging topics.

STRUCTURE ET MÉCANISMES MOLÉCULAIRES DES ARN

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

Team 2 "RNA interactions and NMR"

Over the review period, the team has produced several publications that rank as internationally leading (2 of them distinguished in Faculty of 1000); for example their development of a novel method for producing recombinant RNAs in high yield, which is likely to revolutionize the structural biology of RNA and RNA-protein complexes. A strong multidisciplinary approach has been adopted by the team to work on projects ranging from the development of new RNA technology, structure determination by NMR and crystallography, screening and inhibitor development. Beside their substantial peer-reviewed research output, they also have successfully applied for patents protecting their technology. Based on past performance this team is the strongest grouping within the laboratory.

The team proposes several extremely interesting and ambitious projects. Many of these projects focus on innovative technology development, such as developing a new co-expression system that circumvent problems associated with instabilities in isolated components by enabling production of intact protein-RNA complexes. Several important biological areas will also be addressed. In particular the potential synergies with team 1 were viewed as a positive strength of the laboratory and future collaborative programmes should be actively encouraged, for instance the structural biology of protein-RNA complexes involved in viral translation initiation. The quality of the team is high and together with the multidisciplinary nature of the projects, will provide an excellent training environment for PhD students and postdoctoral workers. Productive links exist with industry and of particular note is work on the design and testing of selective inhibitors for peptide deformylase as potential novel antibiotics. Their future work aims to build on these collaborations.

The current team leader has shown to be a highly creative scientist, particularly with respect to the development of technology. By nature this leads to collaborations, and the team has many, which is a great plus. However, a by-product of these many collaborations is the involvement of the team in many different projects, to the point where it is difficult to identify the team with a specific biomedical focus. With the shift to new leadership, it is advisable for the team to focus on a few specific project areas to which the entire group would identify and to which the team's various technologies could be applied. This would allow the team's efforts to generate a more fundament impact on biomedical science, and would generate an exciting environment for students and postdoctoral fellows. The group leader will assume a new role as Director of the unit with a young researcher taking over as head of the team. This is an outstanding leadership team in place for the next 4 years, which combines an established leader who has excellent overview and focus on methodology, with a young researcher more daily involved in running the laboratory and applications. While she has already demonstrated the qualities necessary to successfully lead a research group, careful mentoring should be in place to ensure further development of her independence. Indeed, the effectiveness of the team over time will depend on her ability to grow as a leader, which will require intellectual space for her to develop research that is of her design and specifically recognized as such on the national and international level.

INTERACTIONS ARN/PROTÉINES-RMN

Note de l'équipe	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+

Team 3 "Signal transduction and membrane transport"

The activities of the lab have focused on two general themes: 1- drug efflux pumps and 2- signal transduction. In the field of drug efflux pumps, a number of proteins have been purified and some structures have been solved. These structures have made some impact in the field and certainely constitute proofs of principle that the lab can handle membrane proteins. Perhaps more interesting and original are the biophysical studies which have been initiated, notably the innovative use of cubic phase to "force" the components together: whether this method will provide results reflecting the reality of the interactions taking place in the system remains to be seen, but it is at least a promising start which is a testimony to the original approach that the group is taking. Overall, the work has yielded interesting results, although it is not yet entirely clear whether the work will be at the forefront of the drug efflux field. In the field of signal transduction, the work on prolactin is noteworthy. Finally, work on plant elicitins, and on actin has been productive. It must be acknowledged that in the context of a massive refurbishment operation which has limited the number of PhD studentships available to the lab and also has inevitably disrupted research, the production of the lab has been reasonable.

The future projects in the next review period include structural and biophysical studies of drug efflux pumps and prolactin receptors, structural studies of P. falciparum virulence proteins, and work on the vascular endothelial receptor. The evaluation committee believes that, although these projects are interesting, they may overstretch a rather small team and that limited resources may be better used to focus either on themes that are relevant to other activities in the unit (RNA technology, RNA structure, RNA-protein interactions in transcription and translation) or on themes where critical mass can be identified (drug efflux).

In the new group leader, the unit has identified an excellent leader. It seems important at this stage when she is taking over from the present group leader that the team's research themes be clearly identified and focused. Of particular importance is the need to generate critical mass in a focused area of research in which she can clearly make a name for herself and build her reputation as an independent leading structural biologist.

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A	A	A	A+	A

Team 4 "Crystallography of small and macromolecular complexes"

The team has extensive experience in small molecules synthesis and crystallography. The traditional activities of the team comprised biomimetics and metaloenzymes studies for which several different enzymatic systems are investigated (nitrile hydratase, hepcidine, urate oxydase). The team appears to be recognized for its expertise in structural enzymology as indicated by the abundant publications list (half of the full list of the unit). However few publications of high standard have been produced and overal impact of the team is not what can be expected from the size and the experience of the team. On the other hand, the team has some interesting collaborations with another group of chemical synthesis in Paris 5 University. Another positive outcome of the team is a long-term partnership with a company on the design of new antibacterial agents. Until recently, the team was uniquely composed of researchers with a lot of teaching duties. Some of them are very productive but others seem to have some difficulties to publish their work (except in collaborative papers). Recently, one full time researcher migrating from team 3 joined the team. This arrival signed the beginning of the reinforcement of the protein cristallography potential.

The future projects presented by the new group leader (who just joined the unit) include structural genomic studies of ribosome biogenesis and metallodrug complexes studies. It is expected that solving 3D structures will provide functional information on the assembly of the complex.

The committee feels that, although the ribosome biogenesis project is interesting, the field is huge when compared with the human resource. Efforts to focus on common projects have to be made and previous group leaders should help to progressively shift some activities on the new project. This is a prequisite for competitiveness in such an ambitious project. This is the challenge for the new group leader. The committee encourages him and would bet he will succeed.

CHIMIE ET BIOCHIMIE STRUCTURALE

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	B	Non noté	A

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

Overall, the committee got the impression that technicians, students, post-docs and permanent researchers were generally pleased with the stimulating friendly atmosphere within the unit.

One important point raised is a lack of lab meetings. However, the director was unanimously approved, even if the council laboratory was not formally consulted.

The research units includes 7 ITAs (6 from CNRS and one from university). Over the past 4 year period, three persons left laboratory (one retired, 1 IE and two mobilities, T and AI); there were four arrivals (one mobility AI for administration and three recruitments, T, AI and an IR). The scientific technical staff is assigned to one specific team for a part of time and for the other part, collective responsabilities or technical expertise are given to the lab. One of a team does not have technical staff.

Technicians are quite satisfied with their working conditions and they are well integrated to the life of the unit.

Three critical points were identified :

- Concerning Security and Health, a person is ACMO and this seems to be compatible with scientific activity of the laboratory. All aspects linked to health and safety regulation are well managed, all types of risk were well identified. But there is a problem for secure transport of very heavy charges like gas bottles for NMR. Accomodations were asked from the university without results.

- A plan for continuing education (PFU) was written by the administrative AI who is responsible for contact with CNRS but access to scientific training is very limited. Only training organized by CNRS, free training or that organized by instrument manufacturers were accepted. No financial support was obtained from CNRS delegation for other scientific training.

- Finally, the technical staff is very anxious about their status modification if the operation of the lab is given up by the university. Indeed, the personnel chose CNRS for the status, the carrier and the national mobility.

6 • Recommendations and advice

– **Strong points :**

- Quality of past accomplishments, including important methodological developments;
- High productivity for a small size unit;
- International visibility;
- Small size unit with emerging researchers;
- Good synergy and atmosphere in the unit;
- Prominence of the past and the future director.

– **What needs to be improved :**

- Internal management : set up a laboratory council
- Weekly scientific meetings should be held for the entire Laboratory in order to have an enriching environment for students and postdocs, and to invigorate the permanent staff and stimulate them to contribute beyond their technical specialization. This is an important forum for practicing presentation skills. In this vein, presentations should routinely be given in English - perhaps once in every two or three turns for each member of the Laboratory. A weekly meeting should be viewed as a valuable tool for recruiting students.

– **Recommendations :**

- One suggestion to consider is to re-define the research organization of the laboratory around projects addressing specific biomedical problems. This provides a ready means to identify the application of technologies and participation of various teams to multiple projects within the Laboratory as a whole, as opposed to within specific teams. This organization stress the multi-disciplinary and collaborative nature of research in the Laboratory.
- Continue to reinforce team 1 in order to provide it with the required critical size.
- Help and support the new team 4 leader to produce synergy between the competence in his new team.

LABORATOIRE DE CRISTALLOGRAPHIE & RMN BIOLOGIQUES

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

UNIVERSITÉ
PARIS DESCARTES

Le Président
Axel KAHN

Paris, le 1er avril 2009

DRED 09/n° 129

Monsieur 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 de comité de visite concernant l'unité « **UMR 8015 Laboratoire de cristallographie et RMN biologiques** » rattachée à mon établissement.

L'Université a pris bonne note des remarques du comité de visite et veillera, en partenariat avec le CNRS, à ce que les recommandations faites soient suivies d'effet.

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

Le Président de l'Université

Axel Kahn

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Paris, le 31 mars 2009

Note à l'attention d'Axel KAHN
Président de l'Université Paris Descartes

Objet : *Rapport du Comité de Visite de l'AERES concernant le renouvellement de l'UMR8015 (février 2009)*

J'ai le plaisir de vous informer que le Rapport du Comité de Visite de l'AERES n'appelle pas d'observation de ma part.

Frédéric DARDEL
Porteur du renouvellement de l'UMR8015