LJC - Laboratoire Joliot-Curie

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Joliot-Curie Laboratory

From the

CNRS

ENS Lyon

Mai 2010

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et de l'enseignement supérieur

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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 : Joliot-Curie Laboratory

Requested label : USR CNRS

N° in the case of renewal: USR 3010

Name of the director: M. Philippe BOUVET

Members of the review committee

Chairperson

M. Pierre LEGRAIN, CEA France

Other committee members

M. Malcolm BUCKLE, ENS Cachan, France

M. Andrew TRAVERS MRC Laboratory of Molecular Biology, Cambridge, UK

M. Marc VICTOR, Université Paris 6

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

M. Agamemnon CARPOUSIS, CoNRS member

Observers

AERES scientific advisor

Mrs. Anne PLESSIS

University or School representatives

Mrs. Chantal RABOURDIN-COMBE, ENS Lyon

Research Organization representatives

Mrs. Florence NOBLE, CNRS INSB

M. Bernard FOURCADE, CNRS INP

Report

1 • Introduction

The visit took place on Tuesday, March 2nd, 2010. The director of the laboratory made a general presentation of the history of the unit, followed by presentation of the four main research themes by the project leaders (past activities and projects). Discussion with representatives of the ENS and the CNRS allowed the committee to better appreciate the notion of "hotel à projets" which is the basis for operations of this unit. In the afternoon, the laboratory was visited, posters were discussed, the visiting teams activities were presented and specific meetings with the various personnel took place (PhD and post-docs; scientists with permanent positions; administrative staff, technicians and engineers). A final discussion with the director before a closed meeting between committee members ended the day.

The laboratoire Joliot-Curie (LJC) is a recent structure, aiming at the development of biological research in an interdisciplinary environment. It is located at the heart of the Ecole Normale Supérieure (ENS) in Lyon, with physics, chemistry and biological laboratories surrounding it. Started in 2004, with the arrival of scientists from varied origins, it was officially created in 2007 as a joint structure between CNRS (Life sciences division) and ENS as an "hotel à projets".

The director of the laboratory manages the unit. However, until recently, all researchers were in teams that were officially still attached to their origin laboratory (Physics, Chemistry, Biology). This is changing with the new structure put in place.

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	Minimum 2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	10	Minimum10
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	7	Minimum 5
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	4.8	4.8
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	5.25	Minimum 2
N6: Number of Ph.D. students (Form 2.8 of the report and 2.7 of the project file)	16	Minimum 6
N7: Number of staff members with a HDR or a similar grade	6	Minimum 6

2 • Overall appreciation on the research unit

Note : this section deals with the management of the JCL unit and its structure (hotel à projet). Scientifc appreciation of the resident team "Mechano-Genetics of the Cell"is given at the end of the document. The comitee was not asked to evaluate the research and projects of the visiting teams.

- Summary

The laboratory has been built up from scratch over 5 years under an innovative structure (hôtel à projets). It has been very successful in the past four years at building a scientific interdisciplinary group, mostly formed by physicists and biologists, dedicated to biological sciences. During the past 4 years, the structure of "hotel à projets" was also modified and clarified through iterative discussions with the CNRS, the major reference organisation and the Ecole Normale Supérieure (ENS), the hosting organisation. A new scientific project is now proposed with an associated organisation which has been adopted in 2007. As such, a resident laboratory (the only team under evaluation here, called "Mechano-Genetics of the Cell") will conduct interdisciplinary research in conjunction with visiting teams to be recruited for a 3-5 year contract. Almost one new team might be hosted every year. The process involves a scientific advisory board whose work and recommendations should be considered as the most important input for the recruitment of new teams and projects.

The committee's recommendation is to increase significantly the number of projects (in the resident and the visiting teams) conducted by biologists.

Specific support from CNRS and ENS is required for this atypical interdisciplinary laboratory, especially in the case of lack of success at ANR calls at early stages of new projects. Such a well publicized support would increase the attractiveness of this laboratory, beyond the regional Lyon scientific community, for visiting teams as well as for additional postdocs.

- Strenghts and opportunities

Interdisciplinarity and enthusiasm for scientific projects and innovative technologies/methodologies are two major characteristics arising from the visit. This is reflected by a very good scientific communication between scientists at all level (PhD students, post-docs, technicians and engineers, permanent scientists).

- Weaknesses and threats

A lack of decidated funding (including positions for visiting PI) supporting specifically the visiting teams might limit the attractiveness of the Unit.

- Recommendations to the head of the research unit

The laboratory should make the appropriate recruitments of visiting teams in a close interaction with the Scientific Advisory Board.

- Production results

A1: Number of permanent researchers with or without teaching duties (recorded in N1 and N2) who are active in research	12
A2: Number of other researchers (recorded in N3, N4 and N5) who are active in research	7
A3: Ratio of members who are active in research among permanent researchers [(A1)/(N1 + N2)]	1
A4: Number of HDR granted during the past 4 years	1
A5: Number of PhD granted during the past 4 years	14

3 • Specific comments on the research unit

- Appreciation on the results

Evaluated only for the resident team "Mechano-Genetics of the Cell", see section 4

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

This Unit is clearly identified as a major player in the field, both at the national and international level. As a whole, the laboratory (roughly 12 permanent scientists) has a very strong publication record : from 2005 to 2009, 60 publications for which the laboratory made a major contribution and 29 as a collaborative work. In addition, 9 publications were under revision or submitted for 2009 (7 major and 2 collaborations). Publications belong to physics and biology journals illustrating well the interdisciplinary nature of the laboratory. Several publications in Physical review letters (10 ; IF 7.2), in Mol Cell Biol (3 ; IF 5.9), Nucleic Acid research (3 ; IF 6.9) and EMBO J (4 : IF 8.3). One publication in each of the following journals (PNAS, Current Biology, Nature Struct Mol Biology).

- Appreciation on the strategy, management and life of the research unit

Meetings with the visiting committee were conducted in a friendly and extremely open format; clearly the participants had discussed in some detail beforehand and had prepared a number of topics that they wanted to discuss without prompting from us. Generally the atmosphere was extremely positive with a unanimous and enthusiastic backing for the structure and future of the unit. The cafeteria is definitely a key space for exchanges and more generally, the premises are well organised.

Specific points were raised at each meeting.

PhD and Postdocs: The only concern was about a lack of administrative information coming for the "top". Otherwise, they were very satisfied by the general spirit and atmosphere.

Technicians, Administrative and Engineers: Very positive general feeling. Mention of a lack of human resource for specific tasks (administrative and for microscopy which is a growing demand area). Some personnel are under a semi permanent CDD status which is appreciated (allows personnel to work in an attractive environment) although insecure in the French system.

Researchers with permanent positions: The unit was viewed as a unique possibility for the interchange of ideas across disciplines.

The system of regular seminars involving invited speakers as well as internal seminars is well established, well organised, well attended and supported by an adequate budget.

The fact that all groups are of necessity transitory is considered to be stimulating. It is accepted that this is particularly stressful especially for visiting teams who feel a specific pressure to perform well in a relatively short time. They recognise however that conditions are very good with excellent access to equipment, platforms and, of course expertise.

The decision to recruit a visiting team is made by the Directory board, after the recommandations made by the scientific board, but all the researchers seemed to agree that they had a say in the matter through a personal contact with the director. Since the consensus was that the future of the unit is directly correlated with the nature and composition of visiting teams it was pointed out quite clearly that the decision to invite visiting teams is crucial.

Infrastructure is very good with excellent access to a lot of common equipment.

- Appreciation on the project

The "Hôtel à Projet" is an excellent system. Interdisciplinarity has clearly been favoured in this Unit. However, since more and more funding is coming from external grant sources such as ANR, the next 5 years will be crucial in that weakening of financing from the CNRS and the ENS could destroy this structure.

Although the current structure is fortunate that they have a consensus on the management by the present Director, the committee perceives that this may alter with the change in composition of the unit and that some more formal structure for the choice of incoming visitor teams will be required. Therefore the committee identifies here a key role for the scientific advisory board.

See section 4 for the appreciation of the resident team "Mechano-Genetics of the Cell".

4 • Appreciation on team

Team: Mechano-Genetics of the Cell

Team leader: M. Philippe BOUVET

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	6	5
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	5	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	4.8	4.8
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	3.25	2
N6: Number of Ph.D. students (Form 2.8 of the report and 2.7 of the project file)	13	8
N7: Number of staff members with a HDR or a similar grade	4	4

- Appreciation on the results

Six research projects were part of the past contract. Most of them led to very significant scientific contributions. Details are presented below. As a whole, the laboratory conducts a very original research, mostly performed by physicists, chemists and biologists, on biological molecules and assemblies (DNA, DNA binding proteins, nucleosomes and chromatin).

Project 1: Structure and dynamics of nucleosome remodelling. It describes the roles of variant histones and a histone chaperone in nucleosome remodelling: The work is of high quality and internationally competitive with some publications in high profile journals (13 publications, including 2 in EMBO J). The studies on variant histones form the foundation for what is now a highly fashionable area of research. Because some members of the initial team have now left certain areas have now been successfully spun-off to other laboratories with whom valuable contacts are maintained.

Projects 2 and 3: Chromatin and functional organisation of the genome and sequence effects on the structure and dynamics of DNA molecules: This work, based on wavelet multi-scale analysis methods, revealed long range correlations in the genomic sequence which correlate with the spatial organization of nucleosomes. Nucleosome Free Regions (NFR) located at both gene extremities have been shown to induce periodic ordering of nucleosomes along gene sequences, in agreement with the “parking” model proposed years ago by Kornberg and Stryer (NAR, 1988). This work brought out a major advance in the understanding of nucleosome positioning, both in vitro and in vivo. Publications in top journals confirm the international recognition of this group (more than 20 publications with a prominent authorship including 6 in Phys. Rev. Lett. and 2 in PNAS).

Project 4: Dynamics of protein-nucleic acid interactions

Project 4.1: Role of TRF-2 in t-loop formation and recombination. This project was developed, thanks to the "visiting team concept" in place in the "hôtel à projets" favouring interdisciplinary collaborations with the use of several platforms present in LJC. It provides solid insights into the mechanism of action of a telomeric DNA binding protein TRF2. Furthermore the group has suggested a role for TRF2 as a blocker of telomeric junction by resolvases through stabilisation of T-loops. The group is now planning to move to another institute but will carry on with the project initiated at the LJC. The excellent initial studies (4 publications including 2 in EMBO J and 1 in Nat. Struct. Mol. Biol.) carried out in the LJC context are testament not only to the scientific expertise present in the team but also to the success of the 'Hotel à projets' concept around which the LJC is centred.

Project 4.2 The accessibility of nucleosomal DNA-to-DNA repair enzymes: This project is actually more closely connected to Project 1. As such comments addressed above to project 1 are equally applicable here.

Project 5: Dynamics of biomolecular assemblies

Project 5.1 dealt with the modelling of large-scale dynamics on proteins and seems to be somewhat misplaced in the present project. The work essentially carried out revolved around protein modelling approaches (3 publications in 2006) and in collaboration with EPFL in Lausanne the elaboration of a topology-based network model for protein dynamics (3 publications 2005- 2008). The link with the project 5.3 is not clear.

Project 5.2 describes the functionalisation of interfaces for the study of proteins by AFM, and illustrates the expertise in AFM and physicochemical manipulations present in the laboratory.

Projects 5.3 to 5.5 describe an amazing study on the conception, development and application of a novel imagery technology based on scanning surface plasmon microscopy (SSPM). This promising technique is being developed in the laboratory into a high-resolution imagery platform allowing access to potentially unique insights in the study of higher order nucleosomal structures with important implications in the field. The group has 3 patents and 16 publications illustrating not only the fertility of this group's imagination but also its capacity to explore, develop and define a novel area. This is a highly successful group operating in the top echelons of national and international science (18 publications, including 4 in Phys. Rev. Lett.). The success of this group is again a testament to the potential of the LJC operating system.

Project 6: Interaction of the cell with its environment

Project 6.1 Swimming of bacteria population in the vicinity of a surface: The work involves tracking the trajectory of individual E. coli bacterium by video microscopy. Bacteria close to a surface swim in circles. This 'trapping' is due to hydrodynamic properties near the surface. These studies are being extended to tracking the trajectory of bacterium upon exposure to chemorepellents. Results have not yet been published but two manuscripts are in preparation.

Project 6.2 Dynamic light scattering as an investigative tool for the study of the internal dynamics of a living cell nucleus. This work, performed in collaboration with the Physics laboratory of the ENS, has analyzed Dynamic Light Scattering (DLS) in the nucleus of a living cell showing that the nucleus exhibits a large range of relaxation times extending from milliseconds to seconds. This study was extended to the analysis of DLS in nuclei in which DNA replication was inhibited. This is a novel application of DLS although it is not clear how relaxation times will be attributed to specific processes such a chromatin remodelling. For the period covered in the scientific report, three articles describing the technique have been published including an article in Biophys J.

- Production results

A1: Number of permanent researchers with or without teaching duties (recorded in N1 and N2) who are active in research	8
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)]	1
A4: Number of HDR granted during the past 4 years	1
A5: Number of PhD granted during the past 4 years	14

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

During this period,14 students defended a PhD. Only four scientists possess a HDR, but that number will increase soon to 6.

The team has established several key collaborations that led to significant publications, among them the Centre de Génétique Moléculaire (Gif, CNRS), Ecole Normale Supérieure (Paris) and Institut Jacques Monod (Paris, CNRS). Focused international collaborations occur with laboratories from India, China and the United States.

Staff of the team (seven different scientists) is often invited for conferences and seminars, in France (over 35) and abroad (25). The team has good connections with several universities abroad (India, China). The number of postdocs is low (4 compared to 12 permanent scientists). This may be due to a shortage of funding.The funding of research is mostly obtained through ANR and region grants. Little funding through industry or international funding agencies. The laboratory has made several patents for SSPM applications.

- Appreciation on the strategy, management and life of the team

The team is a succesful interdisciplinary team. In the future the emergence of cutting edge projects will be even more successful if more scientists with a strong biological training join the laboratory and bring in new projects in relation with existing ones.

Several members of the laboratory contribute intensively to teaching at the ENS. The laboratory itself is embedded in the ENS and contributes greatly to the interdisciplinary nature of the ENS.

- Appreciation on the project

These two sections describe a logical continuation of two major topics related to previous scientific activity. Overall the approaches are both innovative and feasible. They address important questions in chromatin organisation and biology. Some individual projects - for example the SSPM experiments and the reconstitution of chromatin with nucleosomes and regulatory proteins - are challenging and at the cutting-edge technically and consequently for success may require technical modifications.

The chromatin project, devoted to the functional organisation of the genome, rests on the "N-domain" segmentation of the human genome. The N-domain borders, which have been uncovered in this very group, locate the origins of replication which have been shown to coordinate replication and transcription. This project aims at understanding in a quantitative way how these functions are encoded by nucleosome positioning and chromatin fiber structure. However the project could be (and actually should be) more ambitious insofar as the group masters the segmentation of the whole genome by N-domain borders as well as the overall nucleosome positioning. Therefore they are encouraged to try hard to elucidate the entire cell nucleus architecture in relation with chromosome functions. Expertise in systems biology might be a key advantage in this task.

This overall activity for the next years is well centred in the heart of present expertise of the laboratory. It will most probably continue to deliver very high quality research. However the committee feels a lack of vision in terms of biological key questions and new emerging concepts in the highly competitive field of epigenetics. The committee strongly recommends that the new cell biology teams to be recruited (see below) develop projects in close relationship with the above biophysics and biochemical projects in order to compete at the highest level with best international experts in the field.

This third part of the project corresponds to the desire to develop new cell biology projects in a multidisciplinary approach. Four topics are presented; none of them reach the level of interest of previous projects. In addition some of them clearly present a risk of defocus of the themes of the laboratory in terms of biological questions, raising the question of expertise and competitiveness of the group in those areas.

Mechanical properties of the nucleus and its relationship with the cytoplasm: This topic is a fast growing field in cell biology. Major discoveries in the understanding of nuclear structure and organisation are currently made by various groups coming from different cell biology fields and using various innovative technologies and methodologies. The LJC might certainly contribute to this area, but this requires at least two prerequisites: i) building up from ongoing research in the laboratory for example exploring the nucleolar structure and its dynamics with an expected key role for nucleolin and using the SSPM technology developed in the laboratory; ii) recruiting a visiting team expert in cell biology and bringing into the laboratory new biology expertise and concepts

Mechanical and dynamical restructuration of cells: Here the topic focuses on the biophysical bases for asymmetrical cell division related to oscillation of the mitotic spindle. Again, the topic is of first interest and corresponds to a highly competitive field. However, instead of limiting the LJC contribution to innovative technologies and modelling tools, the committee suggests that a cell biology group be incorporated in the laboratory as a visiting team bringing inside new concepts related to cell division, (including asymmetrical division), in a broader vision of the cell metabolism;

Mechanics and dynamics of isolated circulating cells: the example of bacteria: The project, which is a continuation of the work in the report, extends these studies to the 3D tracking of bacteria swimming near a surface and to the impact of the nature of the surface on swimming behaviour. The analysis of the influence of the near surface hydrodynamics on bacterial swimming appears to be sound although, from the biological point of view, the work is very descriptive and the results seem trivial in light of the extant literature on bacterial motility. The small team performing this work is isolated from the larger community of microbiologists whose input is essential to frame pertinent biological questions. Given the modest scientific productivity of the team and the committee's view that the project is not likely to lead to significant new insight into pertinent biological questions, the committee strongly recommends that this line of research be closed

Mechanics of cells assembled in tissues : It is proposed to address the role of physical forces in the morphogenesis of the plant shoot apical meristem (SAM). The SAM was chosen as model system that would be amenable to studies by live imaging techniques. Developing a coherent project on this relatively vast area of research would require the close cooperation of a large team of biologists and physicists. The LJC lacks sufficient biologists with the expertise necessary to develop the project, and it needs to reinforce its core competences in epigenetics and chromatin before expanding in other directions. For this reason, the committee strongly suggests that the line of research be dropped from the plans for the future unit.

The projects are supported mostly by ANR and regional grants. Sharing of resources seems to be the rule in this laboratory. A more proactive policy for the recruitment and/or allocation of postdoctoral fellows is suggested.

Most projects related to chromatin structure and function are original and could lead to cutting edge scientific results, especially if more biological questions are brought into these projects.

- Conclusion :

– Summary

Structure and function of DNA in the context of chromatin organisation are being studied as the major topic and have led to very significant publications. Various techniques and methods have been installed in the laboratory (including AFM, various microscopies, DNA modelling,) and others have been developed in house (scanning surface plasmon microscope imaging or SSPM) with significant results.

The committee's recommendation is to address key biological questions in close relation with succesful present projects, such as epigenetics and chromosomal organisation, relation and function within a eucaryotic cell.

– Strenghts and opportunities

A strong scientific background has been built on focused topics (DNA/chromatin structure) with various approaches that constitutes a very positive basis for further structure/function studies.

– Weaknesses and threats

A deficit in biologists (compared to other disciplines) has in the past constrained the ability of LJC to tackle major biological scientific questions relevant to the very same field (related to epigenetics). This field is now very active and the LJC will need to strenghen its biology expertise to support the competition.

– Recommendations

In conclusion, this is an extremely enthusiastic group of highly motivated and on the whole excellent scientists who have created an organisation that provides a unique possibility for young scientists to develop ideas in a specific context. This success is certainly due, at least in part to an appreciated leadership of its Director. Based on this experience, the concept of 'Hôtel à projets' can be seen a success. The laboratory should now attract key biologists in the field of epigenetics and related topics to capitalize on the very succesful research it has built in this field.

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+

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Le Directeur général de l'ENS de Lyon

à

Monsieur Pierre Glorieux
Directeur de la section
des Unités de recherche
AERES
20, rue de Vivienne
75002 – PARIS

Lyon, le 7 avril 2010

Monsieur le Directeur,

Je vous remercie de l'envoi du rapport d'évaluation du Laboratoire Joliot Curie USR 3010.

Le jugement très positif porté par le comité sur cette structure récente et « atypique » (hôtel à projets) conforte l'ensemble des tutelles (ENS de Lyon et CNRS) dans leur volonté de soutenir l'interdisciplinarité et de poursuivre leur politique pro-active dans ce domaine. Les suggestions et recommandations formulées par le comité permettront de mieux cibler le recrutement d'équipes visiteuses et/ou résidentes à l'avenir et d'intensifier la réussite des projets en cours.

Je vous invite à trouver, ci-jointe, la réponse du directeur du laboratoire, Monsieur Philippe Bouvet.

Je vous remercie ainsi que les évaluateurs pour la qualité de leurs travaux et vous prie d'agréer, Monsieur le Directeur, l'expression de ma sincère considération.

Olivier Faron

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LABORATOIRE Joliot-Curie ENS LYON

Laboratory Joliot-Curie

ENS-CNRS USR3010

Comments on the report from the visiting AERES committee

We thank the visiting committee of the Laboratory Joliot-Curie (USR 3010) for the report that evaluates our activity and for the very useful comments and suggestions.

We fully agree with the committee that there is a deficit of biologists in the laboratory compared to other disciplines. An important task of the next quadrennial contract will be to attract biologists to reinforce the epigenetic projects and also to develop cell biology projects (like the Mechanical properties of the nucleus) as suggested by the committee. The recruitment of biologists will be made either directly by the resident team, or by recruiting new visiting teams that develop biological projects in connection with the interests of the resident team.

We would like also to mention about the project "Mechanics and dynamics of isolated circulating cells" that this project recently received funding through an ANR project with collaborators located in the Pasteur Institute. We recognize that during the past four years progresses on this project have been slow and the biological question not really at the centre of the research. We strongly believe now that, thanks to the interaction through the ANR consortium and to the experimental set up that has been put in place in the laboratory, we will be in very good position to address major biological questions on chemotaxis.

On behalf of the Laboratory Joliot-Curie

Philippe Bouvet

Director of the Laboratory

Lyon, April 8th, 2010