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

Section des Unités de recherche

Evaluation report

Research unit :

Laboratory of Molecular Oncology and Pharmacology of the Ecole Normale Supérieure de Cachan

March 2009

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

mars 2009

Evaluation report

The research unit :

Name of the research unit : Molecular Oncology and Pharmacology (LOMP)

Requested label : USR CNRS

N° in case of renewal :

Head of the research unit : M. Christian AUCLAIR

University or school :

Ecole Normale Supérieure de Cachan

Other institutions and research organization :

CNRS

Date of the visit :

February 3rd, 2009

Members of the visiting committee

Chairman of the commitee :

Mr Jean-Jacques TOULMÉ, University of Bordeaux 2

Other committee members :

Mr. Yves POMMIER, NIH Bethesda, USA

Ms. Françoise GUERLESQUIN, University of Aix-Marseille 2

M. Jeffrey HAYES, University of Rochester, USA

M. Jean-Louis MERGNY, Muséum national d'Histoire naturelle Paris

M. Serge ROCHE, University of Montpellier

M. Claude CARON DE FROMONTEL, University of Lyon

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

Ms. Valérie SCHREIBER, CoNRS representative

Observers

AERES scientific representative :

M. Philippe BOUVET

University or school representative :

M. Jean-Yves MERINDOL, ENS Cachan

Research organization representative (s) :

M. Thierry MEINNEL, CNRS

Ms. Urszala HIBNE, CNRS

1 • Short presentation of the research unit

- Number of lab members : 10 including
  - 5 researchers with teaching duties
  - 1 full time researcher (also member of UMR8113)
  - 3 PhD students, all with a fellowship
  - 1 engineer, technician or administrative assistant
- Number of HDR : 5
- Number of students who have obtained their PhD during the past 4 years: 6
- Number of lab members who have been granted a PEDR : 1
- Number of publishing lab members: 6 out of 6

2 • Preparation and execution of the visit

A door-closed meeting with the head of the laboratory took place at the very beginning of the day.

The information was confirmed that the only CNRS researcher mentioned in the written proposal did no longer want to be associated to the project. (The committee members were informed of that a few days prior to the visit).

We then heard a general overview of both the past scientific activity and the project by the head of the laboratory. Five successive talks were given by every researcher of the team, covering both the scientific and technical aspects. At the end of the day we met simultaneously three senior researchers. The technicians and the PhD students/post-docs were met the day before, during the visit dedicated to the UMR 8113; it is reminded that the members of the present LOMP project were previously part of the 8113 Unit located at the same site. For the same reason the technical facilities shared by the two laboratories were also seen the day before. A door-closed meeting was organized with CNRS and ENS representatives and the head of the laboratory. It was jointly decided to hear the senior researcher that decided to leave the project. No key information was given during this interview but the researcher's decision appeared irreversible.

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

The LBPA (UMR8113 ENS Cachan-CNRS) created in 2002 was an interdisciplinary research unit composed of seven teams (23 researchers and 12 technicians) that remained located on two different sites till 2007. They are now all located on a single site in a brand new building at the ENS Cachan.

The members of the present project (LOMP) corresponded to team #1 in the former Unit. They developed activities along two main lines: i) understanding the mechanisms regulating malignant transformation, tumor phenotype maintenance and tumor invasion, ii) developing technologies for drug discovery. This covers both fundamental and translational research. The research projects are strongly oriented towards clinical applications for cancer treatment with close collaborations with research units and clinical departments of Institut Gustave Roussy and Hôpital Saint-Louis. The team has very strong commitment with the industry. Actually several technicians paid by a company are working daily in the laboratory, in good agreement with the goal of a CNRS USR.

The activity of the researchers is excellent but the number of projects is rather large given the limited number of people. Members of the LBPA team #1 authored about 30 papers, 8 of which published in journals with an IF>5 (J Exp Med, Blood, PNAS, J. Biol. Chem....). Three patents have been filled since 2004 with the company that has collaborators within the laboratory. One patent is being licensed. Most of the team #1 members, including the head of

the laboratory, have a heavy teaching load, which was reported to be of high quality by the ENS representative. Three PhD students are presently in the laboratory.

The laboratory members contribute to three ongoing EU contracts, including two networks of excellence (NoE): Conticanet and CliniGene. The team got also 4 ANR grants (in 2008). This ability to raise EU and ANR funds makes LOMP a well funded laboratory and demonstrates the quality of the research being carried out.

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

A first project deals with molecular mechanisms of the malignant phenotype reversion process. A functional screening approach allowed the identification of the actin-cytoskeletal associated protein zyxin as an important regulator of F-actin assembly. This is an innovative line of research. It is now planed to screen for activators of zyxin function using an in vitro actin polymerization assay. A second project is dedicated to molecular and cellular mechanisms of tumor invasion. Specifically, it aims at unravelling the role of the serine/threonine kinase PKD1 in oncogenic signalling leading to breast cancer tumorigenesis. A third project is focused on anticancer drug design and biotherapies. One important aspect includes the targeting of c-Kit tyrosine kinase alleles in tumorigenesis by specific inhibitors and antibodies. The identification of molecules able to inhibit the IGF-IR pathway, a pathway that plays a critical role in transformation, invasion and apoptosis protection constitutes a fourth project of interest with respect to the screening platform. The team identified PKD1, a kinase able to inhibit the IGF-IR pathway and would like to determine the role of this kinase in cell proliferation, adhesion and tumor growth. Finally an interesting approach resting on phage display-derived antibodies and intrabodies for anticancer therapy appears promising.

Several aspects of these projects (in vitro polymerization assays as well as the combination of pharmacological tools to target oncoproteins such as Kit) are interesting with some novel and smart approaches. The study of molecular mechanisms underlying the function of targeted proteins and the attempts for identifying inhibitors are very timely: this interesting project would have deserved a more in depth description. The project on mast cells brings limited innovative aspects. Nevertheless, the developed in vitro and in vivo models are interesting and the results will be transferred to the platform. The field is higly competitive but the project deserve to be developed thanks to the large number of availble kinases. Some parts of the project might have been better justified. For instance, the tumor suppressor function of zyxin has not been validated in cancer and the role of PKD1 in neoplastic transformation is still obscure. Also IGF, EGF and FGF pathways, involve multiple partners making the project difficult to manage for a team of limited size and the choice of MCF7 cells might not be suboptimal. Indeed, this mammary carcinoma cell line expresses the estrogen receptor, which might interfere with the growth factors pathways studied. Moreover, the results obtained in this cell line would probably not allow the conclusion to be extended to other tumor types sharing alterations of the IGF signalling pathway.

The screening platform is of potential high interest given the number of targets available. The idea of having molecular modelling might even improve this potential however there is no description of this platform nor is mentioned how it will be operated.

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

- **Management:**

The head of the laboratory is a highly recognized scientist. He has a very good publication record and his work is frequently cited (H number = 37). He brightly demonstrated his ability to run projects with a high potential for translation to the industry. However as he is supposed to retire in about two years the question of the future director of the Unit is raised. Even though the committee has been told that a possibility is presently being investigated no clear cut answer has been given to this question.

- **Human resources:**

All scientists (professors and assistant professors) do have strong research activity and fair productivity. They undoubtedly have a recognized expertise in their area. They also have strong networking activity. But there is no collaborative link between the different members of the laboratory that consequently can hardly be viewed as a

« Unit ». For instance no indication has been reported of laboratory meetings. The departure of the CNRS researcher will likely have no impact due to his lack of interaction with the other laboratory members. The situation of the technicians needs to be clarified in particular the position of one technician shared with LBPA seems rather uncomfortable. Technicians in charge of the platform will be hired on private contracts, Positions for an Assistant Engineer and a secretary will be requested to the CNRS and the ENS, respectively. It was not clear either how the USR platform will be managed.

- **Equipment and facilities:**

The laboratory gets access to a number of services (Imaging, L3) however the rules for sharing these facilities with LBPA are not clearly defined. The exact nature of the services that will be provided by the USR platform and its functional organization are rather obscure. But funding of the equipments and functioning seems to be already available or at least is anticipated.

6 • Recommendations and advice

- **Strong points :**

Recognized expertise of all scientists in the team.

Activity connected to translational research, demonstrated by several patents and strong links with two biotechs.

Ability to attract funding (4 ANR grants, 2 NoEs, CPER grants).

Efficient scientific networking (coordination of a NoE and many publications in collaboration).

Important involvement and responsibilities in teaching (notably the head of the laboratory).

Impressive number of kinases (over 50) that may be tested in parallel.

- **Weak points :**

The link between the different projects is weak; collaboration and contact between scientists of the laboratory are limited.

Each theme is led by a single scientist (full or assistant professor). The critical mass may not be reached for international competitiveness.

Limited interaction with local laboratories

Mid-term governance since the director of the unit is supposed to retire in about two years.

- **Recommendations :**

Clear commitment of the trustees (ENS ?) to hire a new lab head.

Recruitment of young scientists with full time research position (CNRS or INSERM) is essential for the development of the project. Increasing the size of the teams with more students and postdocs will be critical in the near future.

Collaborative projects involving several scientists from the lab should be encouraged.

The relation between this laboratory and LBPA need to be specified, and several critical issues should be agreed upon (location, access to facilities,…, technicians).

The relationship with private companies needs to be clarified.

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	A	C	B