Signalisation intracellulaire Rho GTPases et progression tumorale

Rapport Hcéres

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

Section des Unités de recherche

Evaluation report

Research unit:

Intracellular signaling, Rho GTPases and tumor progression

University Paris 11

March 2009

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

Section des Unités de recherche

Evaluation report

Research unit :

Intracellular signaling, Rho GTPases and tumor progression

University Paris 11

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 : Intracellular signaling, Rho GTPases and tumor progression

Requested label : UMR_S

N° in case of renewal : U749

Head of the research unit : Mr Jacques BERTOGLIO

University or school :

University Paris 11

Other institutions and research organization :

INSERM

Date of the visit :

November 10, 2008

Members of the visiting committee

Chairman of the commitee :

Mr Yannick JACQUES, University of Nantes

Other committee members :

Mr Gareth JONES, King's College London, UK

Mr Marc PIECHACZYK, IGMM, Montpellier

Mr Gilles FAVRE, University Toulouse 3

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

Mr Patrick LEGEMBRE, CSS INSERM representative

Observers

AERES scientific representative:

Mr Marc BONNEVILLE

University or school representative:

Mr Dominique EMILIE, Paris 11 University

Mr Jacques BITTOUN, Paris 11 University

Research organization representative (s) :

Mrs Chantal LASSERRE, INSERM

Mr Eric SOLARY, Institut Gustave Roussy

Evaluation report

1 • Short presentation of the research unit

- Number of lab members : 17 including:
  - Researchers with teaching duties : 1
  - Full time researchers : 6
  - PhD students : 6, all of them with a fellowship
  - Technicians : 4
  - Administrative assistants : 1
- Number of HDR : 4, all of them are PhD students avisors
- Numbers of PhD students who have obtained their PhD : 9
- Average length of a PhD during the past 4 years : 3.5
- Numbers of lab members who have been granted a PEDR : 0
- Numbers of "publishing" lab members : 5 out of 7

2 • Preparation and execution of the visit

The visit was well prepared. All members of the review panel received before the site visit the necessary scientific and administrative documents for a proper evaluation of the scientific activity of the Unit and its project. It has however been felt that the written document could have been more explicit on a few points: internal organisation of the laboratory, respective scientific responsabilities of the researchers.

The site visit was well organized. The time schedule was perfectly followed. After the scientific presentations made by the director of the research unit and his collaborators, the expert review panel could meet the representatives of Paris 11 University and Institut Gustave Roussy. He could then meet the different staff categories: researchers, PhD students, technicians and administratives.

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

The research aims of U749 these last years have been essentially dealing with basic research. Its scientific activity has been focused on the study of signal transduction mechanisms involved in growth factor (cytokines) action, cell division, cell transformation and tumor progression in different cellular models. Globally, the scientific goals have been reached with a production of 25 peer-reviewed publications for the period 2004-2008 and a mean impact factor of 10,3 (1 J Exp Med, 3 Blood, 2 Mol Cell Biol, 1 Oncogene,…). This production has been very positively appreciated by the review panel, considering the relative geographic isolation of the laboratory. A good national and international renown of the laboratory in its specific fields, with good publication citation rates, has also been acknowledged. However, heterogeneous scientific output has been noted between the different principal investigators and sub-groups of the unit (see below §4).

The laboratory has several ongoing scientific partnerships and collaborations at the national and international levels. It is labelized by the Ligue contre le Cancer (2006-2008), is granted by the Agence Nationale pour la Recherche (ANR Blanc 2007-2009), by the Réseau national des Génopoles (RNG), by the GEFLUC and ARC.

However, It is not engaged in real national or international research networks and efforts in this sense should be made.

In the project for the next 4 years period, it is proposed to keep the fundamental research core that is the hallmark and expertise of the Unit, and also to improve the capacities of the laboratory to address issues relevant to cancer (oncogenesis, biomarkers and novels targets) and to enter translational research projects. In line with this last aspect, moving of the Unit to Institut Gustave Roussy that hosts numerous teams involved in various aspects of cancer research will provide very good opportunities to reinforce existing collaborations and stimulate new ones. The review panel has strongly encouraged this strategic evolution. However, it has also pointed out a too large number of scientific projects with respect to the size of the unit, and therefore recommends a narrowing of the research topics to limit dispertion and improve overall competitivity. An effort has already been made by the unit by merging several ongoing projects around two axes: tumor progression in colon cancer and signaling in normal and malignant lymphocytes (leukemia/lymphoma).

As mentioned before, the laboratory has been essentially developing fundamental research programs and until now, there has been no real socio-economical translation (patent applications, industrial partnerships) of the knowledge generated. The moving of the laboratory to the IGR and engagement of more cancer-oriented research programs that could lead to novel diagnostic/prognostic tools as well as identification of novel therapeutic targets should create conditions favouring such transfer towards the socio-economic sphere.

There is a good implication of staff members in training of students through their involvement in different university teaching programs and through PhD supervising.

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

Although the project has been presented as a single team laboratory, the written document as well as the site visit presentation have clearly enabled the review panel to distinguish 4 projects each driven by separate principal investigators. Two of them dealing with « the molecular mechanisms of resistance to apoptosis » and « the contribution of HEF-1 and SOCS-1 to colon carcinoma » are within the axis 'tumor progression in colon cancer". The two others (« Gab2/Shp2 signalling pathways » and « Signalling and Rho GTPases ») are within the axis "signalling in normal and malignant lymphocytes". Significant heterogeneity among these 4 groups has been noted, with respect to staff allocated, definition of objectives and tasks, and foreseen feasability/success.

The project « Signalling and Rho GTPases » has been evaluated as a competitive, high standard and promising project, structured through solid external collaborations and financial ressources, and linked to important national expertise programs (RNG, Ligue nationale contre le Cancer programme CIT). A young researcher (CDD Junior inserm) with a strong CV and likely high potential should eventually join this team, which has been considered as an excellent point by the review panel.

The project addressing « the molecular mechanisms of resistance to apoptosis » is also scientifically solid, and has recently led to important publications (J Immunol 2008, Oncogene 2008). The panel has noticed that although the project is original and should lead to novel findings in cell signaling pathways linked to anoikis, more efforts should be made to more specifically establish its relevance to cancer, including transfer of the findings to the clinic (biomarkers, prognosis, diagnosis). Besides, the human ressources and funds allocated to this team have been judged too weak and should be reinforced to ensure effectiveness and competitivity. Specific actions in this sense (grant applications) should be undertaken by PI. Another suggestion of the review panel is that this team could be merged with the one currently working on HEF-1 and SOCS in order to strengthen it.

The HEF-1 project is run by a PI whose recent research output is quite limited (no publications since 2005). There seems to be a need for a new start that could be found through establishment of much tighter links with the PI coordinating the « cell apoptosis » project (see above). The second project (SOCS-1), run by another PI, was felt by the review panel as not sufficiently well defined and based on too preliminary observations.

The « Gab2/Shp2 » project is run by a brilliant associate professor (MCU) who joined the Unit one year ago. It is very ambitious with a large proteomic analytical program. However, due to the limited human ressources available (the PI is involved part time, together with a PhD student), this project appears very risky and its achievement not realistic. The feeling of the review panel in that the PI's thematic independance is too early, and he should be kept for a while under the guidance of the head of the research unit, enabling him to develop his scientific qualities under a protective environment that will create favourable conditions for the development of his own project in the future. This would also have the advantage to consolidate the Flag project of the laboratory.

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

In terms of management, the different categories of staff (researchers, students, technicians) considered that the lab was well run by the director and the scientific staff readily stuck to the director scientific strategy. They were also very satisfied by the choice made within the laboratory of a general sharing of the resources (financial, technical, services, weekly internal scientific meetings opened to all the staff). The review panel felt that there was a deep gratitude of the staff for the strong involvement of the director.

In terms of human ressources, the laboratory is a small sized unit (17 lab members) with a good balance between researchers (7), technical staff (5) and students (6 over 3 years). However, as already pointed out, there is still now a too large dispersion of the research projects in relation with the human ressources.

The next moving of the laboratory to IGR is very well accepted by the staff, that is aware of the opportunities that will be opened (access to seminars, increased visibility and attractivity). The review panel is also very favourable to this moving that will break the geographic isolation of the laboratory, allow development of new collaborations and enhance the attractivity of the laboratory for new young scientist (students, post-doc, researchers). In terms of emergence, moving to IGR will also provide better conditions for promising young PIs.

The research coordinator of IGR presented the integration of this laboratory as a very positive point for IGR that at present lacks specific expertise in molecular signalling. It was felt by the review panel that IGR is willing to offer U749 the necessary conditions and ressources for installation and future development of its research objectives. However some restrictions were raised by one of the PI who considered that the space allocated to the unit after moving was too small. The review panel feels that this could be a critical point and recommends IGR in connection with the university and Inserm to be vigilant on that aspect.

6 • Recommendations and advice

— Strong points :
  - Good scientific production with regards to the geographic isolation and to the limited scientific human and financial resources.
  - Two strong research projects among the four (« Signalling and Rho GTPases » and « the molecular mechanisms of resistance to apoptosis ») that are well recognized at the national and international levels.
  - Two promising young researchers.
  - Mutualisation of the ressources, acknowlegment by the staff of the quality of the direction, solidarity between the staff members.

— What needs to be improved :
  - Too many sub-projects and a too large heterogeneity in the scientific levels of the projects.
  - Two research groups (HEF-1/SOCS-1; Gab-2/ SH-2) whose projects are weaker and not realistic.
  - One researcher with poor scientific output in the last years
  - Lack of socio-economical transfer.

— Recommendations :

Overall, the review panel has evaluated the scientific activity and project of the Unit as of good quality. It supports the strategy of the Unit to keep its fundamental research specificity while improving its involment in cancer oriented research. However, there are two weaker groups diluting the strength of the Unit and it is recommended that the corresponding sub-projects be given up or restructured around the two strong and leading axes carried by the two Pis running the « Rho GTPase » and « apoptosis » projects. This would have also the advantage to reinforce the leading axes that somehow lack human resources and increase the competitivity of the Unit to reach the high level standard of IGR. This will probably require a strong involvement of the director in the managing of the human and scientific ressources of the Unit. The review panel is confident in the quality of the director to carry out this necessary reorganization.

Moving to the IGR environnment is felt as an important opportunity to make the necessary restructurations of the laboratory. It is recommended to be vigilant on the conditions (especially space allocated) of installation of the Unit at IGR.

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

Inserm

Institut national
de la santé et de la recherche médicale

Unité 749
Signalisation dans la prolifération cellulaire et l'apoptose
Dr. J. Bertoglio, Director
direct phone : 33 1 46 83 55 08
E-mail : jacques.bertoglio@u-psud.fr

Chatenay-Malabry, le 26 Mars 2009

Monsieur le Directeur
Section des Unités de Recherche
AERES

Re : EVAL-0911101C-S2100012402-UR-RPRELIM

Dear Colleague,

We thank the committee for its evaluation of our research program, and of our strengths and weaknesses as a group. We were indeed aware of both, and we will take the suggestions into account while continuing to work towards comforting our strengths and increasing our efficiency on some aspects, through improved collaboration between the team members. We do share the views of the committee that our moving to Institute Gustave Roussy should help us to do so in the near future. We were glad that the committee understood and supported this geostrategic move of our unit.

Sincerely yours,

Jacques Bertoglio, MD
Directeur de Recherche à l'Inserm
Directeur Inserm U749

Faculté de pharmacie – Paris Sud – 5, rue Jean Baptiste Clément – 92296 Chatenay-Malabry – France
Phone : 33 1 46 83 57 84 Fax : 33 1 46 83 54 96