Génétique des tumeurs

Rapport Hcéres

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

Section des Unités de recherche

Evaluation report

Research unit :

Genetic of human hematological tumors

University Paris 11

March 2009

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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

March 2009

Evaluation report

The research unit :

Name of the research unit : : Genetic of human hematological tumors

Requested label : UMR_S INSERM

N° in case of renewal :

Head of the research unit : M. Olivier BERNARD

University :

Université Paris 11

Other institutions and research organization:

Institut Gustave Roussy, INSERM

Date of the visit :

January 15th, 2009

Members of the visiting committee

Chairman of the commitee :

M. Patrick AUBERGER, University of Nice-Sophia Antipolis

Other committee members :

M.s Ruth RIMOKH, University of Lyon 1, France

M. Paresh VYAS, University of Oxford, England

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

M. Daniel BIRNBAUM, Marseille, CSS representative

Observers

AERES scientific representative :

M. Philippe BOUVET

University or school representative :

M. Jacques BITTOUN, University Paris 11

M. Dominique EMILIE, University Paris 11

Research organization representative :

Ms. Chantal Lasserre, INSERM

1 • Short presentation of the research unit

- Numbers of lab members including
  - researchers with teaching duties: 1
  - full time researchers: 5
  - PhD students : 3, all with a fellowship
  - engeneers, technicians and administrative assistants : 4, including 1 CDD
- Numbers of HDR and of HDR who are PhD students avisors : 5
- Numbers of PhD students who have obtained their PhD during the past 4 years: 5
- Average lenght of a PhD during the past 4 years: 4 years
- Numbers of lab members who have been granted a PEDR : 0
- Numbers of "publishing" lab members: 6 out of 6

2 • Preparation and execution of the visit

This INSERM unit (formerly INSERM E-0210 : Genetic of human hematological tumors) was previously located at the Necker hospital. The present application for a joint Université Paris 11/INSERM unit entitled « Tumors Genetic » brings together 13 scientists, engineers and technicians from INSERM, University and other institutions and 3 PhD students. This team will join the Institut Gustave Roussy (IGR) to participate in the reorganisation of scientific groups at the site. As this team has long standing and ongoing collaborations with other teams at the IGR, the move to IGR has great scientific merit. The preparation and execution of the visit was well done and appreciated by the committee.

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

The science performed by this unit during the past four years has been internationally competitive and of very good overall quality. More specifically, this team has made important contributions in the field of oncohaematology with the characterization of the NUP98 translocations and the discovery of TET2 mutations in myeloid diseases. Another very interesting and competitive aspect of the activity concerns the OTT-MAL translocation and the phenotypic characterization of *Mal*-/- and *Srf*-/-mice.

The overall publication record of the unit is high with very good princeps publications as principal authors in the field during the past four years including 3 artciles in Blood, 4 in Leukemia, 1 in Oncogene, Gene Chromosome and Cancer. Two high-impact publications are currently in revision and the committee is confident that they will be accepted soon. The national and international collaborations also allowed contributions in high impact factor journals including Cancer Cell, PNAS, Blood (4 articles) and Mol cell Biol (2 articles).

The team leader has a strong national and international esteem, attested by three invited conferences in the US in 2007 and 2008. In addition, he has shown great competence in obtaining international and national fundings from the Leukemia Research Fund (UK), the Fondation de France, ARC, INCA (X3). Of note, the team has a LNCC label (2009-2011).

The location of the Unit at the IGR totally makes sense since this team has long standing and ongoing collaborations with several teams already present on the site. This will reinforce the existing collaborations and foster the development of new partnerships with other teams of the IGR. It will contribute to the development of a centre of excellence in haematology.

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

Although the proposal is in direct line with the previous program, a new aspect dealing with structural and functional analysis of solid tumours will be explored. This will be possible because a new team of cytogeneticists and researchers already located at the IGR will join the unit. The opportunity to develop this project which is out of the scope of haematology has been discussed. The conclusion of the committee is that this aspect should be developed if it becomes internationally competitive.

The main objectives of this application are:

1- The study of megakaryoblastic leukaemia and more specially the identification of initiating leukaemia cells, the function of SRF and its cofactors in the OTT1-MAL transformation and the analysis of the oncogenic events that cooperate with OTT1-MAL;
2- The functional analysis of the alterations of NUP98
3- The identification and characterization of a new gene (TET2) which is inactivated in myeloid malignancies and the study of its function in haemopoiesis in germ line mutant models;
4- The structural and functional genomic analysis of epithelial cancer cells;
5- The role of NOTCH in normal and pathological megakaryocytic differentiation and more generally in myeloid differentiation and the development of new therapeutical approaches.

The members of the committee were very impressed by the outstanding quality of the presentations. The program focuses on onco-haematologic questions of very high scientific interest. Most aspects of the research are highly original and interesting and should have important fundamental and potential clinical implications. This is particularly true for the objectives 1, 3 and 5 for which the group is internationally competitive. For instance, the discovery of TET2 mutations in myeloid diseases is a fantastic observation and the OTT-MAL and NOTCH-1 projects are also excellent. While quite interesting the NUP98 and lung stories will be probably less competitive and focusing on the most attractive aspects of these projects would be desirable.

Finally, the technological strategies are modern, highly coherent and include several very pertinent murine models of haematopoietic malignancies and chromosomal translocations. However, the committee thinks that it will be difficult to develop all the very interesting aspects of this project without reinforcing the team. The team director is aware of that and told us that he will rapidly prioritize the most attractive and competitive programs.

In conclusion this is a highly coherent, pertinent and attractive project. Most aspects are well focused and as such have excellent feasibility. The ratio between fundamental and clinical research is excellent. The record of previous publication is very good. Moreover, two manuscripts in high impact journals and dealing with the TET2 and NOTCH-1 stories hopefully will be rapidly accepted.

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

After meeting with the researchers, engineers, technicians and students the committee concluded that the environment and the atmosphere of this research unit are excellent and that all the staff is in line with the objectives and the strategies of the director.

Moreover, the students versus researchers ratio is quite good, taking into account the number of HDR in the lab (5). Ideally, this team will greatly benefit from the recruitment of one or two post-doctoral positions in a near future.

6• Recommendations and advice

– **Strong points :**

Very good previous contributions in the field of onco-haematology. Highly innovative and original research program developed by an internationally competitive team in the field. The project is also a very good mixture of basic and medical science research. The TET2 project is innovative and internationally competitive. This is also true for the OTT-MAL /SRF and the Notch-1 projects;

The dynamism and international notoriety of the team director;

The excellent network of national and international collaborations including some of the most pertinent and best national and international teams in the field;

The team has proven very effective in initiating new and very original research programs;

The presence of outstanding young scientists in the team who develop internationally competitive programs;

The integration of the team at the IGR (environment, collaborations, platforms) and in addition to INSERM, the strong support of the different institutions (IGR, University and CHU);

The ability of the team to improve its publications in high impact factor journals.

- **Weak points :**

The NUP98 and lung projects are also of interest but will have probably less impact than the three other projects. Moreover, the project concerning the solid tumor aspect is not directly connected to the other points.

To face competition in all these very interesting questions, it will be necessary in the next four years to structure the plethora of questions to favour the most attractive and competitive ones.

- **Recommendations :**

To succeed the new unit will have to overcome several challenges

Integrate within the IGR network and specifically within the «haematological centre» (select of specific program with task force);

Integrate in situ's parts of the unit, solid tumor work and bioinformatics (develop a pilot program);

Select and develop the most promising programs;

Continue to develop appropriate murine and cellular models (secure enough space);

Secure (more) PhD students of high quality;

Develop European ties and obtain European grants;

Continue to publish in high impact journals;

Attract interelated teams of young investigators.

Génétique des tumeurs

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-SUD 11

Le Président de l'Université Paris-Sud 11

à

Monsieur Pierre GLORIEUX
Directeur de la section des unités de recherche
AERES
20, rue Vivienne
75002 Paris

Orsay, le 20 mars 2009.

N/Réf. : 75/09/GCo/LM/LS

Objet : Rapport d'évaluation d'unité de recherche
N° S2100012412

Monsieur le Directeur,

Vous m'avez transmis le quatre mars dernier, le rapport d'évaluation de l'unité de recherche « Génétique des tumeurs hématologiques humaines», et je vous en remercie.

L'université prend bonne note de l'appréciation et des suggestions faites par le Comité.

Les points à améliorer seront discutés avec le directeur d'unité dans un esprit constructif pour l'avenir de la recherche à l'université.

Voici le message que le directeur d'unité a souhaité vous faire parvenir :

« ... On behalf of all members of the proposal, I want to thank the member of the visiting comity for their efforts to evaluate our work as well as their comments and very constructive criticisms. We are please to let the comity know that the two submitted manuscripts have now been accepted for publication.
We fully agree with the comity comments and we will take very seriously the comity's recommendations, and will carefully prioritize our projects.
Thank you very much again for taking time to prepare the report. We are grateful for the positive feedback we have received thus far. »

Je vous prie d'agréer, Monsieur le Directeur, l'expression de ma sincère considération.

Guy COURRAZE
Président

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Paris le 10 mars 2009

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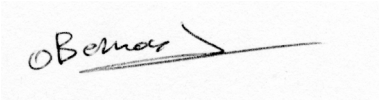
Thank you very much again for taking time to prepare the report. We are grateful for the positive feedback we have received thus far.
With best regards,



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