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Thérapie cellulaire en pathologie cardio-vasculaire

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:

Cellular Therapy in cardiovascular pathology

University Paris 5



February 2009



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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: Cellular Therapy in cardiovascular pathology

Requested label: Inserm

N° in case of renewal: U633

Head of the research unit: M. Philippe MENASCHE

University or school:

University Paris 5

Date of the visit:

21st January 2009



Members of the visiting committee

Chairman of the committee:

M. Roberto LATINI, University of Milano, Italy

Experts:

M. Andreas ZEIHNER, University of Frankfurt, Germany

Ms. Marisa JACONI, University of Geneva, Switzerland

M. Johnatan LEOR, University of Tel-Aviv, Israel

CNU, CSS INSERM representatives:

M. Philippe LECORVOISIER, INSERM CSS representative

M. Alain LEGUERRIER, CNU representative

Observers

AERES scientific representative:

M. Bernard LÉVY

University or school representative:

M. Bruno VARET, University of Paris 5

Ms. Marie-Claude LABASTIE, University of Paris 5

Research organization representative:

M. Raymond BAZIN, INSERM



Evaluation report

1 • Short presentation of the research unit

- Number of lab members 22, including:
 - 1 Full time researchers (team #1: 0 + Team #2: 1)
 - 4 Researchers with teaching duties: (Team #1 : 4 (1.3 FTE), Team#2 : 0)
 - 1 Engineers: (Team#1: 1 , Team#2: 0)
 - 6 PhD students: (Team#1:3, Team#2: 3)
 - 3 Technicians and administrative assistants: (Team#1: 1, Team#2: 2)

- Numbers of HDR: 5, 3 are PhD advisors
- Numbers of students who have obtained their PhD during the past 4 years : 2(Team #1:1, Team#2:1)
- Average length of a PhD during the past 4 years: 4
- Numbers of lab members who have been granted a PEDR : 1
- Numbers of "publishing" lab members: 5 out of 5

2 • Preparation and execution of the visit

The program of the visit was established by the team director in agreement with the chairman of the committee.

1.30 pm to 2.15 pm

Presentation by the head of the lab (and leader of team #1): past activity and projects

2.15 pm to 3.0 pm

Presentation by the leader of team #2: project

3.0 pm to 3.45 pm

Poster presentation by team members and students

3.45 pm to 4.15 pm

Three meetings at the same time

Meeting with PhD students and postdoctoral fellows

Meeting with engineers, technicians and administrative assistants

Meeting with researchers with permanent position

4.15 pm to 4.30 pm

Door-closed meeting: Committee members, AERES representative, Lab director

4.30 pm to 5.00 pm

Door-closed meeting: Committee members, AERES representative, University and Research Organization representatives

5.00 pm to 6.30 pm

Door-closed meeting: Committee members and AERES representative



The site visit was well organized; the experts had all needed opportunities to ask questions and to discuss with all the members of the teams. The experts obtained clear and informed responses to all their questions; they had the opportunity to visit the lab and to have serious exchanges with the students and the researchers.

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

The activity of the two research groups aiming to form a new unit is well-known from publications in international peer reviewed journals of high impact and from conferences. The peculiarity of the unit is the extension of the research performed: the issue of regenerative treatment of cardiac disease has been addressed in a comprehensive way ranging from molecular biology up to a multicenter clinical trial, MAGIC. Having the possibility and know-how for conducting experiments in humans, the unit guarantees reliable translation of its research by a final verification of the hypotheses previously made and verified with different in vivo animal models.

The partnerships with several well known and respected international groups ensures the validity of the results obtained by the unit. In particular, the unit is founded by the transatlantic Leducq Fondation and EU projects, which are considered the strongest indicator of the relevance of the research ongoing in the unit.

Although prematurely stopped for reasons independent of the responsibilities of the unit, the MAGIC trial with the involvement of several cardiac surgery departments in different countries besides France, indicates the importance and relevance of the hypothesis tested.

4 • Specific appreciation team by team

Team #1

During the last four years, the team's research was focused on the selection, isolation, culture and implantation of skeletal muscle progenitors in the injured myocardium. The focus of the team 1 is moving from skeletal muscle progenitors to embryonic stem cells selected for specific antigens. New methods of cell transplant are being tested (i.e. epicardial patches made with new biocompatible materials) with the general aim of repairing the heart from chronic injury (i.e. chronic heart failure, ischemic heart disease). The team has full experience of the field as demonstrated from curricula, previous publications and participations to major scientific international and national meetings. During the last 4 years, the team # 1 published 28 original papers in the better specialty journals corresponding to their activity: European Heart J, J of Thorac and Cardiovasc Surg, Transplantation, JBC, Cardiovascular Research, Stem Cells. Major results, published in the Lancet in 2005 by the team's member (Transplantation of cardiac-committed mouse embryonic stem cells to infarcted sheep myocardium: a preclinical study), have a high number of citations. The team and future unit leader is a regular invited speakers in most of major cardiovascular international meetings.

— Strong points:

One strength of the approach adopted by team#1 is the comparative design of experimental studies, aiming at assessing whether the new cell type/way of transplant is superior to the old one previously in use: this allows the research to advance and focus on best options for the clinic.

Team#1 showed, both from 4-year past research and from the planned future activities, a scientific consistency in going from bench to bedside. This complete itinerary which is seldom seen in other research groups will require a high level of involvement of both teams (basic and translational/clinical research) to build a strong Unit.



– Weak points:

The main weak point in the overall program is the fact that team#1 has only one person with permanent position dedicated to research full-time.

– Recommendations:

The Committee thus recommends selecting during the early phase of the project at least one more researcher as a candidate for a new permanent position in Team 1.

Nom de l'équipe : Cellules souches adultes

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+	B	A

Team#2

This team is working on one of the hottest research areas, the human embryonic stem cells (ESC), their fundamental properties and potentials for cardiac regenerative medicine, also using the mouse system as comparison ESC model to identify common regulatory pathways and/or differences. The group provides a strong background in a cutting hedge research field together with excellent and successful methodologies and has demonstrated top quality publications that have raised the laboratory at a very high level internationally. Of particular note and outstanding are: Nature Protocols 2008; Stem Cells 2007; Developmental Cell 2006.

The team leader has been honoured by 2 important Awards: the Pfizer prix 2003 in Switzerland and the "Prix d'excellence scientifique" from the France-Israel Foundation in 2008.

Among numerous talk and conferences given nationally and internationally, the team leader has also been invited as speaker to important Conferences, such as the American Heart Association Meeting in 2007 (Orlando, US), the Stem Cell meeting on Reprogramming organized by the Stem Cell Network North Rhine Westphalia (Dusseldorf, D), the European Society of heart failure (Milan, I in 2008 and Les Diablerets, Switzerland in 2009), and the Kestonesymposia meeting in US in 2007.

Top quality strategies are convincingly employed to address fundamental cell biology questions enabling the efficient generation of cardiac cell populations as well as the methodology for a fast translation into the clinical arena. Not last the lab also addresses the modeling of cardiac diseases that will enable to design and test new drugs and treatments.

The ongoing international and national collaborations are excellent. Those include:

- the Burhnam Institute, La Jolla, California for High trough-put screening investigations
- The Institute of Bioinformatics, BIOPOLIS in Singapore for bioinformatics analyses
- The Massachusetts General Hospital, Boston, Massachusetts, for cardiac progenitor and valvulopathies studies
- Harvard University , Boston, for iPS and ES cell expertise
- The Technion Institute, Haifa, Israel, for collaboration on hES cells
- One CNRS lab (Hôpital Marie Lannelongue, Le Plessis Rombinson) for animal models of heart diseases and electrophysiology studies



- The Institute of Myology, (Paris) for laminopathies studies.

The team#2 displays solid experience and personnel able to secure the ongoing projects and the leadership is demonstrating fruitful synergies and complementarities with the one of team#1.

– Strengths:

Quality and originality of the results;
Excellent network of collaborations.

– Weak points:

None, apart the present physical non-negligible distance between the 2 teams. However, mid-term solutions to bring closer the 2 teams are under evaluation with concrete propositions.

– Recommendations:

The consolidation of the laboratory with a stable position for a junior scientist or at least a highly qualified technical personnel that could secure the heavy work with cell culture.

Nom de l'équipe : Cellules embryonnaires

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+

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

– Management:

The director of the unit clearly identified the limitation in its previous research as being the limited involvement in basic research, and indicated the solution in a merging of the unit with another group, mainly devoted to investigating the molecular mechanisms of embryonic and progenitor cell differentiation and homing. The challenge of making the unit out of two previously distinct well appreciated research groups appears to be adequately considered and dealt with, considering also the new facilities that will be operative in the next few months.

– Human resources:

The human resources were carefully verified by the committee, by personal interviews with the doctoral and training fellows of the two groups composing the unit, those involved in basic research and those mostly devoted to in vivo translational research. The scientific personnel revealed good knowledge of their roles in the unit and were happy to be involved in their projects.



– Communication:

The director of the unit clearly expressed its aims and projects for the future. The plans were exposed in a clear way so that it appeared evident and plausible the evolution from the previous years of scientific and clinical activity.

6 • Recommendations and advice

– Strong points:

Strong background in cardiac surgery both in experimental animals and in humans guarantees the correct conduction of the challenging experiments planned, with strict direct comparisons of different strategies.

Scientific honesty to go from bench to bedside in stem cell therapy is remarkable.

The creativity of the basic research team will allow new hypotheses to be verified in vivo.

– Weak points:

A major limitation may be seen in the relative scarcity of staff personnel, so that most of the researchers have fellowships limited to 2 to 3 years duration. This may limit the continuity of a research which requires specific skills needing long time to be acquired and practiced in a reproducible way. The major difficulty that the unit

will face in view of the committee is the merging of the two groups since not only the good agreement and common feelings of the two heads but also a continuous communication between the personnel will be needed and supported over the years.

– Recommendations:

Support best fellows so that they may be given the possibility of applying for a permanent position in the unit;

Pursue with energy and creativity the merging of the research personnel with regular meetings, discussions and seminars.

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

Le Président
Axel KAHN

Paris, le 3 avril 2009

DRED 09/n° 132

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-S 633**
Thérapie cellulaire en pathologie cardio-vasculaire » rattachée à mon établissement.

L'Université a pris bonne note des remarques du comité de visite et veillera, en partenariat avec
l'INSERM, 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

DIVISION DE LA RECHERCHE
ET DES ECOLES DOCTORALES

Paris, le 3 avril 2009

UMR-S 633 Thérapie cellulaire en pathologie cardio-vasculaire

Retour sur le rapport du comité AERES – Observations de portée générale

Pas d'observations.