Intéraction hôte-greffon-tumeur-ingénierie cellulaire et génique

Rapport Hcéres

HCERES

High Council for the Evaluation of Research and Higher Education

Research units

HCERES report on research unit:

Host-graft-tumor Interactions

Cell and Gene Engineering

Under the supervision of the following institutions and research bodies:

Université de Franche-Comté - UFC

Institut National de la Santé et de la Recherche Médicale - INSERM

Evaluation Campaign 2015-2016 (Group B)

HCERES

High Council for the Evaluation of Research and Higher Education

Research units

In the name of HCERES,[1]

Michel COSNARD, president

In the name of the experts committee,[2]

Alain LE MOINE, chairman of the committee

Under the decree No.2014-1365 dated 14 november 2014,

[1] The president of HCERES "countersigns the evaluation reports set up by the experts committees and signed by their chairman." (Article 8, paragraph 5)

[2] The evaluation reports "are signed by the chairman of the expert committee". (Article 11, paragraph 2)

Evaluation report

This report is the sole result of evaluation by the expert committee, the composition of which is specified below.

The assessments contained herein are the expression of an independent and collegial reviewing by the committee.

Unit name:	Host-Graft-Tumor Interactions – Cell and Gene Engineering
Unit acronym:	
Label requested:	INSERM – Université
Current number:	UMR 1098
Name of Director (2015-2016):	Mr Philippe SAAS
Name of Project Leader (2017-2021):	Mr Philippe SAAS

Expert committee members

Chair:	Mr Alain LE MOINE, Institute for Medical Immunology, Erasme Hospital, Université Libre de Bruxelles, Brussels, Belgium
Experts:	Mr Salem CHOUAIB, Gustave Roussy Cancer Institute, Villejuif
	Ms Els VERHOEYEN, École Normale Supérieure de Lyon (representative of the CSS INSERM)
Scientific delegate representing the HCERES:	Mr Kamel BENLAGHA
Representatives of supervising institutions and bodies:	Mr Lamine BOUBAKAR, Université de Franche-Comté
	Ms Marie-Ange LUC, INSERM
	Mr Jean-Christophe PAGES, Établissement Français du Sang
	Mr Emmanuel SAMAIN, UFR sciences médicales et pharmaceutiques
Head of Doctoral School:	Mr Patrick PLÉSIAT, Doctoral school n° 554, « Environnement-Santé »

1 • Introduction

The unit is subdivided in two complementary teams. The team TIT (Tolérance et inflammation en transplantation) is headed by Mr Philippe SAAS and the team TIM-C (Thérapeutique Immuno Moléculaire des Cancers) is headed by Mr Christophe BORG. The TIT involves 7 subgroups: 1) "modulations des réponses immunes" – headed by Mr Sylvain PERRUCHE; 2) "immunomodulation et immunopathology" located in Dijon –headed by Mr Bernard BONNOTE- "labelled lipSTIC labex"; 3) "études cliniques en transfusions" headed by Mr Pierre TIBERGHIEN; 4) "transplantation inflammation lipoproteins et complications" headed by Mr Philippe SAAS and Mr Didier DUCLOUX, "labelled lipSTIC labex"; 5) "leucémies dérivées des pDC" headed by Ms Francine GARNACHE-OTTOU; 6) "cellules dendritiques et sous populations lymphocytaires en allogreffe de cellules hématopoïétiques"; 7) "maladie résiduelle et greffe d'ovaire" headed by Mr Christophe ROUX. The TIM C contains 3 subgroups which are 1) "activité signalisation des interactions hôte-greffon-tumeur", headed by Mr Christophe BORG; 2) "activité biologie moléculaire – thérapie cellulaire et génique", headed by Mr Christophe FERRAND and 3) "activité antigènes et réponses immunitaires", headed by Mr Olivier ADOTEVI. For the next contract, TIM-C will be joined by a new research group (EA3922) working on autophagy and cancer, which will reinforce the basic research side of the team.

History and geographical location of the unit

The "host-graft-tumor Interactions – cell and gene engineering" (UMR 1098) was created in 2001 at the Établissement Français du Sang (EFS-BFC) and was labelled UMR 1098 in 2012 by the INSERM. Research activities at the UMR 1098 are located in Besançon for 90% and in Dijon for 10%, the two universities being merged in the consortium COMUE UBFC (COMmunauté d'Universités et Établissements Université Bourgogne Franche-Comté). UMR 1098 is located in different buildings in the university, the Hospital campus or the EFS facilities. UMR 1098 was originally focused on allogeneic immune responses and their regulation (graft versus host disease (GVHD) after stem cell transplantation, or host versus graft reactions in solid organ transplantation), Graft Versus Leukemia effect (GVL) as well as reactions after transfusions. Later, host-tumor interactions became an important topic of the unit that can be perceived in the concept of "mirror image" (unsuitable mechanisms involved in one direction might be exploited in the other one). In parallel, mechanisms of immune mediated inflammatory diseases (IMID) also became a transverse thematic. Importantly, all subjects are related to the clinical practice of the Centre Hospitalier Régional Universitaire CHRU, and most of them are the continuation of previous research. The UMR 1098 unit has evolved from adoptive allogeneic immunotherapy to immune cell-based therapies based on advanced therapy medicinal products (ATMP), including allogeneic NK cells, apoptotic leukocytes, monocyte-derived suppressive cells and skin substitutes (the skin engineering platform). A large biomonitoring platform dedicated to biotherapies and innovative technologies (directly connected to a biological resource center and a clinical investigation center) has been created including up to 28 sample collections and biological follow-up of patients from more than 54 clinical trials. So far, there are more than 15,000 samples collected. The unit obtained the ISO 9001 certificate in 2008 that was renewed in 2015.

Management team

Mr Philippe SAAS is the head of the unit.

HCERES nomenclature

SVE1_LS6, SVE2_LS8

Scientific domains

TIT and TIM-C scientific subjects are related to inflammation and immunity, in the contexts of transplantation, cancer, hematopoietic stem cell transplantation and red cell transfusion.

Unit workforce

Unit workforce	Number on 30/06/2015	Number on 01/01/2017
N1: Permanent professors and similar positions	31 (9.5FTE)	40 (13.6FTE)
N2: Permanent researchers from Institutions and similar positions	3	3
N3: Other permanent staff (technicians and administrative personnel)	20 (18.1FTE)	21 (19.1FTE)
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	8 (2.6FTE)	
N6: Other contractual staff (technicians and administrative personnel)	6 (5.1FTE)	
N7: PhD students	28	
TOTAL N1 to N7	**96 (66.3FTE)**	
Qualified research supervisors (HDR) or similar positions	26	

Unit record	From 01/01/2010 to 30/06/2015
PhD theses defended	28
Postdoctoral scientists having spent at least 12 months in the unit	3
Number of Research Supervisor Qualifications (HDR) obtained during the period	4

2 • Overall assessment of the unit

Introduction

The unit is dedicated to the understanding of immunological mechanisms, inflammation and immunity in different clinical contexts involving immune system with a typical translational approach. These contexts include allogeneic immune responses in renal transplantation or hematopoietic stem cell transplantation, blood transfusions, auto-immunity and malignancies. Identification of biomarkers of disease evolution and follow-up of treatment responses has become an important goal of the unit. Another major objective is the development of innovative therapeutic strategies by using new Advanced Therapy Medicinal Products (ATMP) produced by the different internal teams in the unit, in a GMP (Good Manufacturing Practice)/GCP (Good clinical practice) manner (apoptotic cells, SuperMApo, HuMoSC, UCPVax, Mecaskin). Clinical trials and patient cohorts have significantly progressed compared with the 2011 evaluation. Consequently, major grants and patents have been obtained by the unit.

Global assessment of the unit

The unit has performed excellent translational research, with a high number of publications in very good international journals and an important number of theses defended. Notable developments regarding new biotherapies including ATMP or cell therapy as well as innovative biomarkers have been obtained. The management and team atmospheres are excellent as attested during the discussions with all team members (scientists, technicians and students). The integration in the university campus and the hospital (FHU) is remarkable and strengthens the future existence of the unit. The next five-year plan is convincing, with pertinent questions regarding the FHU/CIC context and unit expertise. In this excellent context, the committee might regret the incapability to recruit young researchers or post-docs. An increased number of full time scientists, completely dedicated to basic research, by allowing publishing in very high impact factor journals, might also enhance scientific excellence and attractivity for post-docs.

Strengths and opportunities in the context

There is a compelling and remarkable promotion of translational research with constant concern to evolve from basic science to clinical trials (e.g. cell-based therapy studies) and with a great involvement of physicians. The questions that are addressed are topical and highly relevant for both basic and translational research. The established patient cohorts and clinical studies supported by a BioMonitoring platform are impressive. The ISO 9001 certification (2008 certification attesting for an established quality management process) is a useful tool for constant quality improvement.

The small shift in the research strategy is also well motivated by the increase in the team size and in the expertise of the team members, including the clinicians. The unit expertise is also highlighted by the strong immuno-monitoring platform and the good technical support.

The strong support of the university, the hospital and EFS, as well as the involvement of the University of Franche-Comté COMUE development and education/training initiative are obvious strengths. The management of two M2 master degrees (M2), dealing with Host-graft and host-tumor interactions, or Molecular and cellular signalization, both headed by a senior scientist of the unit are the basis for the recruitment of master students and further PhD students.

Several national and international collaborations have been set up, grants from public institution (with a high capacity to obtain competitive grants such as PHRC, INCA) and industrial partners have been obtained.

Weaknesses and threats in the context

The research staff is limited in the number of full-time scientists. Most of the scientists are either permanent professors that can only dedicate part of their time to research, or Medicine Professors with heavy teaching and clinical duties. The lack of attractivity probably results in the small number of post-docs and still remains a real issue.

The spread of projects with sometimes only little interactions between internal teams and the competitive characteristics of some thematics (i.e. T CAR…) compared to the relatively small size of the team might be an issue. Although most of the projects show a significant originality and a very strong clinical perspective, the clinical translation may benefit from a more thorough mechanistic analysis.

The cost of development and the difficulty of obtaining the authorization of Advanced Therapy Medicinal Product (ATMP), as well as the European competitive aspects are clear threats.

In addition, the scattering of offices and lab facilities has been considered as a weakness by the committee.

Recommendations

Most of the senior researchers have heavy teaching duties and/or hospital duties and the mentoring of students should be reconsidered. Indeed, due to these duties, they have reduced time for supervision of master and PhD students. The main challenge is now to increase the number of full-time senior researchers and post-docs in order to maintain the quality of the research, to stabilize the teams and to keep focus on the unit's strengths.

In some approaches, a more thorough mechanistic analysis might strengthen the fundamental aspects of the research and might improve the impact factors of publications.

Because of the complexity/multiplicity of subjects that will be developed in the next 5 years in team 1 equivalent, the committee recommends that the new foreseen director be mentored by the former director.

International visibility of team 2 could further increase by favouring submissions to high rank/profile journals in a more systematic way, and also by participating to European networks in addition to the very good ATMP activity. Focusing on a reduced number of projects could improve the impact of Team 2 publications in the future. They should continue their efforts to try to patent their findings, as this is a source of industrial collaborations and grant money as they have experienced in the past. We also recommend to gather the teams in the same location to reinforce their interactions; this is planned and should be realized in the near future.