PI3 - Physiopathologie de l'immunodépression associée aux réponses inflammatoires systémiques

Rapport Hcéres

HCERES

High Council for the Evaluation of Research and Higher Education

Research units

HCERES report on research unit:

Pathophysiology of injury-induced immunosuppression

PI^3

Under the supervision of the following institutions and research bodies:

Université Claude Bernard Lyon 1 - UCB

Campagne d'évaluation 2014-2015 (Vague A)

HCERES

High Council for the Evaluation of Research and Higher Education

Research units

In the name of HCERES,[1]

Didier HOUSSIN, president

In the name of the experts committee,[2]

Martin ANGELE, 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 result of the evaluation by the experts committee, the composition of which is specified below.

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

Unit name:	Pathophysiology of injury-induced immunosuppression
Unit acronym:	PI[3]
Label requested:	University Lyon 1
Present no.:	
Name of Director (2014-2015):	NA
Name of Project Leader (2016-2020):	Mr Guillaume MONNERET

Expert committee members

Chair:	Mr Martin ANGELE, University of München, Germany
Experts:	Mr Jean-Daniel LELIÈVRE, University Paris Est Créteil (representative of the CNU)
	Mr Jean-Louis VINCENT, Université Libre de Bruxelles, Belgium

Scientific delegate representing the AERES:

Mr Joost VAN MEERWIJK

Representatives of the unit's supervising institutions and bodies:

Mr Marc BONNEVILLE, Institut Mérieux

Mr Denis FOUQUE, Université Lyon 1

Ms Marie-Claire MAZE, Hospices Civils de Lyon

Sylvie RICARD-BLUM (represntative of ED n°205 "École Doctorale Inter-Disciplinaire Sciences-Santé" - EDISS)

1 • Introduction

History and geographical location of the unit

The proposal for the creation of a research unit was presented with research-groups with two different and complementary backgrounds: (i) academic field (clinical immunology and department of anaesthesiology and intensive care medicine, E. Herriot hospital, Hospices Civils de Lyon, HCL) (ii) diagnostic company (Institut Mérieux). Between both research groups a long-lasting collaboration exists since 2002 with the creation of a joint unit ("Laboratoire Commun de Recherche" – LCR). This research unit has been dedicated to the discovery of biomarkers in inflammatory contexts. Since 2008 the group focuses on sepsis induced immunosuppression.

Most of the future team's members come from the team "Haemostasis, inflammation, and sepsis", currently headed by Mr Claude NEGRIER. This team decided to split into three teams as the developed projects diverged. Therefore, team-members involved in research dedicated to sepsis decided to build a new team in collaboration with bioMérieux, the PI[3].

The LCR is located in the E. Herriot hospital, as are the Clinical Immunology lab and Anaesthesiology and Intensive Care Medicine department of HCL. Thus, the LCR will constitute the core location of the PI[3] lab with 600 m^2 space.

Management team

The PI[3] will be managed by the scientific board which will include the four subgroup leaders (Ms Fabienne VENET, Mr Vincent MALLET, Mr Julien TEXTORIS, and Mr Guillaume MONNERET), Mr Alexandre PACHOT (director of the Medical Diagnostic Discovery department at bioMérieux), and Mr Thomas RIMMELÉ (Head of Anaesthesiology and Intensive Care Medicine department, E. Herriot hospital).

This team will be headed by Mr Guillaume MONNERET.

AERES nomenclature

SVE1_LS6 Immunology, microbiology, virology, parasitology

Unit workforce

Unit workforce	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions	3	3
N2: Permanent researchers from Institutions and similar positions	5	5
N3: Other permanent staff (without research duties)	4	4
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers from Institutions (postdoctoral students)		1
N6: Other contractual staff (technician)	3	3
TOTAL N1 to N6	**15**	**16**

Unit workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	2	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	3	4

2 • Overall assessment of the unit

Global assessment of the unit

The group developed a high level translational research that aimed to decipher the aspects of immunosuppression induced by sepsis, essentially in intensive care units (ICU) patients. This topic has a high impact since septic complications remain the number one cause of death in ICU. This work is original and well recognized. This conclusion is supported by a quite large number of articles published in peer-reviewed journals, including 140 research papers, 10 review articles, as well as 33 invited lectures in international congresses and 5 patents in the last 5 years. The creation of the PI[3] research unit relies on a strong and sustained collaboration between bioMérieux and HCL. This collaboration has already proven successful in terms of patents, publications and grants. Moreover, the research group has been very active in training with 8 PhD students in the last 5 years. Working at the interface between academic and industrial institutions, the group profits financially from both worlds. In this respect, the estimated expenses of the group are covered by the REALISM project (IRT Biosater), which will provide substantial contribution for the next 4 years. Finally the group collaborates with innovative and well-established international research groups.

Strengths and opportunities in relation to the context

The research group has an impressive experience in clinical research with good access to patient samples and clinical data, which represents the basis for translational research. It focused on an original idea (sepsis-induced immunosuppression); its very good translational research allowed it to describe several biological prognosis markers.

The collaboration with an industrial group is very rewarding for both parties.

From a financial standpoint, the group will be able to cover the estimated costs for the next 4 years. The studies cover various areas in the field of sepsis attempting to address mechanisms of immunosuppression following sepsis from different perspectives. The findings of the proposed studies may result in clinical trials giving an opportunity for new therapeutic interventions in septic patients.

The group has established international collaborations.

Weaknesses and threats related to the context

The research focus of the group, immunosuppression and immunomodulation of sepsis and trauma, has been addressed by a number of research groups in the last decades, but did not have much clinical implication yet. In particular, clinical trial-attempts which focused on the modulation of single factors failed after promising results in experimental models.

Nevertheless, the topic is of great clinical interest. As mentioned above the research group addresses potential mechanisms of immunosuppression following sepsis from different approaches. The diversity of research aims within the proposal may represent a weakness but could also be considered as strength since this may result in innovative interacting projects.

Recommendations

The research should emphasize commonalities between the distinct aspects of sepsis-induced immunosuppression proposed. This may help to enhance the benefit of the collaboration between the sub-groups and find fruitful interactions between the proposed studies.

Immunomonitoring, as suggested in the proposal, should be used as a platform for individualized therapy (personalized medicine) and as a basis for patient inclusion in clinical trials.

Research developed by the team is descriptive and the expert committee feels that it is important in the future to add in vitro mechanistic experiments or animal models. Finally, interaction with clinicians should be increased in order to develop trials initiated by the team. The group should be more directly involved in the conduct of trials rather than having an ancillary role of blood analyses.

Increasing the diversity of the patient populations should also be recommended. The planned study of patients after cardiac arrest is a good example.