Thérapeutiques cliniques et expérimentales des infections

Rapport Hcéres

HCERES

High Council for the Evaluation of Research and Higher Education

Research units

HCERES report on research unit:

Thérapeutiques Cliniques et Expérimentales des Infections

Under the supervision of the following institutions and research bodies:

Université de Nantes

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]

Benoit GUERY, 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:	Thérapeutiques Cliniques et Expérimentales des Infections
Unit acronym:	
Label requested:	EA
Current number:	3826
Name of Director (2015-2016):	Mr Gilles POTEL
Name of Project Leader (2017-2021):	Mr Karim ASEHNOUNE

Expert committee members

Chair: Mr Benoit GUERY, University of Lille

Experts: Mr Antoine ANDREMONT, Hôpital Bichat, Claude Bernard, Paris

Mr Ferhat MEZIANI, University of Strasbourg

Scientific delegate representing the HCERES:

Ms Catherine SCHUSTER

Representative of supervising institutions and bodies:

Mr Fréderic BEN HAMOU

Ms Brigitte DRENO, University of Nantes

Head of Doctoral School:

Ms Corinne MIRAL, École Doctorale n°502 "Biologie-Santé"

1 • Introduction

History and geographical location of the unit

The unit "Thérapeutiques Cliniques et Expérimentales des Infections" is issued from the EA 3826 headed by Mr Gilles POTEL since 1987. The AERES evaluation held in 2011 noticed an important dispersion in projects addressed by the team. This main weakness led the group to split the initial team into two separate research entities: the unit "thérapeutiques cliniques et experimentales des infections" headed by Mr Karim ASEHNOUNE and the unit "Microbiotas, Hosts and Antibiotic Resistance (MiHAR) headed by Mr Eric BATARD and Mr Didier PELETTIER. The current unit associates a very large clinical network to a more basic research team, giving a great opportunity to evaluate clinically relevant questions. The thematic of the new unit will be based on translational research and the role of host immune response to bacterial infections.

The laboratory is located in the medicine faculty building in Nantes. The laboratory is expected to move into the new "Institut de Recherche en Santé" (IRS-2) (expected date: June 2016), close to the new university hospital "Ile de Nantes".

Management team

For the next period, the unit will be headed by Mr Karim ASEHNOUNE, replacing Mr Gilles POTEL the former head of the unit.

HCERES nomenclature

SVE1-LS6

Scientific domains

The scientific field covers all the aspects of the host-pathogen relationships from the consequences of bacterial infections on cells of the immune system to the role of antibiotics and virulence factors on immunity in both animal models and immune cells from patients.

Unit workforce

Unit workforce	Number on 30/06/2015	Number on 01/01/2017
N1: Permanent professors and similar positions	11 (5.5 FTP)	5 (2.5 FTP)
N2: Permanent researchers from Institutions and similar positions		
N3: Other permanent staff (technicians and administrative personnel)	5 (3.1 FTP)	5 (3 FTP)
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	1 (0.5 FTP)	
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (technicians and administrative personnel)	2	
N7: PhD students	7	
TOTAL N1 to N7	**26 (18.1 FTP)**	
Qualified research supervisors (HDR) or similar positions	10	

Unit record	From 01/01/2010 to 30/06/2015
PhD theses defended	5
Postdoctoral scientists having spent at least 12 months in the unit	
Number of Research Supervisor Qualifications (HDR) obtained during the period	**5**

2 • Overall assessment of the unit

Introduction

The unit evaluated in 2011 had shown a high dispersion of the projects; this main weakness led the group to split the initial team into two research entities. It was recommended to focus all the projects on a limited number of themes.

In the past five years, the EA focused on pathophysiology of extracellular bacteria. More specifically, experimental models were generated in order to improve the knowledge of pharmaco-kinetic/dynamic parameters of antibacterial drugs. The research also included epidemiology of bacterial infections and resistance of bacteria to antibiotics. The present scientific field, more focused, will cover the study of acquired immunosuppression after an acute stress, leading to nosocomial infection in humans, more specifically the role of dendritic cells and NK cells in infection. The current unit associates a very large clinical network to a more basic research team giving a great opportunity to evaluate clinically relevant questions.

Global assessment of the unit

This unit is mainly focused on 4 general themes; (i) study of acquired immunosuppression after an acute stress during a nosocomial pneumonia: the group developed a clinical network for treatment testing, and built a biocollection. Mouse models were also generated (haemorrhage and pneumonia). The group used clinical samples as well as mouse models to evaluate the response to severe trauma and brain injuries; (ii) role of dendritic and NK cells after Methicillin-Sensitive *Staphylococcus Aureus* (MSSA) or *P. aeruginosa* pneumonia; this was performed in immunocompetent mice models; (iii) role of virulence factors in the immune response upon bacterial infections: the group generated a model of *E coli* osteo-articular infection along with cell co-culture approaches. The group also performed a collaborative work using *P. aeruginosa* in a pneumonia hypoxic model; (iv) modulation of the host immune response by antibacterial agents: a pre-clinical approach was used in this last part of the research showing the activity of new molecules in animal models. In these models, the host immune response is also evaluated.

Globally the unit uses a large number of models, a large number of pathogens and it is quite difficult to identify a united program, even though part of the initial unit has left.

The EA 3826 represents a laboratory in which the University of Nantes and local supporting companies (pharmaceutical and biotech) have heavily invested, both in scientific personnel and via other supports, indicating that, from their standpoint, the unit represents a sound investment for the future. The scientific production is of overall good quality and the level of publications is good, although not equally distributed among the team members. The laboratory attracts a large number of master and PhD students but no post-doctoral scientists. The unit has obtained a significant level of financial support, via contracts with the private sector (pharmaceutical, biotech) and national granting agencies. In contrast, European and international funding remain rather modest. Despite the strong scientific activity in the unit, the overall orientations and goals of the projects do not appear particularly integrated among team members, although an increase in intra-team collaborations has occurred over the period. A wider use of state-of-the-art rodent models of infection developed by the team in the studies carried out will allow reaching higher impact science for the entire unit.

Strengths and opportunities in the context

The first strength of the unit is a large clinical network: the team can either prospectively or retrospectively (using the biocollection) set up studies to answer clinically relevant questions studying human response to sepsis or potential therapeutic interventions. From these data, the unit can construct pathophysiological hypotheses that can be evaluated in cells and animal models. Along these lines, the unit associates basic researchers to hospital-based doctors, which is definitely an asset for translational research. Thus, the group can easily start very large clinical trials.

The second strength of the unit is to possess a large number of animal models and several cell culture models. They, therefore, can easily test the hypotheses coming from the bedside. Together with the number of models, the unit has the opportunity to evaluate a large number of antibiotics and, more interestingly, to focus on antibiotic associations on “difficult-to-treat” pathogens like multi-drug resistant or pan-resistant bugs.

The third strength of the unit is the large number of excellent specialty papers published in various domains and the important established collaborations.

The unit appears to be undergoing a strong positive evolution, getting important research results, with increasing scientific productivity and international attractiveness. The research is of high interest and highly relevant, in the context of hospital-acquired pneumonia and pneumonia of the host acutely immunosuppressed, in order to improve organ failure in intensive care units. A strong rational appears between human pathologies and the research project developed. Following recommendations of the previous AERES committee, the unit focused its research axis on theses aspects. The strength of the unit relies on the internationally recognized expertise of its members in the host-pathogen interaction domain including the generation of animal models adapted to the their project. The research scope is quite supported by institutional agencies, such as “région Pays de la Loire”, and by big pharmas and the laboratory is deeply connected to university and medical school.

Weaknesses and threats in the context

If the clinical network is a great strength and an important opportunity, the committee felt that it is very difficult to identify a clear line of research, due to the number of infection animal models with, finally, an evaluation of several antibiotics in the different models.

The committee feels that the topics are chosen based on the opportunities of collaborations rather than built up in a research program rationale.

Analyzing the projects of the unit as well show a high dispersion, with even new models (e.g. spinal cord injury or phagotherapy).

Given the type of the university and/or university hospital positions of the team members, many of them have to dedicate a significant amount of their time to education, teaching and training.

The technical support is quite limited given, the specific objectives and the relative large number of faculty and research staff. A significant increase of its international competitiveness hinges on strengthening such technical support. Despite the solid competence of the unit members, funding for the development of specific instrumentation will be difficult to obtain, given the positioning of this group at the moment. The international visibility of the unit, despite the high quality and competence of the researchers must be enhanced in order to attract excellent students and post-docs form abroad.

Recommendations

The clinical network should be the platform of the project, with a narrowing of the topics mostly based on the choices that have to be made with the basic research models. It seems impossible to address in one unit so many areas of research with so many different pathogens and models. The common determinant is the host immune response that can be declined from the clinical data to the cellular and animal models. However, the committee suggests choosing one pathogen and one clinical target.

The laboratory might concentrate resources, both financial and human, on the two promising projects and work to better position the unit in the national and international landscape.

The committee encourages the unit to reach a more aggressive publishing policy, based on prioritizing research goals to the most significant translational purposes.