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IECM - Immuno-endocrinologie cellulaire et moléculaire

Rapport Hcéres

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HCERES

High Council for the Evaluation of Research
and Higher Education

Research units

HCERES report on research unit:

Cellular and Molecular Immuno-Endocrinology

CMIE / IECM

Under the supervision of the following
institutions and research bodies:

ONIRIS - École Nationale Vétérinaire, Agroalimentaire
et de l'Alimentation, Nantes Atlantique

Institut National de la Recherche Agronomique - INRA

Université de Nantes

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

Roberto Mallone, 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: Cellular and Molecular Immuno-Endocrinology

Unit acronym: CMIE / IECM

Label requested: UMR

Current number: EA4644 - USC1383

**Name of Director
(2015-2016):** Mr Jean-Marie BACH

**Name of Project Leader
(2017-2021):** Mr Jean-Marie BACH

Expert committee members

Chair: Mr Roberto MALLONE, Paris Descartes University

Experts: Mr Fabrice LAURENT, INRA UMR 1282-ISP Centre INRA Val de Loire, Tours
(representative of the CSS INRA)

Ms Eliane PIAGGIO, Curie Institute, Paris

Ms Anne WOJTUSCIZYN, Montpellier University

Scientific delegate representing the HCERES:

Mr Jean GIRARD

Representatives of supervising institutions and bodies:

Mr Frédéric BENHAMOU, Nantes University

Ms Marie-Anne COLLE, ONIRIS, Nantes

Mr Christian DUCROS, INRA, Departement Santé Animale

Head of Doctoral School:

Mr Frank BOURY, ED 502 "Biologie et Santé"

1 • Introduction

History and geographical location of the unit

The CMIE Laboratory is a “one-team unit” jointly affiliated with the Nantes University (Faculty of Medicine) and Oniris (Nantes Atlantic College of Veterinary Medicine, Food Science and Engineering, EA 4644). The CMIE Laboratory is also an INRA “under-contract” unit (Animal health department, USC 1383).

Initially created for the study of type 1 diabetes (T1D) pathogenesis, prevention and treatment (possibly by beta-cell replacement), the unit - under the direction of Mr Jean-Marie BACH - kept the T1D autoimmunity expertise and developed other fields such as: 1) the renewal of destroyed beta cells using hematopoietic or hepatic progenitors; 2) a translational research program on the use of spontaneous canine tumors for human cancer research, which led to the creation of a separate unit; 3) graft immune protection; 4) immune therapeutic approaches; and 5) identification of biomarkers for T1D.

The unit research activities are currently centered on three recent themes on T1D:

- 1) the role of the autonomous nervous system in the control of the autoimmune reaction;
- 2) the role of beta-cell-derived microRNAs in the autoimmune process and research of new biomarkers of the disease;
- 3) development of bio-artificial pancreas and xenogenic cell therapy (with the creation of the start-up Xenothera).

Management team

The head of the unit is Mr Jean-Marie BACH. He is assisted by a coordination committee composed of Mr Jean-Marie BACH, Ms Steffi BÖSCH, Ms Lucy CHAILLOUS, Ms Julie HERVÉ, Ms Blandine LIEUBEAU, Ms Mathilde MOSSER, Mr Grégoire MIGNOT.

HCERES nomenclature

SVE1_LS4 Physiologie, physiopathologie, biologie systémique médicale

Scientific domains

The unit research activities are centered on three recent research programs on type 1 diabetes. They range from preclinical research using spontaneous/transgenic mouse models of diabetes or pigs to human research. The current axes were initiated at the time of the previous evaluation and one new recent project:

1. role of the autonomous nervous system in the control of the auto-immune reaction, including a new project emerged in 2014 on the role of stress in the control of immune responses in pig;
2. beta-cell-derived exosome-associated microRNAs: role in the autoimmune process and potential significance as new biomarkers of diabetes (human, dog);
3. development of a bio-artificial pancreas (macroencapsulated islets from piglet or human).

Unit workforce

Unit workforce	Number on 30/06/2015	Number on 01/01/2017
N1: Permanent professors and similar positions	3	6
N2: Permanent researchers from Institutions and similar positions	3	3
N3: Other permanent staff (technicians and administrative personnel)	6	6
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	1	
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (technicians and administrative personnel)		
N7: PhD students	1	
TOTAL N1 to N7	15	
Qualified research supervisors (HDR) or similar positions	2	

Unit record	From 01/01/2010 to 30/06/2015
PhD theses defended	2
Postdoctoral scientists having spent at least 12 months in the unit	1
Number of Research Supervisor Qualifications (HDR) obtained during the period	1

2 • Overall assessment of the unit

Introduction

The CMIE lab is a “one-team unit” jointly affiliated with the Nantes University (Faculty of Medicine) and Oniris (Nantes Atlantic College of Veterinary Medicine, Food Science and Engineering) (EA 4644), and is an INRA “under-contract” unit (Animal health department, USC 1383).

From 2004 to 2011, under the direction of Mr Jean-Marie BACH, the CMIE unit (single-team unit) studied diagnostic and therapeutic approaches for type 1 diabetes (T1D) and strategies for beta-cell replacement. During this period, the CMIE unit also initiated a translational research program on the use of spontaneous canine tumors for human cancer research that ended in 2012 with the creation of a new ONIRIS research unit (AMaRoc).

The unit research activities are now centered on three recent research programs on T1D. They range from preclinical research, using spontaneous/transgenic mouse models of diabetes or pigs, to human research. The current axes were initiated at the time of the previous evaluation and there is one new recent project:

1. role of the autonomous nervous system (ANS) in the control of the autoimmune reaction, including a new project emerged in 2014 on the role of stress in the control of immune responses in pig;

2. beta-cell-derived exosome-associated microRNAs: role in the autoimmune process and potential significance as new biomarkers of diabetes (human, dog);

3. development of a bio-artificial pancreas for T1D patients (macroencapsulated islets from piglet or human). This project also led to the creation of the start-up Xenothera (www.xenothera.com).

While these projects emerged during the previous evaluation period (2010-2015), they have led to a refocusing of the unit research on better-selected topics with the highest potential impact. In particular, previous projects on autoreactive CD8+ T cells, myeloid-derived suppressor cells, role of heme oxygenase and carbon monoxide, implication of Cxcr1 in T1D and beta-cell replacement using hematopoietic or hepatic progenitors are not further pursued. This seems a wise decision in the current landscape of increasing research competition and may increase the scientific yield of the team in the long term. For all the themes presented, this refocusing effort should be further pursued to fully dissect the ambitious hypotheses put forward and improve the publication targets. Despite major improvements in this sense, all themes still suffer from an excessive dispersion of scientific questions and models.

The past production on these subjects is of moderate impact. The future programs are of heterogeneous impact. Despite the remaining weaknesses, the unit seems to have evolved in a promising direction as compared to the previous evaluation. In particular, the integration into the ECTIS IHU is a major improvement towards increased visibility, with ongoing collaborations that have already produced one high-impact publication (J Clin Invest 2015).

Global assessment of the unit

The CMIE lab is a “one-team” unit, with a strong pre-clinical expertise in T1D, highly integrated in the Oniris Veterinary Medicine College, the INRA Animal Health Department and the Nantes Faculty of Medicine. This allows unit members to propose a research program with good translational potential and in line with the “One health, One Medicine” concept, i.e. integrating scientific questions addressed to both human and animal health with productive exchanges between the two. The research staff has a mixed educational profile (veterinary, pharmacist, medical doctor and scientific), providing diversified expertises, and a good ratio of Researchers/Engineers-Technicians. The unit features strong collaborations at the regional level, while national and international collaborations and visibility are more limited at present. The unit seems well managed by a dynamic director and has an important involvement in teaching duties. The past programs on HO-1 and T1D have led to some good impact publications. If the total number of publications compared to the previous evaluation period is roughly similar, publications in leader positions are more limited (10 out of 23 in the last 5.5 years), but this decrease is somehow offset by a few excellent publications. These last years, the unit has consolidated its expertise in T1D, and the refocusing of efforts on more selected topics may improve the publication performance in the future. They have contributed to the creation of one start-up. They have had limited success in fund raising and personnel recruitment, of Post-docs in particular. They had to face the departure of a key young staff, but, fortunately, benefit from the recruitment of two young assistant professors and the future arrival of two senior professors among which one has clinical veterinary duties, which opens new possibilities for studying diabetes and obesity phenotypes in outbred dogs. One technical staff member is retiring this year but will be replaced. The unit presents a project well balanced in terms of task force repartition and ranging from fundamental research to therapeutic approaches. However, future themes are of heterogeneous impact and robustness, and the justification of some WPs in the 3 research themes proposed is debatable.

Strengths and opportunities in the context

There is an integrated “One Health, One Medicine” approach to research, with a good cross-talk between human and animal investigations and translational profiles.

There is a broad complementarity of education and expertise of the staff (veterinary, pharmacist, medical doctor and scientific).

There is a dynamic management and team life.

The proximity of the Veterinary School favours the development of animal models of veterinary and/or medical importance.

The unit is excellently integrated into a local network of collaborations (notably with the IHU ECTIS).

There are good collaborations with non-academic partners (themes 1 and 3).

Additional permanent staff has been recruited (2 assistant professors, themes 1 and 3).

There is expertise in preclinical T1D (murine models, human), and opportunities are offered with the relevant and less competitive pig and dog models.

The unit hosts a biocollection of T1D PBMC samples within the GOFEDI network.

The unit has created a niche in the miRNA domain (and particularly in exosome-associated miRNAs) in T1D.

Another niche is represented by pig and pet experimental models.

The unit has gained expertise in ANS-immune system crosstalk.

There is a synergy with the Xenothera start-up, which offers funding opportunities for the unit (contract, Cifre).

There is good technology transfer potential, with 2 patents already filed.

An "Animal Immunomonitoring" platform has been created, which may attract additional academic and industrial partnerships.

There is an excellent involvement in teaching at the master and doctoral levels, including in summer schools.

The level of publications is improving.

Weaknesses and threats in the context

National and international collaborations and visibility are limited.

There has been limited success in fundraising, and no funding from international agencies.

Theme 2 has no funding at present.

Participation to international meetings is poor.

There are difficulties in recruiting non-permanent staff at the postdoctoral level.

The number of PhD students over the past years (and associated publications) has been limited.

Scientific animation on-site is limited.

A talented assistant professor strongly involved in theme 1 has left the unit.

There is strong competition on theme 1.

The staff members display a heterogeneous level and impact of publications, with a limited number of articles in key authorship positions.

The rationale for some WPs in the research themes does not rely on solid preliminary data and/or hypotheses.

There are technical hurdles associated with some themes.

Research efforts are somehow dispersed on several challenging questions, making the overall project over-ambitious.

Scientific crosstalk among themes is limited.

Recommendations

- develop a national and international network of collaboration ;
- increase funding, including international agencies ;
- improve recruitment of postdoctoral researchers ;
- improve scientific animation onsite by more regular scientific meetings within the unit and by organizing seminars by invited speakers ;

- capitalize on the opportunities offered by Oniris and local collaborations, e.g. use of pig/dog models and expertise on neonatal pig islets ;
- refine some WPs of the research themes by refocusing theme on the basis of solid preliminary data and funding opportunities.