

Endothélium, valvulopathies et insuffisance cardiaque

Rapport Hcéres

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HCERES

High Council for the Evaluation of Research
and Higher Education

Research units

HCERES report on research unit:

Endothelium, Valvulopathy and Heart Failure

EnVI

Under the supervision of
the following institutions
and research bodies:

Université de Rouen

Institut National de la Santé Et de la Recherche

Médicale - INSERM

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

Stéphane Heymans, 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: Endothelium, Valvulopathy and Heart Failure

Unit acronym: EnVI

Label requested: UMR_S

Current number: UMR_S 1096

**Name of Director
(2015-2016):** Mr Vincent RICHARD

**Name of Project Leader
(2017-2021):** Mr Vincent RICHARD

Expert committee members

Chair: Mr Stéphane HEYMANS, Maastricht University, The Netherlands

Experts:

- Mr Régis BORDET, University of Lille 2 (representative of the CNU)
- Mr Thierry COUFFINHAL, University of Bordeaux
- Mr Pierre MARQUET, University of Limoges (representative of the CSS INSERM)
- Mr David SMADJA, University Paris Descartes
- Ms Soraya TALEB, University Paris Descartes

Scientific delegate representing the HCERES:

Mr Patrick LACOLLEY

Representatives of supervising institutions and bodies:

Ms Marie-Joséphine LEROY-ZAMIA, INSERM

Mr Cafer ÖZKUL, University of Rouen

Head of Doctoral School:

Mr Patrice LEROUGE, Doctoral School n° 497, « École doctorale Normandie de Biologie Intégrative, Santé et Environnement - BISE ».

1 • Introduction

History and geographical location of the unit

The cardiovascular research group was founded in the early 1990s as a university research group (“équipe d’accueil”) and received its first INSERM label in 1999 (as “équipe mixte INSERM”, EMI 9920). This was followed by creation of an INSERM unit (U644) in 2004 that was renewed in 2008. All these research groups were directed by Mr Christian THUILLEZ, professor (PU-PH) in pharmacology. In 2012, the unit was created again as INSERM U1096 (new pharmacological treatments on endothelial protection and heart failure) under a new direction (Mr Vincent RICHARD). The present application thus corresponds to a renewal of this research group, under the same direction (Mr Vincent RICHARD, professor [PU-PH] in pharmacology at Rouen University medical school and Rouen University Hospital).

The unit is situated at the medical campus and University Hospital in Rouen. The main location is within Rouen University medical school’s research building that hosts all the pre-clinical research activities of the unit, while clinical research is performed at the clinical departments of Rouen University Hospital (“CHU”) located immediately adjacent (5 min walk) to the medical school. This main hospital (hôpital Charles Nicolle) hosts most of the clinical departments for whose research is fully or partly included in the unit (i.e. cardiology, cardiac surgery, thoracic surgery, vascular surgery, pharmacology, hematology, intensive care, imaging) while 2 departments (Internal medicine and nephrology) are still located in a nearby (6 kms) hospital (hôpital de Bois Guillaume). The unit is integrated within the local research federation (“Structure Fédérative de Recherche”, SFR) Institute for Research and Innovation in Biomedicine (“IRIB” and also coordinates an inter-regional network (Amiens, Caen, Lille, Rouen) that received at the end of 2014 a “FHU” label (“Fédération Hospitalo-Universitaire”).

Management team

The unit will be directed by Mr Vincent RICHARD.

HCERES nomenclature

SVE1_LS4

Scientific domains

Endothelium, valvulopathy and heart failure.

Novel pharmacological approaches for endothelial protection.

Innovations in aortic stenosis/aortic valve implantation.

New strategies for the treatment of heart failure.

Unit workforce

| Unit workforce | Number on 30/06/2015 | Number on 01/01/2017 |
|---|----------------------|----------------------|
| N1: Permanent professors and similar positions | 17 | 15 |
| N2: Permanent researchers from Institutions and similar positions | 1 | 1 |
| N3: Other permanent staff (technicians and administrative personnel) | 12 | 14 |
| N4: Other professors (Emeritus Professor, on-contract Professor, etc.) | | |
| N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.) | | |
| N6: Other contractual staff (technicians and administrative personnel) | | |
| N7: PhD students | 16 | |
| TOTAL N1 to N7 | 46 | |
| Qualified research supervisors (HDR) or similar positions | 19 | |

| Unit record | From 01/01/2010 to 30/06/2015 |
|---|-------------------------------|
| PhD theses defended | 12 |
| Postdoctoral scientists having spent at least 12 months in the unit | 1 |
| Number of Research Supervisor Qualifications (HDR) obtained during the period | 4 |

2 • Overall assessment of the unit

Introduction

The scientific domain of the cardiovascular research group consists of research topics on endothelium, valvulopathy and heart failure. This research focus is in line with the preclinical and clinical history and strengths of the unit at the Rouen University medical school and research.

Global assessment of the unit

Overall, this unit has major strengths, including an excellent translational approach of research, a strong platform for endothelial phenotyping in the cardiovascular and pharmacological field, and many very experienced technicians and researchers. With this approach, the unit is strongly supportive for the clinical professors, and the experimental and clinical units work together in an outstanding mutual understanding.

The next challenge should be to increase the European visibility of the group by getting even more involved in EU networking opportunities. In line with this, developing (from inside) or attracting (from outside) young or senior talents may help to overcome the missing layer between PhD students and the researchers. In a limited time frame, it may help to choose some very promising projects and put existing technicians and researchers within the unit on 2-3 focused projects to increase the impact of the projects. Also making use of novel technologies and the availability of clinical samples will increase the impact of the translational work of the unit.

Strengths and opportunities in the context

- excellent translational approach of research;
 - the research lab is very supportive for clinical professors;
 - many clinical professors are within the research group and hospital holding dual positions;
 - there are excellent relationships between the preclinical and clinical parts of the unit, with many residents that hold a master or PhD on an experimental topic;
 - unit members have a strong activity of publication, both within the unit (n = 87) and outside (n = 104, particularly clinical papers);
 - there is an excellent transfer of research results to the clinics or as patents (3 patents filed over the previous period).
- strong pharmacological, endothelial phenotyping and platform in the cardiovascular field;
 - ISO9001 quality process was recently awarded;
 - there is an excellent organization of the unit in subgroups and technical platforms;
 - the imaging and phenotyping platforms are excellent (in particular magnetic resonance imaging, MRI).
- the unit has good relationship with industrial companies;
- the unit includes young talented people heading new research lines;
- unit members have an excellent participation in teaching and training programs;
 - unit members show major participation in coordinating master courses and in the different programs of the doctoral school;
 - the unit's director has a major participation in coordinating the doctoral school.

Weaknesses and threats in the context

- there is an unclear strategy how to get involved in European projects and networks;
 - the unit has little involvement in EU projects;
 - the unit has little involvement in EU working groups or committees of the ESC, HFA or other EU based societies.
- there is a lack of interlayer between PIs and PhD students;
 - there are many PhD and master students, but few post-docs;
 - the unit's attractiveness for post-docs is unclear (also related to EU visibility).
- prospective patient cohorts and biobanks are lacking;
 - despite a strong translational focus of research, biobanking and databases are lacking behind.
- focus in research projects and international visibility may be improved;
 - there are many therapeutic and pharmacological targets;

- few papers were published in journals with the highest impact factor in the specialized domains.
- technological innovations and opportunities are somewhat slow;
 - methodological meetings in between (otherwise excellent) technicians are lacking;
 - in vitro setups, and omics are somewhat lacking.

Recommendations

- the committee recommends to build up prospective clinical cohorts and biobanks, and combine this with easily available technological innovations such as omics in tissue samples, genetic analysis, and in vitro work (cells derived from human samples in vitro). The committee also recommends to invest in - or collaborate intensively with labs involved in - bio-informatics in order to integrate different levels of information, in tissue, blood and phenotyping;
- the committee recommends to collect not only valves, but also blood, DNA and other biosamples in different diseases;
- the committee recommends to develop a clear strategy on what to do with those samples, to focus more specifically, to diversify technologies, and to develop a more integrated research on aortic stenosis, from bench to bedside;
- the committee recommends young that PIs as well as established investigators get proactively involved in European networks, working groups, committees, meetings, etc... in order to increase the visibility of the excellent work of the laboratory, and also to network for getting involved in existing and new EU projects & applications;
- the committee recommends to invest time in methodological developments together with the existing excellent technicians:

The unit may envisage using transcriptomic, proteomic and/or metabolic investigations together with their animal and clinical models to help evaluating more globally the implication of the different pathways in the endothelium dysfunctions they tackle, and modulators thereof;

- the committee recommends to make timely choices of more focused projects, to reduce their diversity and to invest in high impact and promising research projects. The unit should organize the coordination of the different clinicians and researchers, reorganize the different themes around one central focused project once it looks promising (example: lymphangiogenesis). This will also increase the visibility internationally, and the impact of the publications.

The unit may compare more systematically in all their animal/clinical models the pertinence of the different pathways they have been studying, as it does not appear clearly why only certain targets are studied in any given model;

- in concert with the university, the committee recommends to develop young talent program.

Effort should be done to increase the numbers of full-time researchers as well as of international post-doctoral fellows in the different themes.