MITOVASC - Biologie mitochondriale et cardiovasculaire

Rapport Hcéres

HCERES

High Council for the Evaluation of Research and Higher Education

Research units

HCERES report on research unit:

Mitochondrial and Cardiovascular Pathophysiology

MITOVASC

Under the supervision of the following institutions and research bodies:

Université d'Angers - UA

Centre National de la Recherche Scientifique - CNRS

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]

Adam Greenstein, 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:	Mitochondrial and Cardiovascular Pathophysiology
Unit acronym:	MITOVASC
Label requested:	Université - CNRS and INSERM
Current number:	6214 (CNRS) and 1083 (INSERM)
Name of Director (2015-2016):	Mr Daniel HENRION
Name of Project Leader (2017-2021):	Mr Daniel HENRION

Expert committee members

Chair: Mr Adam GREENSTEIN, University of Manchester, UK

Experts:

Mr Bernard GENY, University of Strasbourg (representative of the CNU)

Mr Alain LACAMPAGNE, University of Montpellier (representative of the CoNRS)

Ms Cécile VENDIS, University of Toulouse (representative of the CSS INSERM)

Scientific delegate representing the HCERES:

Mr Jean-Marie ZAJAC

Representatives of supervising institutions and bodies:

Ms Clarisse DAVID, CNRS

Ms Marianne DESMEDT, INSERM

Ms Chantal LASSERVE, INSERM

Ms Armelle LETURQUE, CNRS

Mr Alain MERCAT, CHU, Angers

Mr Jean-Paul SAINT-ANDRÉ, University of Angers

Head of Doctoral School:

Mr Franck BOURY, Doctoral school n°502, Biology-Health Nantes-Angers, EDBS

1 • Introduction

History and geographical location of the unit

The MITOVASC unit at the University of Angers was founded in 2015 and comprises two broad research teams: 1) mitochondria pathophysiology and 2) cardiovascular physiology. The unit has also been designed to co-ordinate the translational research activities of six clinical teams which are not the focus of this report but includes relevant targets for translation of the MITOVASC science into clinical practice (microcirculation, cardiac protection, mitochondrial medicine, vascular inflammation & medicine and endocrinology). Together, the MITOVASC unit and the clinical teams form the MITOVASC Institute. The MITOVASC unit was formerly known as the 'Biologie Neurovasculaire et Mitochondriale Integrée (BNMI)' unit. The restructuring of BNMI into MITOVASC essentially represents the progressive merger and subsequent growth of two groups at Angers: vascular biology and mechanotransduction (head: Mr Daniel HENRION) and Mitochondria Biogenetics (heads: Mr Pascal REYNIER and Mr Vincent PROCACCIO). The group gained momentum in 2014 with the addition of a clinician researcher whose expertise in septic shock complements the vascular group. In 2015, Mr Guy LENEARS joined the Angers mitochondrial team with a remit to develop a mitochondrial medicine research centre for the Région Pays de la Loire. This year the group will be further strengthened with expansion into cardiac research, predominantly based around ischaemia reperfusion, with the addition of Prunier's team.

Management team

The new MITOVASC unit is led by Mr Daniel HENRION who successfully led the previous AERES evaluation in 2010.

HCERES nomenclature

SVE1_LS4

SVE1_LS1

SVE1_LS2

Scientific domains

Scientific domains are clearly delineated.

Within the mitochondrial team: mitochondrial dynamics and bioenergetics, mitochondrial translational research and mitochondrial diseases - mitochondrial genetics and therapeutics and mitochondrial Medicine Research Centre (PREMMI).

Within the vascular team: cytoskeleton in mechanotransduction - neuroeffector systems in mechanotransduction - flow mediated remodeling - fetal programming - environment conditions - vascular dysfunction and metabolism - Gq Protein Coupled Receptors (GPCR) - neurosecretion, stress, vascular sodium channels.

Unit workforce

Unit workforce	Number on 30/06/2015	Number on 01/01/2017
N1: Permanent professors and similar positions	31	17
N2: Permanent researchers from Institutions and similar positions	5	5
N3: Other permanent staff (technicians and administrative personnel)	8 (7 FTE)	11 (9 FTE)
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	8	
N6: Other contractual staff (technicians and administrative personnel)	7 (6 FTE)	
N7: PhD students	21	
TOTAL N1 to N7	**80 (78 FTE)**	
Qualified research supervisors (HDR) or similar positions	29	

Unit record	From 01/01/2010 to 30/06/2015
PhD theses defended	18
Postdoctoral scientists having spent at least 12 months in the unit	9
Number of Research Supervisor Qualifications (HDR) obtained during the period	5

2 • Overall assessment of the unit

Introduction

The MITOVASC unit is designed to investigate the relationship between microvascular blood flow and mitochondrial bioenergetics and how breakdown of this relationship contributes to human disease phenotypes. While there are substantial projects for each domain separately (vascular & mitochondrial), there is an emergent emphasis on collaborative research between the two disciplines and a clear intention stated to continue moving the research into a clinical setting.

The vascular team (Cardiovascular mechanotransduction/CARME) has an internationally leading presence in the field of vascular remodelling and the responses of arteries to flow (i.e. movement of blood through the arterial 'tube') in health and disease thanks in part to the consistently high quality work of the director. Over the last five

years, the vascular team has steadily grown and now includes a number of successful principal investigators. The work is of a common theme (as above) but more specifically there has been recent academic traction in relation to the role of Estrogen Receptor alpha (ER) and G-q protein coupled receptors in the setting of mechanotransduction and shear stress. There is investigation into both common vascular pathologies (ageing, diabetes) and more rare illnesses (pseudoxanthoma elasticum). There is an emphasis on translational aspects with the recent incorporation into the group of clinician scientists with interests in remote ischaemic preconditioning in the setting of cardiovascular disease and septic shock.

The mitochondrial team (Mitochondrial Pathophysiology/MITO) is headed by Mr Guy LENEARS who joined the unit in 2015 and corresponds to the fusion of ex- teams 8 and 10 and a part of Mr Guy LENEARS' team. For the last funding period, the research work was dedicated to the characterization of mutations and genes involved in mitochondrial dynamics and associated with neurological disorders. Important data from the team showed in a mouse model that mitochondrial dynamics is necessary to protect the heart ischemia/reperfusion stress and to adapt to vascular response to hypertension. They explored new therapeutic approaches (impact of resveratrol, idebenone and cyclosporine in Leber Hereditary Optic Neuropathy (LHON) and cysteamine in Huntington's disease). The strategy for the next period is clearly focused on the strengthening of the relationship between clinical and fundamental research. There is close collaboration among the Angers physicians and the five principal investigators for the MITO lab.

The structure of MITOVASC clearly promotes collaboration between mitochondrial and vascular groups and this is illustrated by the growing list of departmental publications investigating, for example, actions of resveratrol or complications of diabetes and hypertension. This process of ‘cross-fertilisation’ is clearly an emphasis for the institute and already beginning to bear fruit.

Global assessment of the unit

This is an ambitious and well-structured unit now, with clear plans for development and growth. There is strong leadership stretching throughout the faculty with defined leads and an emphasis on both basic and translational research. There are opportunities for further integration between the mitochondrial and cardiovascular mechanotransduction. The institute appears to function with significantly fewer administrative support staff than other equivalent sized academic institutes, particularly given the ambitious bench-to-bed side objectives and recent growth in academic research staff.

Strengths and opportunities in the context

The principal strength of the unit is the stable and outstanding leadership provided by the director. There has been a steady growth of the unit under his direction and the MITOVASC institute now represents one of the most important basic science and translational faculties for the University of Angers. The critical mass of the team provides a hub for clinicians who are actively encouraged (and funded) to join MITOVASC by the dean of the medical school and the president of the university. There is strong support from the chief executive officer of the university hospital.

There is a high degree of satisfaction from the staff throughout the unit with opportunities for retention of junior staff. The recent growth of the mitochondrial group is also a notable strength of MITOVASC. The group is now led by Mr Guy LENAERS and, compared with the vascular group (Group 2), is still in its infancy. However, there are substantial oversight structures in place with extensive institutional and national (CNRS/INSERM) funding and the proposed model for growth is ambitious yet realistic. The addition of the clinical groups from cardiology and intensive care provide novel avenues for cross-fertilisation between teams 1 and 2.

Weaknesses and threats in the context

Although the committee noted that the mitochondrial group is still in an early phase of development and establishment, there was a paucity of collaborative projects between the mitochondrial and vascular groups.

There was no specific strategy or pathway in place (or at least not outlined to the committee) for promotion of junior staff at post-doctoral level to attain independent principal investigator status within the institute.

Recommendations

Once the mitochondrial team has been given the chance to establish itself within the university, the MITOVASC uit (and institute) should pursue joint projects and initiatives between vascular and mitochondrial domains as the intersection of these two areas represents a particularly under-researched area within cardiovascular science.

Furthermore, it is very unlikely that the degree of expertise in mitochondrial and vascular research that is found in Angers will be replicated elsewhere, even internationally.

The MITOVASC unit is strongly recommended to pursue a growth agenda through applications to INSERM and the University of Angers for additional tenured positions, especially at junior levels.

The MITOVASC unit could consider a joint scientific advisory board for the institute rather than having one for the mitochondrial unit and one for the vascular unit.

Doctoral students and post-doctoral staff have requested more opportunities for networking amongst themselves in order to promote collaborations, such as funded monthly afternoon sessions.