Phy-Os - Sarcomes osseux et remodelage des tissus calcifiés

Rapport Hcéres

HCERES

High Council for the Evaluation of Research and Higher Education

Research units

HCERES report on research unit:

Bone sarcomas and bone remodeling of calcified tissues

Φ SOS

Under the supervision of the following institutionsand research bodies:

Université de Nantes

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]

Ms Laurence Vico, chairwomen 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:	Bone sarcomas and bone remodeling of calcified tissues
Unit acronym:	ϕSOS
Label requested:	UMR_S
Current number:	UMR_S 957
Name of Director (2015-2016):	Mr Dominique HEYMANN
Name of Project Leader (2017-2021):	Ms Françoise RÉDINI

Expert committee members

Chair:	Ms Laurence VICO, Lyon University, Saint-Étienne
Experts:	Ms Claudine BLIN, University Nice Sophia Antipolis (representative of the CSS INSERM)
	Mr Olivier PEYRUCHAUD, Lyon University
	Ms Katia SCOTLANDI, Rizzoli Orthopaedic Institute, Laboratory of Experimental Oncology, University of Bologna, Italy
Scientific delegate representing the HCERES:	
	Mr Jean GIRARD
Representatives of supervising institutions and bodies:	
	Mr Frédéric BENHAMOU, Nantes University
	Ms Marianne DESMEDT, INSERM
	Ms Meriem MAROUF-YORGOF, INSERM
	Ms Anne ROYER, CHU of Nantes
Head of Doctoral School:	Ms Corinne MIRAL, ED 34 Biology and Health

1 • Introduction

History and geographical location of the unit

The laboratory LPRO "Pathophysiology of bone resorption and Therapy of primary bone tumours" was created at Nantes University in 1999 and under the direction of Mr Dominique HEYMANN. In 2004, the team obtained its first university label as Équipe d'Accueil (EA 3822) and received the same year a recognition both by INSERM and by the "Région des Pays de la Loire" as an Équipe Région-INSERM (ERI7). The team begun with 11 permanent employees and rapidly grew up to 16 permanent employees in 2008. After the AERES evaluation in 2008, the laboratory became in January 2009 an INSERM unit: the UMR_S957 monothematic INSERM unit. In 2012, the unit label was renewed by INSERM and Nantes University. In addition, part of the unit was recognized as "Équipe Ligue Contre le cancer" for five years. At the end of the AERES evaluation, a re-organization in a multi-team unit was discussed. Then from 2012 to 2015, the team still expanded with 4 more researchers (1 INSERM) and 2 more technicians and engineers. Currently, the creation of a unit with three internal teams is proposed. Most of the researchers develop projects on physiology-pathology of bone sarcomas from the beginning, now with complementary approaches: team 1 is focused on bone sarcomas, targeting the tumour cells and their microenvironment (cells, signalling pathways) for new therapeutic strategies; team 2 is focused on the cellular communications in bone pathologies, mainly from tumour origin and in a bone inflammatory context; team 3 studies the genetic, epigenetic and cellular stress aspects of bone physiopathology, with a particular interest in bone sarcomas (but not only). The unit space (816 m^2) is located at the Medical School, close to the hospital [Nantes CHU and "Mère-Enfant" hospital]. This vicinity facilitates the interactions between basic and clinical research.

Management team

For the 2017-2021 period, the director will be Ms Françoise REDINI (INSERM DR2), helped by a co-director Mr François GOUIN (PUPH). The 3 teams are:

- team 1 "Microenvironment of primary bone tumours: Signalling and therapeutic targeting". Director: Ms Francoise REDINI (Inserm DR2) and co-dir. Mr Frank VERRECCHIA (Inserm DR1);

- team 2 "Inflammation and cellular communications in bone pathologies". Director: Mr Pierre LAYROLLE (Inserm DR1) and co-dir. Mr Frederic BLANCHARD (Inserm DR2);

- team 3 "EpiStress: Genetics, Epigenetic, and Cellular Stress". Director: Mr Benjamin ORY (MCU) and co-dir. Francois LAMOUREUX (INSERM CR2).

HCERES nomenclature

SVE1_LS4 Physiologie, physiopathologie, biologie systémique médicale

Scientific domains

The scientific domains are related first to the physiopathology of bone remodelling, mainly in the pathogenesis of primary bone tumours, and secondly to bone reconstructive surgeries based on mesenchymal stem cells. The unit covers basic research, pre clinical and clinical aspects in these fields. The unit proposed novel therapeutic strategies (pharmacological agents, metabolic pathways, epigenetic or stress proteins, cytokine-based therapies, siRNA approaches, immunotherapy).

Unit workforce

Unit workforce	Number on 30/06/2015	Number on 01/01/2017
N1: Permanent professors and similar positions	13	9
N2: Permanent researchers from Institutions and similar positions	13	12
N3: Other permanent staff (technicians and administrative personnel)	10	11
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	2	
N6: Other contractual staff (technicians and administrative personnel)	5	
N7: PhD students	11	
TOTAL N1 to N7	**54**	
Qualified research supervisors (HDR) or similar positions	18	

Unit record	From 01/01/2010 to 30/06/2015
PhD theses defended	26
Postdoctoral scientists having spent at least 12 months in the unit	9
Number of Research Supervisor Qualifications (HDR) obtained during the period	3

2 • Overall assessment of the unit

Introduction

The main area of the research unit is the understanding of the physiopathology of primary bone tumours at the molecular, cellular and tissue levels, with the aim of improving individual medical treatment. Despite the difficulties in attracting funding for such rare diseases, the group managed, through mechanistic approaches, to occupy a first place in the INSERM community. Thus, the Nantes research unit has undoubtedly reached during all these years a national and international recognition in the specific field of bone sarcomas comprehension and disease treatment. The other domain of high visibility is the healing of bone large defects supported by the FP7 REBORNE project.

At the last evaluation, the scientific quality was recognized. It was achieved through successful integration of basic and clinical objectives. It has also been achieved through good governance, dynamism and group cohesion. This great potential regularly grew during the last years and led to a restructuration from a single team unit to a multi-teams unit. Indeed, this unit has now reached a larger size as compared to the previous evaluation in 2011, so that the reorganization into three teams appears fully justified. This reorganization obeys a logical strategy with clearly defined scientific perimeters and thematic complementary.

Global assessment of the unit

The "Bone sarcomas and bone remodelling of calcified tissues" ("Φ SOS") Unit is a research unit historically and mainly devoted to research on the biology of bone sarcomas and, more recently, on bone healing processes. The overall scientific quality of Φ SOS is prominent both in qualitative and quantitative terms. The experts committee judges this Unit to rank within the top 10% of their respective areas of expertise worldwide. The dossier and the various aspects presented during the visit offer a highly coherent and dedicated research structure. Original and specific approaches and ideas guarantee the individuality of the unit. It is important to highlight the really translational research, from bench to bedside and vice versa. The unit is internationally respected (38 invited talks at international meetings) and leads one FP7 that also gave visibility on osseous defects regeneration.

The visibility of the senior scientists in the international research arena is high. The long-term viability of the unit seems to be well prepared, with a recent success to an INSERM competition and the recruitment of other new young researchers.

The 3 teams of this unit have published in journals with high impact factors (J Bone Miner Res, Cancer Res, Biomaterials, PNAS, Ann Rheum Dis, Nature Commun, J Clin Inv) and several important breakthroughs have been reported in cell signalling, epigenetic/genetic, cell interaction/communication, and preclinical models.

Strengths and opportunities in the context

Multidisciplinary approach linking clinicians (including surgeons) and scientists to capitalize on typical translational research.

The reorganization of the unit that has reached a greater critical mass, is naturally favouring synergies and interactions between teams.

Basic science represents an important research component: important breakthroughs in – for example - the characterization of tumour microenvironment and the therapeutic targeting of bone cells, cytokines and their signalling pathways, and in the identification of the role of JQ1 (BET bromodomains inhibitor protein capable of interfering with osteosarcoma development) that generated new hypotheses that may lead to clinical trials.

The unit has publications in the Top journals in their field (at least 1 or 2 per year).

The unit protects the discoveries, with 3 patents since 2012 (2 common to all teams, 1 in team 2).

The unit has a center of shared competences to optimize efficiency and sustainability.

The unit shows good attractiveness with substantial progression in the manpower.

The unit shows a very good integration into the local and regional landscape and has the support of the région Pays de la Loire and of the University of Nantes; the unit benefits from a significant involvement of the hospital.

Weaknesses and threats in the context

Although the experts committee does not have any worry and fully supports the choice of the new director, the departure of the present director, a leader who contributed to the team high visibility and international reputation, might represent a notable loss for the unit. Hopefully this loss might be balanced by a new collaboration with the future lab of Mr Dominique HEYMANN in Sheffield "Sarcoma Research Unit" [the recognition as a "European Associated Laboratory" label is requested from INSERM].

The field of study on bone remodelling of calcified tissues opens up to new pathologies. The experts committee alerts the unit on the importance of maintaining specificity versus other teams working on rheumatoid arthritis or on vascular calcifications.

Recommendations

Progression has been regular and impressive since the INSERM recognition; the team will have to keep pace, including for the funding!

The success and the increased volume of activity will likely require a more "formal" management in order to ensure scientific communication between the teams and to ensure internal communication within the teams so that the remarkable growth will not let anyone out.

The experts committee encourages the project of INSERM associated European Lab with Sheffield.

More postdocs should be recruited from abroad.

Considering the work force, the experts committee recommends to focus the research program in team 3.