CHELTER - Role of intra-clonal heterogeneity and leukemic environenment in therapy resistance of chronic leukemias

Rapport Hcéres

HCERES

High Council for the Evaluation of Research and Higher Education

Research units

HCERES report on research unit:

Role of intra-clonal heterogeneity and leukemic environment in therapy resistance of chronic leukemias

CHELTER

Under the supervision of the following institutions and research bodies:

Université Clermont d'Auvergne – UDA

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]

Mhairi COPLAND, chairwoman 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:	Role of intra-clonal heterogeneity and leukemic environment in therapy resistance of chronic leukemias
Unit acronym:	CHELTER
Label requested:	EA
Current number:	EA CREaT 7283
Name of Director (2015-2016):	Mr Pierre VERRELLE
Name of Project Leade (2017-2021):	Mr Marc BERGER

Expert committee members

Chair:	Ms Mhairi COPLAND, University of Glasgow, UK
Experts:	Ms Florence CYMBALISTA, Université Paris 13/AP-HP
	Mr Éric DELABESSE, Institut Universitaire de Cancérologie de Toulouse (representative of the CNU)
Scientific delegate representing the HCERES:	Mr Kamel BENLAGHA
Representatives of supervising institutions and bodies:	Mr Alain ESCHALIER, Université d'Auvergne
	Mr André SALAGNAC, Centre Hospitalier Universitaire Clermont-Ferrand
Head of Doctoral School:	Mr Jean-Marc LOBACCARO, Doctoral school N°65 « Sciences de la Vie, Santé, Agronomie, Environnement »

1 • Introduction

History and geographical location of the unit

The unit "Role of intraclonal heterogeneity and leukemic environment in therapy resistance of chronic leukemias" (CHELTER) is a re-structured research team issued from the haematology focussed research group of the previous unit "Cancer Resistance Exploring and Targeting" (CREaT). Re-structuring is taking place because the director of the current contract is relocating to the Curie Institute in Paris. The neuro-oncology research component of CREaT will join Imagerie MOleculaire et Strategies Theranostiques (IMOST). The re-structured unit, CHELTER will be established at the Clermond-Ferrand University Hospital (Estaing) in order to be close to the clinical units to which its members are attached and also to the technology platforms being used.

Management team

For the future contract, the management team is formed by Mr Marc BERGER as head of the unit and Mr Olivier TOURNILHAC as deputy head.

HCERES nomenclature

SVE1_LS6, SVE1_LS7

Scientific domains

The restructured unit CHELTER will focus on chronic leukaemias (Chronic lymphocytic leukaemias [CLL], chromic myeloid leukaemias [CML] and Waldenström Macroglobulinemia [WM]), domains in which they have substantial clinical expertise and collaborations. Key research techniques and resources available within the research group include FACS analysis, cell culture, confocal microscopy and biobanking.

Unit workforce

Unit workforce	Number on 30/06/2015	Number on 01/01/2017
N1: Permanent professors and similar positions	5	3
N2: Permanent researchers from Institutions and similar positions	6	
N3: Other permanent staff (technicians and administrative personnel)	1	4
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)	1	
N7: PhD students		
TOTAL N1 to N7	**13**	
Qualified research supervisors (HDR) or similar positions	7	

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

2 • Overall assessment of the unit

Introduction

The newly formed CHELTER unit takes forward the haematological components of the CREaT (EA7283) contract. The main scientific focus is on chronic leukaemias. Since the last evaluation report in 2011, the team has focussed on acquired chemotherapy resistance in chronic lymphocytic leukaemia (CLL). Moving forward, CHELTER plans to expand the area of research interest to include chronic myeloid leukaemia (CML) and Waldenstrom's macroglobulinanaemia (WM), focussing specifically on (i) intra-clonal heterogeneity, (ii) bone marrow microenvironment, and (iii) the leptin-NRP1/OBR axis in CLL and CML; and (iv) TCL1 in WM.

Global assessment of the unit

The group is small with no full time staff members and only 4.8 full time equivalent staff members. Despite very modest funding, the unit has presented extensively at both national and international conferences, has published in peer-reviewed journals and have had students complete PhD and MSc theses. Over the period, the most significant publication from the unit is a large collaborative study demonstrating that multiple recurrent mutations in CLL confer poor outcome.

The unit has strong and experienced leadership from the director and associate director, and is clearly very motivated to continue and expand their ongoing research. Because the unit is so small, it will be important for them to continue to establish collaborations, within their centre, and nationally and internationally. There is a concern that without this, they may not attain the critical mass required for successful research projects in the future. The unit has very good support from the University Hospital which they are affiliated to. Support from the University was more modest.

The panel had concerns regarding the research project presented for the next research contract period, both in terms of the scope of the project and the technical detail provided, as the proposed areas of research are extremely competitive with a number of large, well-funded groups in the same area. Due to the small size of the group and lack of a full time researcher/technician, it was felt that the plan of work may be too ambitious, and should be more focussed on one or two key research questions only.

Strengths and opportunities in the context

Researchers from the unit have contributed to more than 100 articles in international peer reviewed journals since 2010. This consists of 101 clinical and 10 research articles. There are also extensive publications in national peer-reviewed journals and national and international conference proceedings. The majority of these publications are collaborative projects.

There is evidence of extensive national and international collaborative activities. The future project leaders are well known in the French Clinical Networks. The collaborative work recently published in collaboration is of particular strength.

The unit has a clear focus on chronic leukaemias. The research team is well established and there is access to biobank samples from clinical trials with associated clinical data.

Ability of the team to train master degree and PhD students.

Weaknesses and threats in the context

Laboratory-based publications are limited, probably reflecting the small size of the unit and lack of any full time research staff.

There is a requirement for consolidation of collaborations, which are key to the success of this research group, regionally, nationally and internationally. There seems to be limited collaboration between the two threads (CML and CLL/WM) of the research proposal.

Due to the small size of the unit and its relative isolation, it may be difficult to recruit high calibre researchers.

The molecular biology and biomarker research field in chronic leukaemias is extremely competitive with many big groups using NGS technology, which has yet to be set up in this centre. It may be that this lab cannot be competitive in this arena.

Outreach activities are very limited, again reflecting the small size of the group. The unit needs to raise its new profile so that it is more visible to the university and that the local community are aware of it.

Due to the small size of the team, skills are limited. There is currently a lack of a researcher with expertise in molecular biology or bio-informatics. There are currently no full-time post-doctoral researchers in the group. For the proposed studies of the bone marrow microenvironment, access to animal models will be important to validate any results.

Funding is very limited, and there is currently no private or university funding.

Recommendations

This is a small clinical team undertaking both clinical and laboratory research with little support from or interaction with the university. The hospital has been very supportive to allow staff the time to generate research. The success of the unit is reliant of collaboration. The unit should continue to strengthen these productive collaborations. At this time, the unit has no private or university funding. The unit staff are encouraged to apply for university/private funding, and also to get more involved in the university life so that they are more visible to the senior academics and administrative staff there. Consideration should be given to setting up a website for the unit to raise its profile both locally and nationally/internationally.

For the laboratory-based scientific research and supervision of PhD students, there was insufficient group leader and post-doctoral researcher representation at the research laboratory. The research proposed was considered to be very ambitious, and the unit was encouraged to focus on fewer aims in order to achieve their publication goals. Their main strengths are biobanking and flow cytometry. The committee noticed a good atmosphere in the unit. For the PhD students a journal club leading to exchange of scientific information would be an important addition. Consideration should be given to this regular discussion being in English. As the unit is currently in the set up/re-organisation phase, the committee recommends frequent (~monthly) meetings among the group leaders and staff members in order to develop their research strategy fully and identify/apply for funding sources.