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## CTO - Ciblage thérapeutique en oncologie

Rapport Hcéres

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# HCERES

High Council for the Evaluation of Research  
and Higher Education

Research units

HCERES report on research unit:

Targeted Therapies in Oncology

Under the supervision of  
the following institutions  
and research bodies:

Université Claude Bernard Lyon 1 - UCB

Université Jean Monnet Saint-Étienne - UJM

Hospices Civils de Lyon

# HCERES

High Council for the Evaluation of Research  
and Higher Education

Research units

*In the name of HCERES,<sup>1</sup>*

Didier HOUSSIN, president

*In the name of the experts committee,<sup>2</sup>*

Marc REYMOND, chairman of the committee

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Under the decree N°2014-1365 dated 14 november 2014.

<sup>1</sup> The president of HCERES "countersigns the evaluation reports set up by the experts committees and signed by their chairman." (Article 8, paragraph 5)

<sup>2</sup> The evaluation reports "are signed by the chairman of the expert committee". (Article 11, paragraph 2)

## Evaluation report

This report is the result of the evaluation by the experts committee, the composition of which is specified below.  
The assessments contained herein are the expression of an independent and collegial deliberation of the committee.

Unit name:	Targeted Therapies in Oncology
Unit acronym:	
Label requested:	EA
Present no.:	EMR 3738
Name of Director (2014-2015):	Mr François-Noël GILLY
Name of Project Leader (2016-2020):	Mr François-Noël GILLY

## Expert committee members

Chair: Mr Marc REYMOND, University of Bochum and University of Magdeburg, Germany

Experts: Mr Vincent GREGOIRE, Université Catholique de Louvain, Belgium

Scientific delegate representing the HCERES:

Mr Jean ROSENBAUM

Representatives of the unit's supervising institutions and bodies:

Mr Germain GILLET, Université Claude Bernard Lyon 1

Mr Youcef OUERDANE, Université Jean Monnet Saint-Étienne

Ms Sylvie RICARD-BLUM (representative of the Doctoral School EDISS N° 205)

## 1 • Introduction

### History and geographical location of the unit

EMR 3738 was founded in 2003 in Lyon and is a mixed academic unit of Université Claude Bernard de Lyon (UBCL) and Université Jean Monnet St-Étienne. The unit is focused on clinical cancer research and includes three teams with the following specialties:

Team #1: surgery (cytoreductive surgery [CRS] and hyperthermic intraperitoneal chemotherapy [HIPEC]);

Team #2: chemotherapy (predictive pharmacology and early clinical trials);

Team #3: physical agents (radiotherapy);

Team 4 (hadron therapy) was part of EMR 3738 from 2006 to 2014. Since Team 4 leaves the unit at the end of 2014 it is not part of the present research evaluation.

### Management team

The head of the unit is Prof. François-Noël GILLY.

Team leaders are Prof. Olivier GLEHEN (Team #1), Prof. Gilles FREYER (Team #2) and Prof. Françoise MORNEX/ Prof. Olivier CHAPET (Team #3).

### HCERES nomenclature

SVE1\_LS7 Epidémiologie, santé publique, recherche clinique, technologies biomédicales

### Unit workforce

Unit workforce	Number as at 30/06/2014	Number as at 01/01/2016
<b>N1:</b> Permanent professors and similar positions (PU et MCU)	21	18
<b>N2:</b> Permanent researchers from Institutions and similar positions	1	
<b>N3:</b> Other permanent staff (without research duties)	6	6
<b>N4:</b> Other professors (Emeritus Professor, on-contract Professor, etc.) (PrAss)		
<b>N5:</b> Other researchers (PHU, PH) (Emeritus Research Director, Postdoctoral students, visitors, etc.)	10	9
<b>N6:</b> Other contractual staff (ARC, Biatss) (without research duties)	7	7
<b>TOTAL N1 to N6</b>	<b>45</b>	<b>40</b>

Unit workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	13	
Theses defended	17	
Postdoctoral students having spent at least 12 months in the unit (PHU)	3	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	23	20

## 2 • Overall assessment of the unit

### Global assessment of the unit

There have been a number of practice-changing advances in cancer surgery brought about by a small but active pool of French surgical researchers. EMR 3738 belongs to these researchers, and its national and international reputation is outstanding, in large part because of the lifetime achievement of François-Noël GILLY in peritoneal carcinomatosis and his leadership as the President of the UCBL since 2012.

The integration of a surgical team with complementary approaches (chemotherapy and radiotherapy) in clinical cancer research is a strong asset. Over the last research contract period, EMR 3738 has received major public and industrial research funding, and is rich of expertise and resources. Accordingly, the unit has produced significant knowledge and achievements. However, innovative character of research (paradigm changes, breakthrough research) has been decreasing over time, world-class publications are largely missing in the very last years. With 35 researchers, EMR 3738 has the critical mass (including expertise and financial resources) required for successful research projects in the future.

However, the project presented for the next research contract period has not the quality expected. In order to be successful, the research project for the next contract period (2016-2020) should be re-designed, in particular focused and prioritized. This is true for Teams #1 and #3, and to a lesser degree also for Team #2. An active reflexion on potential synergies within EMR 3738 and with external partners should be initiated in order to generate additional value. Preclinical research programs should be urgently implemented as a precondition for future early-phase clinical studies. Organizational management (in particular coordination between clinical and research tasks) and processes (time management) should be improved. Integration of EMR 3738 into a larger cancer research structure in Lyon South might be a strategic opportunity. Team #3 should be monitored with particular attention.

### Strengths and opportunities in relation to the context

Team #1 belongs to the leading groups in peritoneal cancer in France. Examples for this leadership are the National Reference Centre for rare tumors of the peritoneum, the National Reference Centre for trophoblastic tumors and large clinical databases such as the (BIG) RENAPE network for digestive tumors of the peritoneum. Team #2 has demonstrated superior expertise in theranostics based on body fluid biomarkers and mathematical modelization, and receives strong financial support from industry. This team received in 2010 the quality label for early-phase clinical studies (CLIP). Focusing on chemotherapy in the elderly patient is a valid strategic option.

Scientific output of both Teams #1 and #2 is significant; Team #2 has clearly increased this output over the last 2 years. Team #1 is well networked on international level, and has contributed to high-level publications within this framework.

A high number of doctoral students (Team #1, Team #2), training of external teams in France and abroad (Team #1, Team #3), participation to master programs (Team #1, Team #2), participation to collaborative projects

between universities demonstrate a clear commitment to teaching. The creation of a patient association (AMARAPE) raising research funding is remarkable.

### Weaknesses and threats related to the context

Team #1 is answering important clinical questions but the innovative nature of its research might be questioned. Lack of standards in several parameters such as disease definition, quality of surgery and tumor response assessment are and will remain intrinsic limitations of clinical research in peritoneal cancer. Randomized trials are exceptional in this research area, so that the level of evidence delivered (based mainly on registry studies) is not strong enough to compete with systemic chemotherapy studies. It is not even likely that comparative studies will deliver within the next 5 years the proof that hyperthermic intraperitoneal chemotherapy (HIPEC) has a significant effect on oncological outcome in addition to cytoreductive surgery alone, in particular for cancers with signet-ring histology and ovarian cancer. This represents a major threat for Team #1 in the medium-term and requires an alternative strategy for the next research contract.

Modeling disease evolution and therapy response using body fluid biomarkers is a valid and strong scientific project for Team #2. However, for these biomonitoring studies, Team #2 is essentially depending on sample and data collections provided by others. Against this framework, it appears critical that the number of collaborative publications with external partners is low and even decreasing over time. Team #2 has initiated a number of early-phase clinical trials since 2010 but these efforts resulted in very few publications so far.

For Team #1 & Team #2: Preclinical research in the lab or in the animal is not developed enough, although such models are obviously available (rabbit; rodent). The need for such experimental research is explicitly recognized by the head of EMR 3738 and the corresponding resources are locally available, but the scientific project 2016-2020 is not prioritizing such preclinical research at all. For such studies, the choice is to collaborate with external partners. This might be explained by time constraints (the routine clinical duties of most of the team members limit the availability for experimental tasks) and missing expertise, but this is not acceptable: generation of preclinical data is considered critical by the committee since toxicity studies in two animal models are a regulatory prerequisite for investigator-initiated early-phase clinical studies

Synergies between the 3 teams are claimed to be strong but this is not fact-based: only 8 common publications over the last 5 years (out of over 100 listed on PubMed) have been found by the committee (Team #1 with Team #2: 5; Team #1 with Team #3: 3). These figures (under 10 % joint publications) appear too low in an integrated research unit, with plenty of potential synergies.

Team #3 overall appears weaker in term of scientific output, and the publication focus is unclear for the auditors with over 50 publications “off field of research” during the period under observation. A striking observation is the lack of collaboration of Team #3 with other Teams of EMR 3738, in particular with Team #4, which appears a “natural” partner considering their field of expertise and their interest. The nature of this observation is irreversible as Team #4 will leave the unit EMR 3738 - a missed opportunity. The level of collaborations of Team #3 with external partners also appears to be low.

### Recommendations

The committee recognizes the major achievements of EMR 3738 obtained during the last contract period in patient care, research and education.

However, traditional answers should be reevaluated in the light of future challenges and the committee proposes the following comments and recommendations that might help the Chairman to better prepare EMR 3738 for the future:

- to renew his personal spirit and vision as the head of EMR 3738 for the last years of his exceptional career, in order to ensure the sustainability of this research unit. This transition will include scientific, organizational, financial and human resources decisions;

- to find ways to integrate EMR 3738 within existing regional cancer research structures, without losing the existing focus in clinical research. In particular, the criteria and process for selection of clinically relevant results from translational research programs should be defined;

- against this framework, to reshape and precise the research program 2016-2020, in particular by:

- proposing/selecting breakthrough research projects (new questions);

- exhausting potential synergies between research teams #1 to #3;
- refocusing and simplifying research activity on these projects;
- addressing and mastering methodological limitations of research in peritoneal cancer;
- to coach the Team leaders during the transition process (in particular Team #3).