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Biomarqueurs prédictifs et nouvelles stratégies moléculaires en thérapeutique anticancéreuse

Rapport Hcéres

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agence d'évaluation de la recherche
et de l'enseignement supérieur

Department for the evaluation of
research units

AERES report on interdisciplinary unit:
Predictive Biomarkers and New Therapeutic Strategies
in Oncology

Under the supervision of
the following institutions
and research bodies:

Université Paris-Sud

Institut National de la Santé et de la Recherche
Médicale – INSERM

Institut Gustave Roussy

January 2014



agence d'évaluation de la recherche
et de l'enseignement supérieur

Department for the evaluation of
research units

*On behalf of AERES, pursuant to the Decree
of 3 november 2006¹,*

- Mr. Didier HOUSSIN, president
- Mr. Pierre GLAUDES, head of the
evaluation of research units department

On behalf of the expert committee,

- Mr. Gilles FAVRE, chair of the committee

¹ The AERES President "signs [...], the evaluation reports, [...] countersigned for each department by the director concerned" (Article 9, paragraph 3 of the Decree n° 2006-1334 of 3 November 2006, as amended).



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:	Predictive Biomarkers and New Therapeutic Strategies in Oncology
Unit acronym:	
Label requested:	INSERM
Present no.:	INSERM U981
Name of Director (2013-2014):	Mr Fabrice ANDRE
Name of Project Leader (2015-2019):	Mr Fabrice ANDRE

Expert committee members

Chair:	Mr Gilles FAVRE, University of Toulouse
Experts:	Mr Charles DUMONTET, University of Lyon, France
	Mr Alex DUVAL, INSERM Hôpital St-Antoine, Paris
	Mr Jean-Jacques MAZERON, la Pitié-Salpêtrière, Paris
	Mr Pierre VERELLE, University of Clermont-Ferrand

Scientific delegates representing the AERES:

Mr Bernard DASTUGUE
Mr Jacques HAIECH



Representative(s) of the unit's supervising institutions and bodies:

Mr Christian AUCLAIR (Doctoral School n° 418 representative)

Mr Etienne AUGE, University of Paris 11

Ms Marie-Josèphe LEROY-ZAMIA, INSERM

Mr Eric SOLARY, Institute Gustave Roussy



1 • Introduction

History and geographical location of the unit

The INSERM Unit U981 was created by the fusion of several “un-labelled” teams working on translational research (breast, thorax, urogenital, gastro-intestinal). The proposal of this fusion of teams into a single unit was evaluated by AERES in 2008, the unit was created by IGR in 2009 and obtained the support of INSERM in January 2010 (“Equipe labellisée”). The groups constituting the unit which had previously been dispersed inside Institut Gustave Roussy, were then grouped together in 2009 on the 12th floor of the Institute in a laboratory with a surface of 500m², sharing the space with a translational research platform. In September 2013, the Unit moved to a new space with a surface of 1600 m², sharing with a translational research platform.

Management team

The project is presented by the former director.

The decisions related to the Unit are taken by the steering committee which includes each group leader and the representatives of technical staff and post-docs. The steering committee meets once a month. Communication is facilitated by the Unit's website. Staff and fund management is done primarily by the Director of Human Resources of IGR and by the Research Manager of IGR, with whom meetings are organized monthly. Part of funds and human resources is managed by INSERM.

AERES nomenclature

SVE1_LS2 Génétique, génomique, bioinformatique

SVE1_LS7 Epidémiologie, santé publique, recherche clinique, technologies biomédicales

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	5	5
N2: Permanent researchers from Institutions and similar positions	2	4
N3: Other permanent staff (without research duties)	17	18
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	1	
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	5	10
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	31	38



Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	10	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit*	5	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	8	11

2 • Overall assessment of the interdisciplinary unit

This is a strong team at the forefront of international research in translational research in oncology. The future project suggests that the international visibility and competitiveness of the group will be amplified in the future.

Strengths and opportunities related to the context

- Scientific strategy from bed to benchside;
- Excellence of the scientific production in top journals such as NEJM or Lancet Oncol, NSBM, J Clin Oncol;
- Funding secured for the next five years;
- Strong support from the Institute Gustave Roussy;
- Valorisation of the results into patents (16) and start-up companies (1);
- Access to effective core facilities at IGR, including biobanks, molecular biology, omics;
- Excellence of the collaborative networks in which they participate;
- Installation in a new building (1600 m² for the unit);
- Clinicians are key opinion leaders in their fields;
- Attractivity for basic science researchers (2CR, 1 DR only. The equilibrium with clinicians is not optimal);
- Ability to translate results from the lab to clinical trials (3 on going).

Weaknesses and threats related to the context

- Availability of bioinformaticians to reach the critical mass needed for efficient research;
- Limited administrative and technical support from academic establishments.

Recommendations

- Pursue a collective reflexion to control the flux of groups entering and leaving the unit;
- Continue the strategy to recruit new permanent basic scientists;
- Consolidate the representation of students in the steering committee;
- Set up a drug discovery strategy applied to their own targets.



3 • Detailed assessments

Assessment of scientific quality and outputs

The unit, which is dedicated to translational research, has succeeded in its “from bench to bedside” scientific strategy, bringing major contributions to oncology research that has been published in top journals. The unit has performed an exceptional task over the last 5 years at the cutting edge of research in cancer, including novel biomarkers in several types of tumors that could turn out to be not only highly predictive of response to standard therapeutic approaches but also druggable targets useful for discovery of new chemical compounds.

They discovered new pathways of resistance to therapy in Lung and Breast cancer and in melanoma. They developed new technologies allowing them to propose new therapeutic targets, new circulating molecular biomarkers and innovative bioinformatics algorithms for the modelling of drug sensitivity.

They have been productive scientifically, as evidenced by their list of impressive publications. They published 97 papers during the period 2009-2013. In particular, NEJM, Lancet Oncol, J Clin Oncol, Cancer discovery, NSMB, that have directly emerged from the lab can be highlighted. This is particularly impressive considering the number of investigators and the youth of the group.

This unit can be ranked as one of the best research groups in translational research in oncology in the world.

Assessment of the unit's academic reputation and appeal

The unit is well connected in the academic world as supported by the large number of published collaborations (> 40), the number of grants received, and the extensive network supporting the research efforts. Several clinicians are world leaders in their respective fields, particularly in breast and lung cancer and in melanoma. Many researchers of the team have been chairman of renowned international meetings such as AACR/NCI/ EORTC and IMPAKT and participate in the editorial board of international journals such as the Journal of Clinical Oncology. Part of their strength is that they co-supervise PhD students and post docs in world class laboratories allowing them to develop innovative concepts in translational research. The strength of these collaborations is shown by the production of 18 papers in journals with IF > 10 emphasizing the high relevance of the results they published.

Assessment of the unit's interaction with the social, economic and cultural environment

The unit is very efficient with regard to the interaction with the economic world. Not only does it hold a number of funded collaborations with industry but it also features the striking particularities of (i) issuing a large number of patents (16) including 3 which are exploited, (ii) favouring the spin-offing of young companies.

The interface between basic science and the clinics is also very efficient since 3 clinical trials directly coming from the laboratory results have been recently launched.

Lastly, they participated to numerous actions of scientific and medical knowledge diffusion in a very large diversity of media.

Assessment of the unit's organisation and life

One of the major virtues of the unit is the ability to amalgamate several single groups working on single primary models such as breast, Gastrointestinal, lung and other common primary cancers. They have been able to assemble all these different groups under a uniform program of research and the strategy they have developed exploits both the preclinical and biological knowledge as well as the clinical experience and the needs of cancer patients.

The unit is efficiently organized around medical questions, each driven by a couple of researchers comprising a scientist and a clinician. The coordination of the projects is achieved by a functional steering committee including research group leaders that create a lab life favouring the transdisciplinarity and the sharing of the results between the specific tumor types. The coordination between the clinic, basic sciences and the IGR core facilities is well organized and powerful. However, the director should direct his efforts towards the aim of maintaining this organisation in spite of the rapid growth of the unit.



Assessment of the unit's involvement in training through research

The unit has trained numerous PhD but one of their strengths is the training of young clinicians to translational research in oncology, in that they constitute a well-known and attractive center in France. The unit is linked to the ED418 École Doctorale de cancérologie de Paris 11 (director: Mr Christian AUCLAIR).

Assessment of the strategy and the five-year plan

The plan for the next 5 years is clearly described, it is strong and based on results previously obtained from the group but also develops new finding in the field of bioinformatics and the resistance to targeted therapy.

They aim to develop a rational program of research with several key branches based on some of cancer vulnerabilities such as DNA repair deficiency. Also, they are rapidly adapting the vast new knowledge of mechanisms of resistance to targeted therapies, also taking into account the complexities and challenges due to tumor heterogeneity. All these parallel programs have an ultimate aim of establishing new technical tools for diagnosis including circulating markers and new algorithms for use in daily clinical practice. The unit's approach is non-conformist since they are strongly committed to implement clinical trials based on this knowledge and this is one of their strengths. To this end they integrate into projects tumor samples, a choice of biomarkers and the necessary bioinformatic tools for further personalized treatment and drug discovery.

The programs they propose are well designed, original, competitive with a good feasibility although some parts of the projects are risky. They have perfectly integrated the clinical strength of the Institut Gustave Roussy, including, clinics, molecular biology, pathology and omics platforms. International collaborations are in place. It is also a very good point for this unit to have secured funding for the next five years.



4 • Conduct of the visit

Visit date:

Start: January 22 2014 at 8.30 AM

End: January 22 2014 at 6 PM

Visit site:

Institution: Institut Gustave Roussy

Address: Gustave Roussy
114, rue Edouard-Vaillant
94805 Villejuif Cedex

Conduct or programme of visit:

8h15-8h30	Private meeting (Committee and Scientific Delegate)
8h30-8h45	Introduction (Scientific Delegate) and committee presentation
9h-10h15	Scientific talks and discussions
9h15-10h15	Coffee break
10h15- 12h	Meeting (in the absence of the head of the unit) with: <ul style="list-style-type: none">- Scientists and Professors- PhD students and post-docs- Engineers, technicians and administrative staff- Head of the Doctoral School
12h-12h30	Meeting with the head of the unit
12h30-13h15	Lunch
13h30 - 16h	Private meeting and preparation of the report

Specific points to be mentioned

The expert Mr Rafael ROSELL, Institute of Oncology, Barcelona, Spain was absent during the visit.



5 • Supervising bodies' general comments

Le Président de l'Université Paris-Sud

à

Monsieur Pierre GLAUDES
Directeur de la section des unités de recherche
AERES
20, rue Vivienne
75002 Paris

Orsay, le 26 mai 2014

N/Réf. : 138/14/JB/LM/AL

Objet : Rapport d'évaluation d'unité de recherche
N° S2PUR150007977

Monsieur le Directeur,

Vous m'avez transmis le 24 avril dernier, le rapport d'évaluation de l'unité de recherche « BIOMARQUEURS PRÉDICTEURS ET NOUVELLES STRATÉGIES MOLÉCULAIRES EN THÉRAPEUTIQUE ANTICANCÉREUSE » N° S2PUR150007977, et je vous en remercie.

L'université se réjouit de l'excellente appréciation portée par le Comité sur cette unité et prend bonne note de ses suggestions.

Monsieur Fabrice ANDRE, Directeur de l'unité de recherche, n'a pas souhaité apporter de commentaires.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de ma sincère considération.



Jacques BITTOUN
Bâ
Président
91405 ORSAY cedex