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CART - Carcinose angiogénèse et recherche translationnelle

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 unit:

Carcinose Angiogenèse et Recherche Translationnelle
CART

Under the supervision of
the following institutions
and research bodies:

Université Paris 7-Denis Diderot

Institut National de la Santé Et de la Recherche
Médicale





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

Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head

Pierre Glaudes



Grading

Once the visits for the 2012-2013 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).

This score (A+, A, B, C) concerned each of the six criteria defined by the AERES.

NN (not-scored) attached to a criteria indicate that this one was not applicable to the particular case of this research unit or this team.

Criterion 1 - C1 : Scientific outputs and quality ;

Criterion 2 - C2 : Academic reputation and appeal ;

Criterion 3 - C3 : Interactions with the social, economic and cultural environment ;

Criterion 4 - C4 : Organisation and life of the institution (or of the team) ;

Criterion 5 - C5 : Involvement in training through research ;

Criterion 6 - C6 : Strategy and five-year plan.

With respect to this score, the research unit concerned by this report received the following grades:

- Grading table of the unit: **Carcinose Angiogenèse et Recherche Translationnelle**

C1	C2	C3	C4	C5	C6
A	A	A	A+	A	A



Evaluation report

Unit name:	CARCINOSE Angiogenèse et Recherche Translationnelle
Unit acronym:	CART
Label requested:	UMR_S
Present no.:	UMR_S 965
Name of Director (2012-2013):	Mr Marc POCARD
Name of Project Leader (2014-2018):	Mr Marc POCARD

Expert committee members

Chair:	Mr Jean-Jacques FEIGE, University of Grenoble
Experts:	Mr Habib BOUKERCHE, University of Lyon 1 (Representative of the INSERM) Ms Muriel MATHONNET, University of Limoges (Representative of the CNU) Mr Curzio RÜEGG, University of Fribourg, Switzerland Mr Fabrice SONCIN, University of Lille

Scientific delegate representing the AERES:

Mr Jean ROSENBAUM

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

Ms Christine CLERICI, University Paris Diderot

Ms Marie-Josèphe LEROY-ZAMIA, INSERM



1 • Introduction

History and geographical location of the unit:

The CART Unit is located at the Hôpital Lariboisière (Paris, 10ème) in a building which it shares with INSERM Unit 606 (Ms Marie Christine DE VERNEJOU) and with IVS (Institut des Vaisseaux et du Sang, a private research foundation). It occupies 490 m2 and shares some facilities and lab space with IVS. The 4 scientists members of IVS are active participants to the CART project.

The CART Unit is issued from the INSERM Unit 965 that was already directed by Mr Marc POCARD (the proposed Director of the CART Unit). The INSERM Unit 965 was created in January 2009 with the aim to federate several research teams working in the field of angiogenesis: IVS, directed at that time by Mr Gérard TOBELEM; several clinicians from the Digestive Surgery Unit; a world specialist in fundamental angiogenesis research (Mr Jean PLOUET, CNRS researcher, one of the discoverers of VEGF); a start-up company created by Mr Jean PLOUET which wanted to develop Nov- and Netrin4-derived anti-angiogenic drugs; and a few other scientists. Three major and dramatic events affected the first years of life of Unit 965. Firstly, in December 2008, Mr Jean PLOUET suddenly died. Secondly, in 2009, Mr Jean-Michel TOBELEM unexpectedly left IVS to take charge of the Etablissement Français du Sang. Thirdly, the start-up company decided to quit Hôpital Lariboisière and the INSERM Unit 965. Despite these destabilizing events, Mr Marc POCARD succeeded at keeping the Unit alive and driving the remaining members of the Unit towards a common goal, a research of excellence in angiogenesis and at producing a respectable number of high-quality research articles in this field.

Management team:

The CART Unit will be directed by Mr Marc POCARD, a Professor at University Paris 7 and a gastro-enterological surgeon in duty at Hôpital Lariboisière.

AERES nomenclature

SVE1-LS7

Unit workforce:

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	4	5	5
N2: Permanent researchers from Institutions and similar positions	1	2	
N3: Other permanent staff (without research duties)	2	3	
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	2	3	1
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	2	4	2
N6: Other contractual staff (without research duties)	4	5	5
TOTAL N1 to N6	15	22	13

Percentage of producers	80%
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Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	10	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit*	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	8	10



2 • Assessment of the unit

Strengths and opportunities:

The CART Unit has chosen to center its research activities on the study of peritoneal carcinosis, including rare forms of peritoneum-derived cancers named peritoneal pseudo-myxomas (PMP) and the much more frequently observed peritoneal metastases of solid cancers from diverse origins. Despite the recent progress brought by the HIPEC (Hyperthermic Intraperitoneal ChemoTherapy) therapeutic method for the treatment of peritoneal carcinosis, strong improvements are still required and the fundamental mechanisms that drive metastatic cancer cells to home in this specific niche are still to be discovered. The clinical Unit of Mr POCARD at Hôpital Lariboisière is an active member of the National Reference Center for Peritoneal Carcinoses (RENAPE network) and is thereby extremely well positioned for developing a performant translational research on this pathology. It should be noted that very little experimental and translational research are conducted worldwide in this pathology despite its high and growing clinical relevance. Likewise, very few research teams in France are active in studying this condition.

The historical record of high quality angiogenesis research in INSERM Unit 965 and the presence of many lab members from this Unit in the CART project are considered as determinant strengths to study anti-angiogenic therapies as alternatives or as complements to surgery and HIPEC for the treatment of the patients with both primary and secondary peritoneal carcinoses.

The capacity of Mr Marc POCARD to convince several INSERM/CNRS researchers from other Parisian labs to join and study the fundamental mechanisms of peritoneal carcinosis is a good indicator of the attractiveness of the project, of the dynamism of its Director and an important point for setting up an efficient and competitive research team with enough full-time researchers for properly supervising the students.

The Director (Mr Marc POCARD) shows a strong charisma and has set up a nice atmosphere of friendly scientific interaction within his team which is very important for keeping the motivation of the lab members high.

Weaknesses and threats:

The number of full time researchers will be reduced after 2014 due to the retirement of two of them. There is a real need to increase the number of permanent positions to stabilise and possibly bring in further specific know-how of the lab and the capacity to efficiently supervise the students.

The number of projects appears too important relative to the task force of the lab. The most promising hypotheses to be tested should be prioritized and the less competitive ones should be abandoned in order to favor the most competitive and productive projects.

Recommendations:

Besides the translational research on peritoneal carcinosis for which the lab seems to be well prepared, there is a need to develop a more fundamental research on the mechanisms of the disease. This will help to identify new molecular targets and thereby new therapeutic treatments.

Set up an active policy for recruiting new INSERM/CNRS researchers who will help to develop fundamental research on the mechanisms of the disease.

Make priority lists and choices about the numerous projects in order to support the most promising ones with more human resources.



3 • Detailed assessments

Assessment of scientific quality and outputs:

The scientific production of U965 was excellent with 70 publications over the 4-year period (2009-2012), including 18 fundamental publications with a lab member in first or last author position, 24 publications resulting from collaborations and 29 publications resulting from clinical studies. Among the 18 publications of the lab: 2 Am J. Pathol (2010, 2011), 1 J. Hepatol (2011), 1 JCI (2012, in press), 1 Diabetes (2012). Among the collaborative publications, 1 Cell paper from the group of Peter CARMELIET, a world leader in the field of angiogenesis, who solicited U965 for testing anti-PIGF antibodies on its transgenic mouse model of hepatocarcinoma. Among the clinical publication, a remarkable paper in JCO signed by Marc POCARD proposing a new concept for phase 0 clinical assays in oncology with patients undergoing surgery for metastatic disease. This paper, which was cited as "article of the month", is a breakthrough in the design of clinical assays for new antitumoral drugs. U965 also patented the analysis of circulating microparticles for the prognosis of cancer.

Assessment of the unit's academic reputation and appeal:

Mr Marc POCARD is a nationally recognized expert in peritoneal carcinoses and more largely in visceral surgery. As a Director of the CART project, he has been able to attract several INSERM/CNRS researchers to come and work with him on this project. He also convinced one person sponsored by Fondation Rotschild and one person paid by the STAGO company to work in his lab. His collaboration with Mr Peter CARMELIET (Louvain, Belgium), a recognized leader in the field of angiogenesis, is also a proof of the recognized expertise of his lab concerning the mouse models of cancers. Also, two foreign MD (from Russia and from Italy) prepare a thesis in his lab. This effort should be pursued to attract also foreign post-doctoral fellows.

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

The expertise of the lab in the generation of animal models of human cancers has been valorized through a collaborative contract with Roche Pharma. This effort is pursued with the help of Inserm-Transfert. Other industrial partnerships have been signed with Sanofi and Servier.

The research on PMP is sponsored by an American Association named N.O.R.D.

The research on peritoneal carcinoses is sponsored by the National Center of Expertise RENAPE

In 2012, Mr Marc POCARD is organizing an International Clinical Meeting on Peritoneal Carcinoses in Paris with a first-ever pre-meeting about the basic research on this disease. This will certainly help his team to increase its international visibility and recognition on this topic.

Assessment of the unit's organisation and life:

The atmosphere in U965 appears excellent. The students and the technical staff said they were extremely satisfied by the attention brought to them by Mr Marc POCARD and the other PhD mentors. However, the number of researchers holding an HDR (Habilitation à Diriger les Recherches) should be increased in order to allow a larger panel of PhD mentors to take care of the students. Several researchers appear to have the experience and the publication record required to obtain this habilitation.

The animal facility is a laboratory platform run by a single technician who appears to be happy and very proud to assume this important responsibility. Although this seems to work fine (during vacation time of this technician, a student from a school of zootechnicians is hired), it appears as a fragile situation that should be consolidated since the animal tumor models represent the heart of the CART project.

The Unit runs weekly seminars that are well attended.

INSERM and University Paris Diderot have set up a mutualized administrative platform that allows a total delegation of funding management by INSERM. This seems to work well and to greatly simplify the practical life of the secretary of the lab.



Assessment of the unit's involvement in training through research:

What is remarkable in this Unit is the large proportion of MDs among the M2 and PhD students. Presently, out of 5 M2 and 7 PhDs, 7 are MDs from different specialties (4 from Visceral Surgery, 2 from Radiology, 1 from Neurosurgery). Mr Marc POCARD, who manages the option Cancerology in the Master "Surgical Science" at University Paris 11-12, does an excellent job by attracting these young surgeons and radiologists towards research. Reciprocally, the CART Unit greatly benefits from the delicate experimental expertise of these students.

In 2012, Mr Marc POCARD is organizing an International Clinical Meeting on Peritoneal Carcinomas in Paris with a one-day pre-meeting on basic research. This typically shows the strong will of Mr Pocard to bring together the expertises of clinicians and basic scientists in order to address patient-oriented scientific challenges.

Assessment of the five-year plan and strategy:

The research interests of the previous INSERM Unit 965 were centered on angiogenesis. Due to several unexpected events mentioned above, the task force of leader researchers on this field was suddenly reduced. The wish of Mr Marc POCARD to focus the new CART project on the study of peritoneal carcinomas thus appears as a very positive reorientation that takes into account the expertise of the numerous clinicians who actively participate in the project (12 University-Hospital clinicians participate in the project, 7 PhD students are MDs) and the strong link with the Center of Reference on Carcinomas headed by Mr POCARD at the Hospital Lariboisière. The committee strongly supports this very judicious choice. The visiting committee was impressed by the quality of the animal models established in the lab that closely mimic the clinical situation. The visiting committee is convinced that this team will be able to develop an innovative translational research and bring up new technical and therapeutic solutions for the treatment of patients with carcinomas. The committee also thinks that the basic research on the fundamental mechanisms of this disease should represent an equally important priority of the CART project. The arrival of two scientists from the Centre des Cordeliers will allow to investigate mechanistic hypotheses about the role of Hospicells and of the apoptotic pathway. This effort to "understand" the pathology should be further developed, possibly by recruiting new experimental investigators, as it will help to feed the pipeline of therapeutic innovations.

Besides these carcinoma-centered researches, some ancillary projects address cerebral angiogenesis and post-ischemic revascularization. They result from the the previous focus of interest of U965 on angiogenesis. These projects will be important in generating new data on basic aspects of angiogenesis relevant to the central CART project and, on the long term (next 5-year contract), these research themes may nicely complement those developed by teams that will join the future Centre de Recherche Lariboisière.



4 • Conduct of the visit

Visit date:

Start: Friday, December 8, 2012, at 9h30
End: Friday, December 8, 2012, at 17h30

Visit site: Paris

Institution: Hopital Lariboisiere,

Address: Paris

Conduct or programme of visit:

- 9h30 -10h00 : Huis clos - Présentation de l'AERES au comité par le Délégué
10h00 -10h15 : Devant l'unité, présentation du Comité de visite et Présentation de l'AERES par le Délégué
10h15-11h45 : Présentation de l'unité, bilan et projet, incluant les questions (Mr Marc POCARD)
11h45-12h15 : Rencontre avec les représentants de la Tutelle:
Auditoire : membres du Comité, Délégué AERES

12h15-13h : *Déjeuner*

SESSION RENCONTRE AVEC LE PERSONNEL PERMANENT ET NON PERMANENT

Le comité se répartit en trois sous-groupes

- 13h -13h30 : Rencontre avec les ITA titulaires, CDD
Auditoire : membres du Comité, Délégué AERES, sans les Tutelles, ni la Direction

Rencontre avec les doctorants et post-doctorants et/ou CDD « chercheurs », Ingénieurs
Auditoire : membres du Comité, Délégué AERES, sans les Tutelles, ni la Direction

Rencontre avec les chercheurs et enseignants chercheurs titulaires.
Auditoire : membres du Comité, Délégué AERES, sans les Tutelles, ni la Direction, ni les responsables d'Equipes

13h30-13h45 : Rencontre avec la direction de l'unité
Auditoire : membres du Comité, Délégué AERES

13h45-15h45 : Réunion du comité à huis clos
Présence : membres du Comité, délégué AERES



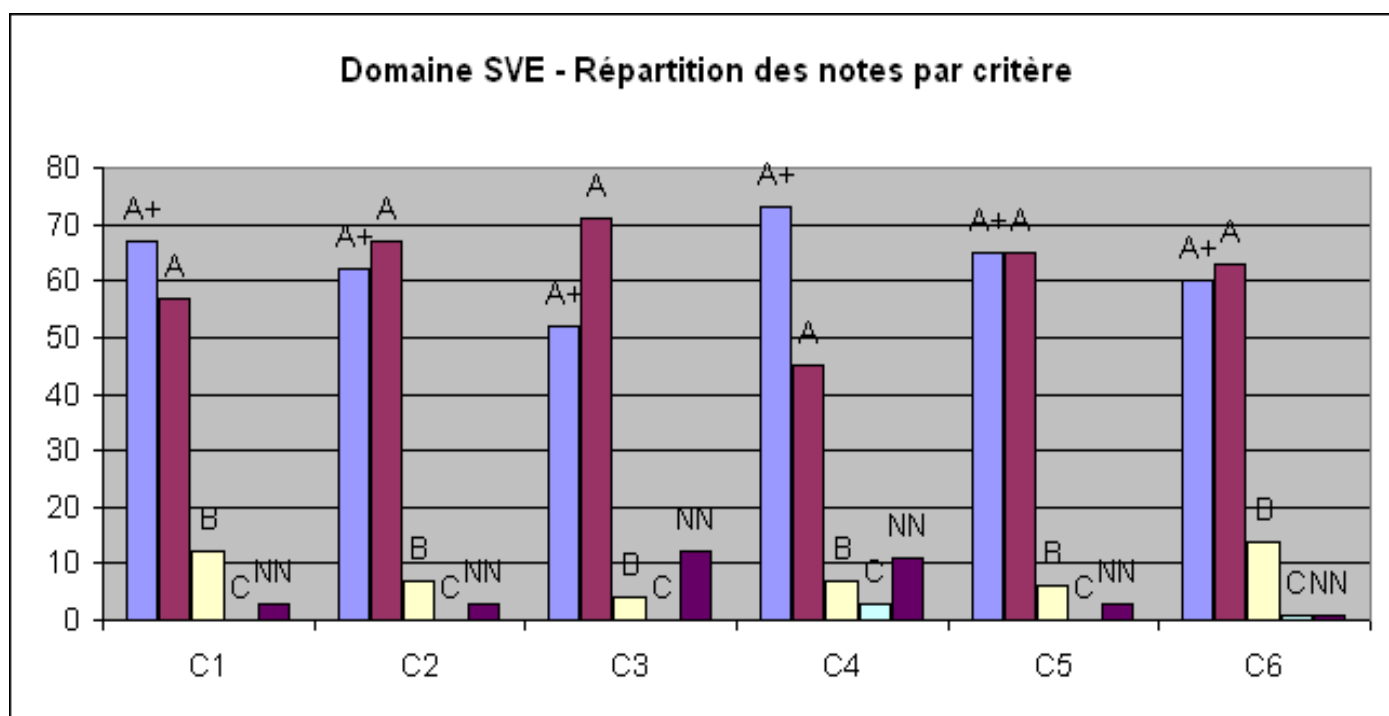
5 • Statistics by field: SVE au 10/06/2013

Notes

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	67	62	52	73	65	60
A	57	67	71	45	65	63
B	12	7	4	7	6	14
C	0	0	0	3	0	1
Non Noté	3	3	12	11	3	1

Pourcentages

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	48%	45%	37%	53%	47%	43%
A	41%	48%	51%	32%	47%	45%
B	9%	5%	3%	5%	4%	10%
C	0%	0%	0%	2%	0%	1%
Non Noté	2%	2%	9%	8%	2%	1%





6 • Supervising bodies' general comments

Le Président

P/VB/NC/YM – 2013 - 045

Paris, le 20 mars 2013

M. Pierre Glaudes
Directeur de la section des unités de l'AERES
20 rue Vivienne
75002 PARIS

Laboratoire « Carcinose Angiogénèse et recherche Translationnelle - CART »

Monsieur le Directeur,

Je tiens, en premier lieu, à remercier les membres du comité de visite de l'AERES pour la production du rapport sur l'unité « Carcinose Angiogénèse et recherche Translationnelle - CART ».

Je me réjouis des appréciations très élogieuses qui sont portées sur ce laboratoire dont vous avez en particulier souligné l'excellente qualité des publications et l'aspect extrêmement innovant de ses recherches dans le contexte national.

Le comité souligne que malgré la jeunesse de ce laboratoire et des événements qui auraient pu fragiliser la structure, l'équipe dirigée par Marc Pocard a remarquablement su maintenir son niveau de recherche et développer son projet collectivement, permettant d'attirer des chercheurs.e.s d'autres laboratoires. Dans ce cadre, l'université continuera d'apporter un fort soutien pour, à la mesure de ses moyens, conforter ce laboratoire et l'association avec l'INSERM.

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

Vincent Berger



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**ANGIOGENESE ET
RECHERCHE TRANSLATIONNELLE
Unité 965
Directeur : Pr. Marc Pocard**

Instituts
thématiques



Inserm

Institut national
de la santé et de la recherche médicale

Paris le 18 mars 13

Madame, Monsieur,

Je soussigné Pr Marc Pocard, directeur de l'unité 965 déclare n'avoir aucune remarque ou observation d'ordre générale à formuler sur l'observation AERES du projet CART et accepte l'ensemble des remarques positives ou négatives formulées dans ce rapport.

Très cordialement,

Marc Pocard