Cancer et transplantation : physiopathologie et réponse thérapeutique

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Cancer et Transplantation: physiopathologie et réponse thérapeutique

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

January 2013

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

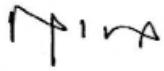
Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head



Pierre Glaudes

The president of AERES "signs[...], the evaluation reports, [...]countersigned for each evaluation department by the relevant head of department (Article 9, paragraph 3, of french decree n°2006-1334 dated 3 november 2006, revised).

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: Cancer et Transplantation: physiopathologie et réponse thérapeutique

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

Evaluation report

Unit name:	Cancer et Transplantation: physiopathologie et réponse thérapeutique
Unit acronym:	
Label requested:	UMR-S
Present no.:	UMR-S 728
Name of Director (2012-2013):	Ms Anne JANIN
Name of Project Leader (2014-2018):	Ms Anne JANIN

Expert committee members

Chair:	Mr Charles THEILLET, University of Montpellier
Experts:	Mr Christophe BORG, University of Franche Comté
	Mr Bruno CLÉMENT, University of Rennes
	Mr Jean-Jacques FOURNIÉ, University Paul Sabatier,Toulouse
	Mr Barry GUSTERSON, University of Glasgow UK
	Ms Laurence LAMANT, University Paul Sabatier, Toulouse

Scientific delegate representing the AERES:

Mr Daniel OLIVE

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

Ms Corinne ALBERTI, Université Paris 7

Ms Marie-Josèphe LEROY-ZAMIA, INSERM

1 • Introduction

History and geographical location of the unit :

The INSERM unit 728 was created in 2005, in continuation of a university Paris 7 structure. The laboratory is part of the Institut Universitaire d'Hématologie (IUH, Université Paris 7) within the University Hospital St Louis in Paris, which has a long time history in haematological malignancies, both at the clinical and research level. Originally the creation of an INSERM team, initially devoted to technological developments in histopathology (ERM 0220) was an initiative of Ms Anne JANIN within the laboratory of Pathology at the Hospital St Louis. The creation of the unit extended and validated the long time effort of Ms Anne JANIN in setting up the central tumor bank at Hospital St Louis. UMR 728 integrated specific research themes on GVH associated tumors and response of cancer to anti-angiogenic treatment. While in the early times the unit was dispersed in 3 locations in adjacent buildings, it has recently been regrouped in a single location within the renovated portion of the IUH. It is also mentioned in the report, with no further detail on the administrative status nor description of the facility and staff involved, that the team of Mr RAYMOND at the Hospital Beaujon in Clichy is associated with the Unit. Hence, UMR-S 728 associates several teams on separate locations over 5 kms apart.

Management team:

The unit is directed by Ms Anne JANIN. No detail given on the persons or group of persons assisting her in the management. No management structure (Codir, CoLab, SAB) is specified.

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	18	18	?
N2: Permanent researchers from Institutions and similar positions	3	3	
N3: Other permanent staff (without research duties)			
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)			
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	Post-docs 4		
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	**25**	**21**	

Percentage of producers	*100%*

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	6	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit*	4	
Number of Research Supervisor Qualifications (HDR) taken	17	
Qualified research supervisors (with an HDR) or similar positions	17	

2 • Assessment of the unit

Strengths and opportunities:

- Dedicated and energetic director with an internationally recognized expertise in pathology,

- Central position in the provision of biological resources facilities at the Hospital St Louis,

- Strong links with the clinical pathology and other clinical platforms (mainly imaging),

- Location within a strong site and ties with the Institute of Haematology (IUH) with excellent clinicians and scientists,

- Easily accessible high level core facilities at IUH,

- Good links with the industry,

- Strong ties with a cognate laboratory at the Shanghai University-Hospital, which it helped to establish,

- Large staff resources,

- A transdisciplinary approach of cancer covering biomarkers, drug targets, imaging and clinical response,

- Strong history in pathology based technological developments,

- Link with clinical oncologists,

- Remarkable input in setting up training program,

- An interesting preclinical program combining xenografts and serial fine needle aspirates to assess response to treatment,

- Collaboration with chemists and physicists on nanoparticles,

- Multidisciplinary environment of PhD/MD students and post-docs from diverse clinical and non-clinical disciplines.

Weaknesses and threats:

At the organizational level:

- Neither a clearly defined strategy nor any identified priority for the coming 5 years,
- No identified program/project with allocation of human resources and technological support,
- No PI identified with responsibilities in the lab,
- No budget allocation plans,
- No emerging young investigator singled out,
- Difficult to assess/ role and contribution of most of the University-Hospital staff.

At the scientific level:

- Most (more than half) of the publications in which the Unit has a lead role correspond to work on GvH by a scientist who has left the unit and it was understood that the GvH theme was going to an end in the unit. The programmed termination of this leading theme opens questions concerning future developments.
- The strategy concerning the improvement of anti-angiogenic treatments was not clearly defined and no associated resources justified.
- The nanoparticles project requires strong scientific support and long-term resources to achieve its goals at the clinical settings.

Recommendations:

- Need to build a management team which include PIs,

- Need to define a strategy, identify priorities and reduce the number of themes for the coming 3 to 5 years and focus resources accordingly,

- Formalize the position of and the projects developed by the scientists in the lab besides the team leader.

3 • Detailed assessments

Assessment of scientific quality and outputs:

Over the period 2007-2012 300 papers and review articles have been authored or co-authored by members of the unit, of which 120 published in journals with IF>5. However, 34/300 have members of the Lab as first or senior authors and were therefore actually produced by the unit 728. Most high impact publications (JCO or NEJM) have been published by one co-author among a relatively large list of clinically collaborating groups. Hence, the scientific output of the unit is judged as fair for a unit of that size.

Assessment of the unit's academic reputation and appeal:

Ms Anne JANIN is an energetic leader, whose action has led her to work with international working groups on biobanking. In addition she has set up an active and long standing cooperation with the University and Hospital of Shanghaï, Jiao Tong University. The strong links that have been established with Shanghai and have persisted since are a clear sign of appeal at the international level. The lab has trained a number of chinese PhD and MD students that have since obtained position and started a carrier in Shanghai.

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

The unit has been active on the valorisation side having filed several patents, some of them being licenced. CIFRE contracts and ongoing contracts with industrial partners. The development of virtual slides and micro-dissection programs and their dissemination is to be noted. Furthermore, several members of the unit, including the director, have participated to radioshows on science or medical matters.

Assessment of the unit's organisation and life:

The unit is presented as a single team/single theme (mono-équipe/mon-thématique) and it is an apparent will of the director to keep this organizational model for the next period. The report's structure does not make mention of specified themes nor of identified groups. However, it was apparent that several projects are developed in the unit, with no clear mention of the PI in charge and the human resources or budget allocated to it. Some points were clarified during the visit allowing to identify two broad research lines, (1) Cancer in transplanted patients, (2) Response to therapy. But globally the scientific management did not appear to follow predefined directions, and the unit's formal organisation should be clearly defined on the basis of the scientific projects.

A- Cancer in transplanted patients

This theme was central to the previous term and has made the reputation of the unit. Investigators contributed to the characterization of TH17 infiltrates in GvH target organs in humans. The team also contributed to the demonstration of the presence of cells of donor's origin in epithelial cancers occuring in recipients of allogenic hematopoietic cell transplantation. The unit has shown that tumors which occur secondary to tissue allograft comprised cells contributed by the graft resulting in chimeric tumors. This work was very largely contributed by a scientist who has left the unit in 2012, putting future developments on this line of research in question. It was not clear whether or not this line would be continued and who was in charge. A further point of concern was the overall lack of in vivo or in vitro models. Most results are description of phenotype or genotyping. If this line of research were to be continued it would be recommended to acquire expertise in the field of pathological assessment of immune cell infiltrates.

B- Response to therapy

This theme covers a rather diverse range of projects with different PIs in charge and different approaches.

1- Lymphoma. The scientist in charge has an outstanding track record at both the clinical and research level (52 publications on lymphoma therapy topic since 2007, including high IF papers, NEJM, Lancet, JCO, Blood…). She investigates agressive B cell lymphomas with cerebral relapse and aims at improving the therapeutic response. This theme deals more specifically with MCL and Myc positive DLBCL and plans to perform combined transcriptome analysis and PET scan imaging. This project is said to involve both clinicians and researchers with no further detail on the personnel (technicians, docs or post docs) nor funds allocated to it. Links with the associate international laboratory of Shanghai Hematology Institute were mentioned with 4 shared PhD students (2 and 2) by both groups within 5 years. This collaboration produced 10 publications since 2007, none with the PI heading this program. Plans are to continue gene expression profilings with human samples and murine models, in search for genes associated with therapeutic response (such as PRDM1 & resp to anti CD20 (RTX) and to bortezomib). It was regretted that this high quality program has no identified staff, team and funding, at least from what the panel understood. Precise delineation of structures, roles, and means involved by the unit on the lymphoma research project should be considered in order to give this project the position it deserves according to its very good publication record.

2- Projects in the field of clinical oncology. These projects are under the responsibility of a clinical oncologist acting at the Hospital Beaujon in Clichy. Original plans were that he would join Hosp St Louis as Chief of Medical Oncology, explaining why he joined the unit. Things went differently but links remained. This scientist has a good track record and has contributed to good papers (NEJM, Clin Cancer Res). His work has allowed to validate the administration of sunitinib (anti-angiogenic) and mTOR inhibitors in the treatment of chemoresistant renal and digestive track cancer. This clinical research activity is associated to biomarkers studies that are being developed within a laboratory (pharmacobiologie des anticancéreux, Hopital Beaujon). Aims of these studies are focused on EMT and its effector or inducing factors. Besides the preclinical assessment of new therapeutic compounds, no hypothesis or perspective were clearly defined in the written report or during the meeting. Of note, the scientist in charge has created a small company which valorizes some of these studies and subcontracts with pharmas. It was felt that care should be taken to draw the exact line of divide between the academic and commercial activities. Globally, the dynamism and the quality of the production of this scientist was positively acknowledged. It would certainly gain from a better definition of objectives and priorities, both at the level of the project per se and for what concerns its interrelations with the rest of the unit.

3- Protein-protein interactions linked to apoptosis. **These projects are under the responsibility of a scientist that** has just joined the unit coming from the UMR 940 located at the IGM, rue Juliette Dodu, Paris. He originally joined the UMR940 as a Avenir young investigator and developed a project on protein-protein interactions linked to apoptosis. His objective is to identify small molecules that would disrupt these interactions. He has a good track record in his field. His project was presented on a poster (out of 15 of diverse impact), thus, the committee could not evaluate its potential in depth. It seems, however, that this full time researcher is entitled to develop a specific line of research and should be helped to do so.

4- Nano-particle as a tool in targeted therapy; this project is developed in collaboration with a laboratory at the ESPCI (Ecole supérieure de physique chimie industrielle) which brings its expertise in the conception and assembly of the nanoparticles. INSERM U728 brings the tumour and the targeting models. The starting idea is to coat the particles with antibodies recognizing cancer stem cells and take advantage of the iron heart of the particles to concentrate them by means of a magnetic field at specific sites of the body where tumors or metastases reside. This project is at a rather early phase of its development and its high level of potential was underlined by the committee. The committee also recommended that great attention be put into the control of the Ig-coupling reactions and the choice of the antibodies used in the coating. This is given the fact that cancer stem cell markers are often a a matter of belief, which will not be enough to ensure efficiency in a therapeutic setting. It is also recommended that responsibilities in this project be clearly assigned to a senior researcher.

5- Xenograft as a model of dynamic tumour response; the laboratory has set up a collection of tumour grafts established from fresh patient material. Preference was given to needle biopsies of metastases, which is a clear originality. They reported a good rate (no specific numbers, though) of take and rapid growth, despite the small amount of engrafted tumour. Plans are to use these grafts as a tool to assess response to therapy. One originality to this project is that they have implemented an approach allowing to monitor dynamically the response, by making sequential needle biopsies under ultrasound on the animal during treatment. This project is judged interesting and must be supported in the future. Recommendations are that specific staff should be identified in charge, with clealry defined resources against specific deliverables in defined tiome frames, with priorities.

C- Biobanking as a Scientific Resource;

The paraffin embedded tissue resource represents a large proportion of the diagnostic cases coming through the department. The frozen material is more limited, but is excellently archived and quality controlled. However, it was not clear how scientists and clinicians accessed these tissues and what the committee structure was that approved access. It is therefore recommended to follow international BioBanking Recommendations, which request that Biobanks are managed by mutidisciplinary research committees staffed with a majority of members independent of the BioBank Team. These recommendations were made to ensure that the resources are made available to the largest scientific community possible to ensure that donors wishes to get the best science from their gifts is ensured. It was not clear that such a structure was in place.

Little information was available on how the scientific life is organized within the unit except a weekly lab meeting for data presentation. In addition, the unit does not run any Lab committee (Conseil de Laboratoire). This aspect could be of particular importance given the existence of two labs located respectively at the Hospital Beaujon in Clichy and at the Hospital St Louis in Paris.

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

The unit has a clear and efficient involvement in training for which it must be congratulated. It is strongly committed in the B2T biology and biotechnology and Masters programs. In addition, the unit is member of a Doctoral School, with several MD and PhD students enrolled. Also, its strong input in biobankers training should be acknowledged.

Of note is the very interesting link and ongoing program with the international INSERM lab settled in Shanghai. This latter might eventually be assessed separately.

Assessment of the five-year plan and strategy:

The review panel noted that no clear scientific five-year plan nor strategy were defined in the written report and could not correct this impression during the visit. This did not come up during oral presentations and nor during private hearings with the director when asked about future plans for the unit.

4 • Conduct of the visit

Specific premises visited:

Institut Universitaire d'Hématologie, Hôpital St Louis, Paris. Locaux au premier étage occupé par l'unité. Locaux refaits à neuf, bien structuré et équipé.

Programme du Comité de visite

Unité Cancer et Transplantation

18 janvier 2013 de 8h30 à 18h00

Délégué scientifique AERES : Mr Daniel OLIVE

Comité Scientifique : Mr Charles THEILLET (Président) ; Experts Mr Jean Jacques FOURNIÉ (CSS8), Mr Barry GUSTERSON, Mr Bruno CLÉMENT, Ms Laurence LAMANT (CNU), Mr Christophe BORG.

8h30 - 9h00 : Huis clos, présentation de l'AERES au comité par le Délégué

9h00 - 9h15 : Devant l'unité, présentation du Comité de visite et présentation de l'AERES par le Délégué

SESSION AUDITION

09h15 - 10h00 : Ms Anne JANIN : Présentation de l'unité, réalisations et perspectives

10h05 - 10h45 : Mr G. BOUSQUET, M. VARNA : Projet ERC

10h50 - 11h20 : Mr WL ZHAO : Laboratoire International Associé Shanghai

11h25 - 12h00 : Mr A. de GRAMONT : Innovation Research Cancer Network

12h00 - 14h00 : Déjeuner de travail

SESSION RENCONTRE AVEC LE PERSONNEL PERMANENT ET NON PERMANENT

Le comité se répartit en trois sous-groupes

14h - 14h45 : **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 »

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

14h45 - 15h00 : Pause

15h00 - 15h45 **Rencontre avec les représentants de la Tutelle**

Auditoire : membres du Comité, Délégué AERES

15h45 - 16h15 : **Rencontre avec la direction de l'unité**

Auditoire : membres du Comité, Délégué AERES

16h30 - 18h30 : Réunion du comité à huis clos

Présence : Membres du Comité, délégué AERES

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

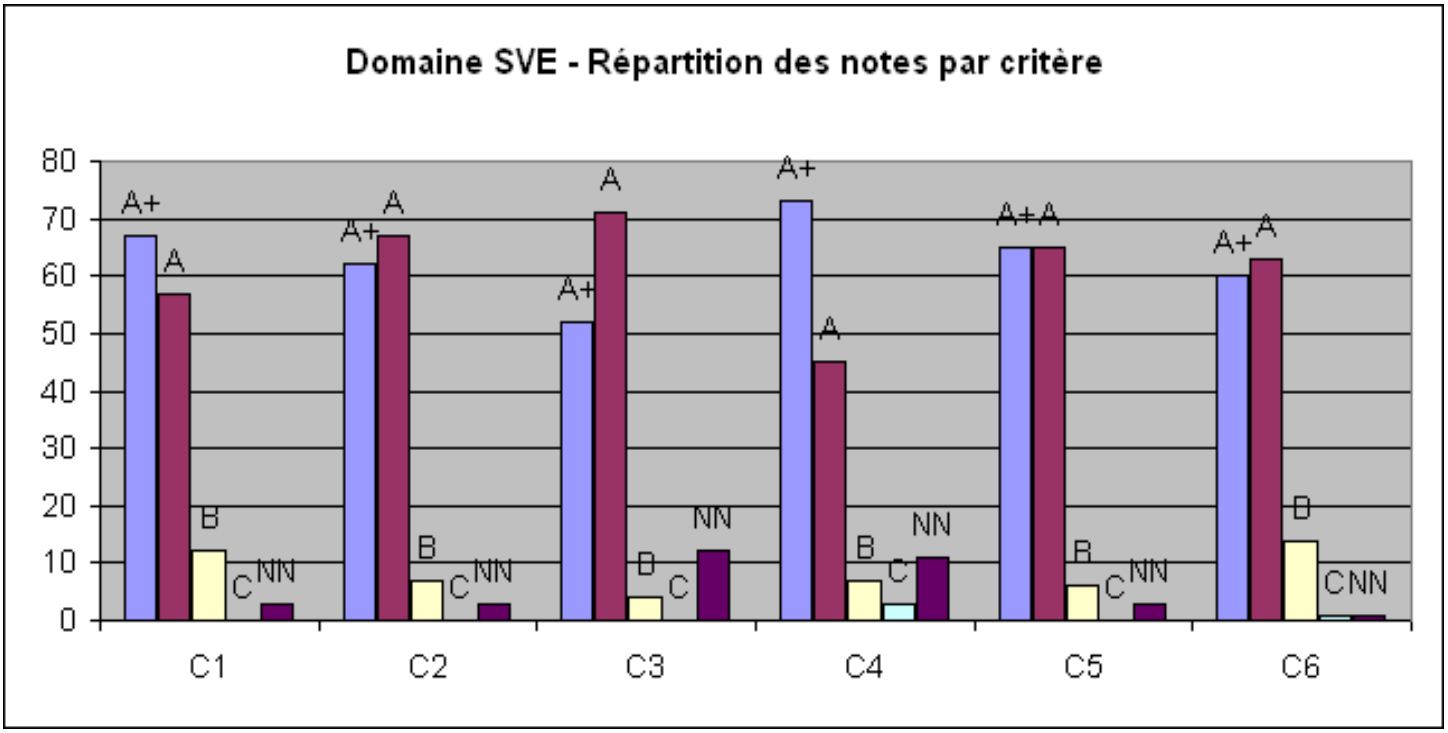
Grades

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

Percentages

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%

Histogram



6 • Supervising bodies' general comments

université PARIS DIDEROT PARIS 7

Le Président

P/VB/LB/NC/YM – 2013 - 088
Paris, le 22 avril 2013

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

S2PUR140006354 - Cancer et transplantation : physiopathologie et réponse thérapeutique - 0751723R

Monsieur le Directeur,

Je vous remercie pour l'envoi du rapport d'évaluation concernant le laboratoire « Cancer et transplantation : physiopathologie et réponse thérapeutique »

Le comité relève le très bon rayonnement à l'international et en particulier les relations privilégiées établies avec la Chine permettant d'assurer, en plus des collaborations scientifiques, des échanges d'étudiant.e.s entre les deux pays. Ceci permet à ce laboratoire de remplir pleinement son rôle académique de formations, ce dont je ne peux que me réjouir.

L'excellent niveau de publications n'a pas été mentionné par le comité comme une force, sans doute du fait de l'erreur, relevée par la directrice, dans le calcul du nombre estimé de publications avec les membres des équipes en premier ou dernier auteur. Quoiqu'il en soit, il traduit une activité indéniable de cette unité que nous continuerons, en association avec l'INSERM, à soutenir à la hauteur de nos moyens.

Sur certaines des remarques constructives formulées par le comité, la directrice a apporté des réponses en formulant des propositions d'organisation, d'allocation budgétaire et de perspectives scientifiques à 5 ans pour chacune des équipes.

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

Vincent Berger

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université PARIS DIDEROT PARIS 7

Inserm
Institut national
de la santé et de la recherche médicale

Laboratoire UMR_S 278
Directeur : Pr Anne Janin

Response to the AERES evaluation report of U728, Director Anne Janin

The members of the research unit U728 thank the evaluation committee for the time and energy devoted to our unit evaluation, their constructive remarks and their assessment of the quality of publications, remarquable in put in setting up training program, good links in industry, clear sign of appeal at international level, four main topics required for research units, together with transdisciplinary project implementation and integration of clinical oncologists.

For the detailed assessment at the scientific level,

1. Cancer in transplanted patients: The studies in Biopsies of GVH patients were initiated by A Janin with E Gluckman since 1981. Before the arrival of G Socié, professor of clinical hematology, in 2002 in the unit, 22 publications were realized on GVH including Am J Pathol, Gastroenterol, Ann Int Med. One unique study was published with him in 2009 on cancer after bone marrow transplantation. Afterwards P Ratajczak post doc and now CR Inserm since 2011, has been PI in this program, with L Verneuil, post doc in the unit and now professor of dermatology, and J Verine PhD in the unit and now associate professor of pathology. The program has been extended to cancers in kidney transplant patients. The first studies are now at maturity and just published in 2012 (without G Socié), in J Invest Dermatol, and in Am J Transplant (ranked as first journals in dermatology and transplantation), and in revision in J Clin Invest (IF 14). For the recommandation to "acquire expertise in the field of pathological assessment of immune cells infiltrates", this expertise has been acquired by staff and pathologists of the unit for a long time, and acknowledged by the Inserm, since we participated in two Ateliers (129 in 2001 and 156 in 2004), and in the participants'training. This expertise of the unit is used for all our publications.

2. Lymphoma: the cooperation with Shanghai institute of hematology began in 2002, and has led to the creation of an Inserm international associated laboratory with W Zhao as PI. When in France, Chinese PhD in the unit train on animal model analyses and electron microscopy. C Thieblemont arrived at the end of 2008, with no previous history or experience of collaboration with China. One common paper with C Thieblemont was published in 2011, another in on-going, from a cotutelle PhD.

3. Clinical oncology: the role and status of A de Gramont has been discussed and clarified in March 2013 with Jacques Grassi Head of the ITMO to which our unit is attached. A de Gramont is director of AAREC Filia Research for 65% of his time and paid for 20% of his time by the unit on a clinical research grant. E Raymond and colleagues are linked with the rest of the unit through their collaboration with Lu He, DR Inserm, the training of students, the use and development of xenograft models and novel predictive biomarkers as well as their interest for relevant expertise in pathology.

4. Protein-protein interaction linked to apoptosis: Our visibility convinced JL Poyet, DR Inserm, to join the unit because the development of his research project needs study of patient-derived cancer tissue xenografts, as models to qualify new anticancer drugs for study in human clinical trials. His position in the unit has been clarified as shown in the next page, as PI for the xenograft as model of dynamic tumor response. Xenograft models development, used by nearly all programs of the unit, is completely paid by the Inserm common budget of the unit.

5. Breast cancer stem cell and hybrid nanoparticles. This transdisciplinary project was designed by A Janin, G Bousquet oncologist, P Ratajczak CR1 Inserm, P Bertheau, M Varna post doc at the ESPCI, P Merlet nuclear medicine, G Lelong IMPMC Chemist. We do agree that this project is at an early phase and needs long-term resources, and apart from the ANR international and ITMO cancer grants already acquired, A Janin as PI has applied for a senior ERC grant. In 2012, after selection in the first round, the project ranked 40$_{th}$ on 100 in the second round (only 30 projects were granted). A Janin was allowed to apply again in 2013 and the project has just been selected in April 2013 for the second round. The Inserm has applied as the host research institution for this ERC project.

6. Biobanking as a scientific resource: as stated in the INCa annual report transmitted to the committee, around 30% of the 5000 new samples are used for research each year. These resources are made available through Material Transfert Agreement to scientific teams in France (U 727 Strasbourg, U 955 Institut Pasteur, CNRS 5238 Clcc Lyon, U954 Nancy, U1050 Collège de France in 2012) and abroad (Universities of Minnesota, Zurich, Genoa, and Regensburg, in 2012).

7. The publication report of our autoevaluation was established according to the Inserm recommendations: between 1/1/2007 and 17/1/2013, 315 publications, mean IF 7.15, total citations 5224, H-index of the unit: 35. The committee stated that "34/300 publications have members of the Lab as first or senior authors". The actual number is 104/300 and not 34/300.

In addition, Nicole Haeffner, in charge of the Inserm bibliometry unit, established for the ERC senior grant appliance the profile of A Janin, H-index 43, belongs to the top 1% scientists in clinical medicine, (ESI Thompson in February 2012 and again in October 2012).

Position and projects developed by the scientists, five-year plan and strategy

* **PI, P Bertheau, Virtual slides**, HU; C Miquel, , M Grossin, A de Roquancourt , post doc D Ameisen, F Bouhidel, staff : L Legres, IR

3-year plan: design and implementation of an automatic module for blur analysis, grant FlexMim,

5-year plan: ponderation of the blur in the anatomo clinic context, use of contextual graphs to modelize pathology practice. Collaboration with university informaticians.

* **PI C Thieblemont, Aggressive lymphoma,** HU E de Kerviler, C de Bazelaire, J Frija, J Brière, P Brice, PhD M Romero, C Benet, staff D Geromin, IR

3-year plan:optimization of microbiopsy process for genomic analyses and xenograft model

5-year plan: development and implementation of a genomic tool dedicated to diagnosis and prognosis in aggressive B-cell lymphoma grants PHRC, INCa, FRM

*** PI P Ratajczak, CR1 and L Verneuil**, **Cancer in transplanted patients**. HU J Verine, A Janin, P Mongiat Artus, V Meignin, PhD M Battistella, staff: M ElBouchtaoui, Tech

3-year plan: chimerism and p53 mutations PHRC and ANR grant

5-year plan: Tumoral microenvironment angiogenesis and immune cells

*** PI E Raymond, Antiangiogenic therapeutic strategies**. A de Gramont, Lu He, DR Inserm, post doc L Xerri, PhD S Albert, J Coelho, staff: H Ming

3-year plan: Characterization of vasculogenic mimicry and Epithelial Mesenchymal Transition in tumors treated by anti-angiogenic agents.

5-year plan: Development of new inhibitors targeting mesenchymal-like tumors cells.

*** PI JL Poyet, DR Inserm, Protein/protein interaction and xenograft as a model of dynamic tumor response** HU M di Benedetto, H Bruzzoni, PhD D Rigue, Staff I Ferreira, IE,

3-year plan: Evaluation of the modulators of protein-protein interactions involved in the regulation of apoptosis we have developed (cell permeable peptides) in human cancer xenografts

5-year plan: Production, evaluation and optimization of small organic compounds derived from the above-mentioned peptides (lead compounds) for the development of novel pharmaceuticals.

* **PI W Zhao, lymphoma and response to chemotherapy**. W Li, Y Fan, Z Wei, staff: Y Dong

3-year plan: autophagy in lymphoma cells and chemoresistance

5-year plan: miRNA oncologic clusters and lymphoma progression

*** PI A Janin Breast cancer stem cells and hybrid nanoparticles**

P Ratajczak, CR1 Inserm, G Bousquet, P Bertheau, P Merlet, post doc: M Varna, PhD L Vercellino, staff C Leboeuf IE, G Gapihan AI,

3-year plan: enginering, functional studies of hybrid nanoparticles, in vivo imaging approach

5-year plan: in vivo photothermal targeted therapy

Management team: P Bertheau, C Thieblemont, P Ratajczak, JL Poyet, E Raymond, A Janin

The Unit Council will assist the Director to coordinate and manage the research activities of the Unit. Each PI will be present or represented by a tenured scientist. The Council will meet each month to discuss scientific strategies, recruitment options, budget issues, equipment needs, problems and obligations inherent to hygiene and security, relationships with the Saint Louis campus. A written report of each Council meeting will be submitted to all members for approval at the next meeting.

Budget allocation: No overhead charges are applied to externally-funded grants obtained by the PIs. The recurrent university budget (24 k€ available for the unit in 2012, reduced from 60k€ after institutional exceptional charges) is shared through all members and dedicated, after discussion with all PIs, to formation, missions and payments for students and trainees. The recurrent Inserm budget (90 k€ in 2012), the only one that can be used indifferently for consumables or for equipment, is used for the charges linked to the technology shared by all programs, particularly for the annual set up of microscopes, cryostats, microtome, laser microdissection, ultrasonography dedicated to small animal, immunohistochemistry device, and the whole budget of xenografts for the unit programs.Because of its critical importance on many in-house or collaborative projects, a particular attention is given to preservation of money till the end of the year for laser replacement for micro dissection.

Pr Anne Janin