PARCC - Paris centre de recherche cardiovasculaire

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Paris-Cardiovascular Research Center

PARCC

Under the supervision of the following institutions and research bodies:

Université Paris Descartes

Institut National de la Santé et de la Recherche Médicale

January 2013

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

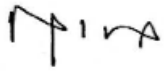
Research Units Department

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 and its in-house teams received the following grades:

- Grading table of the unit: Paris Cardiovascular Research Center

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

- Grading table of the team 1: Endothelial pathophysiology and biomarkers of cardiovascular diseases

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

- Grading table of the team 2: Imaging of microcirculation

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

- Grading table of the team 3: Genetics of rare arterial diseases

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

- Grading table of the team 4: Cardiovascular epidemiology and sudden death

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

- Grading table of the team 5: Innate and adaptative immunity in vascular diseases

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

- Grading table of the team 6: Regenerative therapies for cardiac and vascular diseases

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

- Grading table of the team 7: Physiology, pharmacology and imaging of large arteries

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

- Grading table of the team 8: GPCRs and tyrosine kinase receptors; role and interactions in development and disease

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

- Grading table of the team 9: Pathogenesis of vascular infections

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

- Grading table of the team 10: Immunotherapy and anti-angiogenic therapy in oncology

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

- Grading table of the team 11: Percutaneous arterial repair

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

- Grading table of the team 12: Pathophysiology of the renal tubule, homeostasis and blood pressure

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

- Grading table of the team 13: Pheochromocytomas and paragangliomas: from genetics to molecular targeted therapies

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

- Grading table of the team 14: Genetics mechanisms of aldosterone-related disorders

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

Evaluation report

Unit name:	Paris Cardiovascular Research Center
Unit acronym:	PARCC
Label requested:	UMR_S
Present no.:	UMR_S970
Name of Director (2012-2013):	Mr Alain TEDGUI
Name of Project Leader (2014-2018):	Mr Alain TEDGUI

Expert committee members

Chair: :	Mr Bart STAELS, Université de Lille
Experts :	Ms Marie-Christine ALESSI, Université de Marseille, représentante INSERM
	Mr Jacques BARHANIN, Université de Nice
	Mr Matteo BELLONE, Université de Milan, Italie
	Mr Pierre BONGRAND, Université de Marseille
	Mr Michel BURNIER, Université de Lausanne, Suisse
	Mr Jean-Jacques FEIGE, Université de Grenoble
	Mr Harry HEMINGWAY, University College London, Royaume-Uni
	Mr François MACH, Université de Genève, Suisse
	Mr Paolo MADEDDU, Université de Bristol, Royaume-Uni
	Mr Pierre-Yves MARIE, Université de Lorraine
	Mr Sylvain RICHARD, Université de Montpellier
	Mr Vincent RICHARD, Université de Rouen
	Mr Gian Paolo ROSSI, Université de Padoue, Italie
	Mr Luc VAN BORTEL, Université de Gand, Belgique

Scientific delegate representing the AERES:

Mr Patrick LACOLLEY

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

Ms Chantal LASSERRE, INSERM

Mr Stefano MARULLO, Université Paris 5

1 • Introduction

History and geographical location of the unit

Hôpital Européen Georges Pompidou, 56, rue Leblanc - 75015 Paris

Management team:

Director: Mr Alain TEDGUI; Managing Director: Mr Philippe COUDOL;

Representatives of the scientific team leaders: Ms Chantal BOULANGER, Mr Olivier CLÉMENT, Mr Xavier JOUVEN, Mr Ziad MALLAT;

Translational Research Coordinator: Mr Xavier JEUNEMAITRE; Training Coordinator: Mr Jean-Sébastien SILVESTRE.

AERES nomenclature :

SVE1_LS4

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	46	50	50
N2: Permanent researchers from Institutions and similar positions	18	18	18
N3: Other permanent staff (without research duties)	51	45	
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	6	9	9
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	41	17	17
N6: Other contractual staff (without research duties)	37	18	
TOTAL N1 to N6	**199**	**157**	**94**

Percentage of producers	*100,00 %*

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	29	
Theses defended	32	
Postdoctoral students having spent at least 12 months in the unit*	36	
Number of Research Supervisor Qualifications (HDR) taken	5	
Qualified research supervisors (with an HDR) or similar positions	47	55

2 • Assessment of the unit

Strengths and opportunities

Despite the fact that PARCC is a young center, the achievements of the center since its creation de novo in 2009 are clearly remarkable. This is not only reflected by its structure, the excellent level of scientific production but also by its national and international reputation, attractiveness, training, etc. Altogether, in this very short period of time PARCC has taken its place as a center of excellence in the field of vascular research and medicine.

The scientific production of the center since its creation 4 years ago is astounding considering all possible standards, including impact factors of the publications, citation indexes, and overall impact (including medical impact) of the published discoveries.

In this short period of time, the center has managed and continues to attract or promote a significant number of new young full time researchers. The identification and promotion of new group leaders is also impressive, as is the potential for a number of other future group leaders. Training of PhD students and recruitment of post-docs and technical staff is also excellent.

The center has developed, and keeps developing, an excellent level of external collaborations, as illustrated by the number of collaborative publications in high ranking journals, and this is made possible partly due to the good connection within various prestigious international networks.

The center benefits from a strong leadership, and a highly efficient management team. The strategic choice to organize the center in relatively small (yet productive) teams, which might appear a risky choice, has so far proven to be very effective, giving rise to a number of highly competitive and very well evaluated teams. The evaluating group considers this an essential element which favors the emergence of new themes, individualization of junior researchers and promotion of new team leaders.

The center houses a very strong assembly of coherent technical platforms, unique human tissue collections and cohorts of patients, and solid infrastructures for clinical and epidemiological research, with very good access to the core facilities for all teams. The access to these shared resources appears adequate, as reflected by the reports from the individual teams.

The current and future strategy is defined by continuously giving attention to the translational aspects of research, transfer to patients care and population, and benefits from continuous interaction between experimental and clinical research.

Weaknesses and threats

Diversity of the research themes may be a concern, especially in such a large center that at some point needs to create a strong identity which allows differentiation from other similar centers worldwide. This has to be put in balance with the claimed strategy of the center to privilege quality over extreme focus of research. In this regard some groups diverge from the whole 'vascular' theme (e.g. one group is more focused on tumor biology). Also, the question of developing research oriented toward cardiac diseases in a mostly "vascular" center may also be addressed (e.g. cell therapy of myocardial regeneration, etc.).

As mentioned in the strengths the organization in small groups is adequate and currently very productive. However, at some point, it might result in a certain fragility of teams which largely depend on one single principal investigator.

Recommendations

Now that the center reaches 'cruising altitude', it would appear essential to clearly define the Strategy of PARCC to differentiate the center from other large cardiovascular centers in the world. For example, the evaluating committee remarked the lack of research on cerebrovascular disease, a topic which could be considered. The strategy to attract new, young teams is very encouraged, but it is not clear whether there is sufficient space available for hosting such new teams.

Given the ambitious projects which involve genetic studies, proteomics, etc. the development or close interaction with a center of bioinformatics may be considered.

3 • Detailed assessments

Assessment of scientific quality and outputs

The scientific production of the center, since its creation 4 years ago, is astounding considering all possible standards. All together, the center has published >350 original research articles and >50 review articles. In accordance with the declared aim to privilege quality over quantity, >70 original articles have been published in journals with IF>9 (including >40 articles with members in leading positions) and around half of the articles are published in journals with IF >6. The level of citation of the published articles is also excellent, with >30 articles in top 1% and around 150 in the top 10%. Among these papers, some publications merit to be particularly highlighted based on their originality and impact, e.g. in the field of inflammation/atherosclerosis/aneurisms (J Exp Med 2009, J Exp Med 2010, J Clin Invest 2010), progress in the treatment of rare vascular diseases (Lancet 2010), vascular infections (Science 2011), mechanisms of glomerulonephritis (Nat Med 2011), genetics of renal diseases (Nat Genet 2012), mechanisms of rejection of kidney allografts (Lancet 2012) etc. Of note, most of the teams involved in cardiovascular research also published in the top cardiology journals, including a number of publications in Circulation. Remarkably, the high level of publications is fairly balanced between the different groups.

Assessment of the unit's academic reputation and appeal

Members of the center participated in 7 FP7 programs, and 3 Leducq networks. Three members obtained ERC grants in 2011 and 2012 (2 junior and 1 starting grant). Three members are part of a Labex.

The center's attractiveness is also excellent: around 40 post-docs from >18 countries, and 2 invited professors were hosted since 2009. The center also attracted several high level (young) scientists who joined after its creation, including 2 AVENIR teams, and more recently a very productive group of scientists specialized in renal physiology, as well as several experts in cardiovascular imaging.

All team leaders and several collaborators are regularly invited worldwide to give scientific seminars.

The head of the center served as European Editor for Arteriosclerosis Thrombosis Vascular Biology, and two members were associated editors. Seven scientists from the center are members of the editorial board of prestigious specialty journals

The scientists from the center have developed an impressive network of collaborations in France and internationally, leading to a very high number of collaborative publications in high ranking journals.

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

Production of patents is top level, with 15 patents. Three startups were created based on the findings of the center.

Many recent discoveries from the center have clear potential for medical impact (e.g. identification of a gene responsible for familial hyperkaliemic hypertension, characterization of new diagnostic and prognostic markers of cardiovascular disease, determinants of sudden cardiac death, treatment of Ehlers-Danlos vascular syndrome with a beta-blocker, development of bio-absorbable stents, etc.). Some have additional economic and social impact (e.g. prediction of rheumatic heat disease in Africa and Asia, study of the epidemics of Sickle Cell Disease in Africa; etc.) in which the PARRC investigators take the lead in establishing the prevalence, developing diagnostic protocols and tests.

Assessment of the unit's organisation and life

The center benefits from a strong leadership, and a highly efficient management team, who managed to successfully build an extremely competitive, productive and well organized center within a very short period of time.

The center has made the strategic choice to organize itself in relatively small (yet productive) teams, many of those composed of 1-3 full time researchers. Although a potentially risky approach, it provides also an excellent environment for researchers (especially junior scientists) to develop their own group and receive personal recognition. In fact, in line with this choice of organization, one large team from the center now gives rise to four independent groups (some being reinforced by the inclusion of scientists from another center in Paris), and it must be noted that all 4 groups were very well evaluated individually by the committee. In parallel, a number of reorganizations of the research teams within the center are planned (most of them being already effective) and were all favorably evaluated by the committee during the individual team evaluations. This clearly reflects a strong and effective effort to favor emergence of new themes and individualization of junior researchers. As an example, two team leaders received an ERC starting grant in 2012. The different presentations also allowed the committee to identify several potential team leaders who may emerge within a relatively short period of time.

The coordination of the center is also excellent, with a director assisted by a scientific executive board with representatives of the teams and of the different activities of the center (in parallel to the mandatory Lab council). The director is assisted by a managing director in charge of the administrative and technical platforms. The center also benefits from a scientific advisory board composed of internationally renowned experts in cardiovascular research and medicine, who met twice since the creation of the center and emitted a series of recommendations that were taken in account in the presented project.

The financing rules are clear, in terms of distribution of recurrent grants between transverse activities and between teams, overheads, and established at the level of the scientific executive board.

One of the strongest aspects of the center is that it houses a very strong assembly of coherent technical platforms, including genetically-modified animal facilities, in vivo imaging, molecular imaging, flow cytometry, etc. as well as unique human tissue collections. In parallel, an important aspect is the access to a large series of unique cohorts of patients, and solid infrastructures for clinical and epidemiological research. The access to these shared resources appears adequate, as reflected by the reports from the individual teams.

Despite the large size of the center in terms of number of teams (14) and persons (>250) the personal interactions also appear very good, and are favored by the organization of common events (seminars, master classes, annual retreat). This was also reflected by the group discussions with the students/post doctoral fellows and technicians.

Assessment of the unit's involvement in training through research

Since its creation, the center hosted over 60 PhD students, over 30 completed their thesis so far. Over 100 master students were trained.

Most PhD students are affiliated to the doctoral school *Biologie et Technologie (B2T)* or *Génétique Cellule Immunologie Infectiologie Développement (Gc2ID).* Some students are also affiliated to the ED *Epidemiology and Public Health (ED420)* or ED *Médicament, Toxicologie, Chimie et Environnement (MTCE)*.

The center's director is also coordinator of a specialty in the *Master Biologie Cellulaire Physiologie et Pathologies (BCPP)*. He will be co-leader of a Department in the future doctoral school project at Paris-Descartes.

The discussion with the students during the evaluation visit did not raise any particular concerns, and revealed an overall good cohesion and satisfaction regarding the center, its organization and their own position. Overall guidance of the students by their supervisors also appeared adequate, as well as the student's funding, and perspectives for future careers and post-doc opportunities.

Assessment of the five-year plan and strategy

Individual evaluation of the five year plan of the teams revealed that 11 out of the 14 teams were considered as excellent/outstanding, and two projects were considered as very good.

A vast majority of the projects are supported by inter-team collaborations (around 40 collaborations are identified) and thus benefit from excellent synergy between the groups. They will also benefit from a very extensive and constantly growing network of external collaborations.

The overall project is overall very consistent and reasonably well focused considering the very large size of the center, with the largest portion of the center devoted to research in vascular pathology, angiogenesis, as well as genetics and epidemiology of cardiovascular diseases (this latter aspect slightly diverges from the overall 'vascular' focus by including cardiac and renal research). One team slightly diverges from the overall objectives by proposing research on tumor immunology, however with a significant part of the project devoted to (tumor) angiogenesis. The projects cover a large area of vascular diseases, although mostly excluding (with a few exceptions) the growing field of research concerning cerebrovascular diseases.

Most teams propose a strategy very well balanced between the pursuit of ongoing, validated projects and riskier, innovative projects, thus proposing a globally excellent feasibility. This high feasibility is also largely supported by the examination of the past year's achievements of the center in terms of reaching the proposed goals. Feasibility and overall quality of the projects are also well supported by the extensive and complete technical facilities, clinical platforms, and access to patients' populations or biobanks. One possible exception may concern the genetic and epidemiological studies for which the expansion may at some point suffer from the lack of in house competences in bioinformatics and biostatistics.

The strategy is defined with a continuous and remarkable attention being given to the translational aspects, transfer to patients and population, interaction between experimental and clinical research, and overall valorization of the findings and concepts.

The SWOT analysis is extensive, and the center's project has been also carefully designed in order to respond to the successive analyses and evaluations that originated from the international scientific advisory board.

4 • Team-by-team analysis

Team 1 : Endothelial pathophysiology and biomarkers of cardiovascular diseases

Name of team leader: Ms Chantal BOULANGER

Workforce

Team 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	3	3	3
N2: Permanent EPST or EPIC researchers and similar positions	2	2	2
N3: Other permanent staff (without research duties)	1	3	3
N4: Other professors (PREM, ECC, etc.)	0	1	1
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1	1
N6: Other contractual staff (without research duties)	2	2	1
TOTAL N1 to N6	**10**	**12**	**11**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	5	4

• Detailed assessments

Assessment of scientific quality and outputs

The team developped in the recent years an internationaly recognized excellence in the field of endothelial microparticles (MP), ranging from basic approaches to clinical validation, which are the basis of the now well established concept on the role of endothelial MP in cardiovascular disorders.

The major breakthroughs are: 1) the pathological role of MPs and 2) the validation of MP as biomarkers of various diseases.

1) The pathological role of MPs was demonstrated in atherosclerosis (*JACC 2007, Circulation 2007, Circ Res 2012*), diabetic retinopathy (*Diabetes 2010*) and cirrhosis (*Gastroenterology 2012*), but also for erythrocyte MP in sickle cell disease (*Blood 2012*), as well as of MP as mediators of post-ischemic angiogenesis (*Circulation 2009*).

2) The concept of MP as biomarkers of cardiovascular diseases has been demonstrated in various groups of patients, e.g. coronary artery diseases (*Blood 2012, J Hypertension 2010*), renal failure (*Nephr. Dial.Transplant 2012*) and cirrhosis (*Gastroenterology 2012*). This has also been associated with validation studies in in vivo imaging of MPs (*Radiology 2012*).

The scientific production reflects this high level of innovation, with around 25 original publications in the top specialty journals, e.g. Circulation, Circ Res (x2), Eur Heart J, Blood (x2), JACC, Gastroenterology, Diabetes (x2), Radiology etc. The vast majority of these articles are published in reviews with IF over 6, with 5 articles in the top 5 citations. The international recognition is also reinforced by an excellent production of high impact reviews , e.g. Circ Res 2011 and ATVB 2011 (top 0.1%).

Assessment of the unit's academic reputation and appeal

The team recently obtained an international ANR contract (with Germany and Canada), and is part of a Leducq network. Two post-docs have been trained in the past 3 years, and funding has been obtained to recruit 2 more post-docs.

The team leader authored 5 invited reviews, including Circ Res 2011 and ATVB 2011 (top 0.1%), and 1 invited editorial in the Eur Heart J. The team leader is also presently Associate Editor for Atherosclerosis Thromb Vasc Biol, and reviewer for all the major Cardiology journals.

The team leader also has been invited to give lectures or seminars in 15 international congresses, including for example 4 participations to European Society of Cardiology meetings

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

Four patents have been filed in the past 3 years. Remarkably, the follow-up supportive studies for these patents are supported by 2 ANR emergence grants (including one in 2012, led by a young University/Hospital Researcher).

The caracterization of MP as biomarkers of several diseases is of potential importance in terms of long term clinical impact.

The team has contracts with two industrial partners.

Assessment of the unit's organisation and life

This is a group highly focused around the team leader's theme of microparticles, thus with an a highly coherent scientific objective. One major novel aspect of the future project is the inclusion of a second full time researcher, who is already fully operative, and associated with a top journal publication in 2012.

The inclusion of a series of young clinicians in the project appears very effective, for example one of them is PI on an ANR project.

The level of interaction with other groups within the center is also excellent (6 teams), as already demonstrated by high level joint publications (e.g. in atherosclerosis, angiogenesis, ..).

The organisation of the lab in two adjacent rooms facilitates interactions. One flow cytometer has been acquired in 2012 for MP determination and is included in the flow cytometry unit directed by an engineer from the team.

Assessment of the unit's involvement in training through research

The team is affiliated to the doctoral school B2T (biologie et biotechnologie). 3 PhD theses have been completed between 2010 and 2012. Remarkably, despite the recent completion of these, 2 of these 3 obtained permanent hospital (PH) and University Hospital positions, are now members of the team (including 1 after a post-doc in the USA). The third PhD student is currently a post-doc in the team and will leave for a post-doc in London in 2013. Another PhD student is currently in her second year.

These are excellent results given the small number of effective PhD student supervisors. Inclusion of a second full time investigator already who already received its habilitation to direct research (HDR), and this is also the case for one of the young clinicians in the group.

Assessment of the five-year plan and strategy

The new team 1, with the same team leader and now entitled "endothelial pathophysiology and biomarkers of cardiovascular diseases" will be reinforced by the recruitment of a CR1 CNRS previously member of team 5. This integration in fact reflects ongoing collaborations in the field of erythrocyte MPs, as reflected by a major joint publication in Blood 2012. The project is organized in four tasks.

1) The own project of the rectruited CR1 CNRS researcher, following the Blood 2012 publication, aimed at characterizing the pathological effects of erythrocyte, heme-laden microparticles obtained from patients (either sickle cell disease, diabetic or with CAD). This will be based on a combination of *in vitro* and *in vivo* studies, again with good faisibility. This is a particularly innovative project that will most likely uncover novel important pathological aspects of MP.

2) The pursuit of the clinical characterization of MP as biomarkers, in 4 conditions (silent coronary artery diseases, primary microvascular dysfunction, healthy subjects and diabetic patients). These studies are clear and useful complements of the previous work. The major originality of these studies, compared to the previous ones, is the extension of the concept of MP as biomarkers to heme-loaded MPs. They appear totally feasible given the background expertise, the clinical collaborations, and the external fundings obtained.

3) A new project to understand the role of endothelial autophagy in the development of atherosclerosis. Although this project slightly diverges from the general MP research, the question asked presents a high level of innovation and interest. Indeed, very little work has been devoted to the question of endothelial autophagy, which however most likely plays a role in various cardiovascular diseases. This role is supported by preliminary data on the regulation of autophagy by shear stress. The project involves a series a relevant approaches, spanning from cell culture to (ongoing) development of mice with selective deficiency in endothelial autophagy. Interest will be placed on endoplasmic reticulum stress, endothelial survival, inflammation/permeability, and ultimately atherosclerosis. This is certainly the most novel aspect of the project, although potentially at risk and possibly highly competitive

4) A project to study the pathological role of microRNAs (miRs) packaged in MP. This is also a rather novel approach, directly derived from the team's experience on MPs. The idea that miRs may be involved in the pathogenic effects of MPs is supported by preliminary data obtained recently by the team. Again, the approach will involve cell biology experiments (to decipher the relationship between miRs and MP) and integrated models (to study the functional effects of miRs). Again this is a very innovative approach, developped in the extremely competitive field of microRNAs, supported by international collaborations (international ANR project).

All together, the series of projects are highly original and innovative, and appear reasonably feasible within the anticipated time frame. Major risks are identified in the project, including, as mentioned above, the novelty of the autophagy hypothesis and the strong international competition. However as mentioned before the team has previously demonstrated its capacity to respond to similar challenges, via the development of relevant in house experimental models, as well as the creation of an efficient network of collaborations either within the PARCC or externally.

Conclusion

- **Strengths and opportunities:**

International recognition in the field of microparticles.

Highly focused research devoted to the pathological roles of endothelial microparticles/apoptosis/autophagy.

Very strong and effective leadership and organization of the team.

High level of publications, both in terms of original articles and of highly cited reviews, for a relatively small team (Initially 1 - now 2 full time researchers, 5 University-Hospital researchers, 3 engineers).

Effective integration of a second full time (CNRS) researcher in the team, with expertise that complements that of the projet leader, validated by a common publication in a high impact journal in 2012.

Transversal research approach with molecular, cellular, animal and clinical approaches.

Original and highly innovative novel projects focused on endothelial autophagy and micro-RNA packaging in microparticles.

Excellent level of external funding.

- **Weaknesses and threats:**

The projects focused on endothelial autophagy and miRNA are highly original, however currently based on limited preliminary data, thus this part of the project may be currently considered as being of high risk.

The number of different "projects" as presented (4) may be considered on the high side given the relatively small size of the group, and given the fact that the inclusion of an additional full time researcher was associated with the addition of a new research "project". This comment must be however moderated by the fact that this "new" project is in fact fully related to the group's work on MP and also because the 4 projects are in fact very focused, 3 being tasks of the same project on MP.

- **Recommendations:**

An additional effort needs to be made to reinforce the team in terms of full or part time researchers, and post-docs.

Attention should be put to the development of a network of international collaborations (e.g. autophagy?) that should help reaching the fixed objectives in a context of high international competition.

It is also important that the group, possibly in association with other international leaders in the field of MPs, develops joined strategies to fully establish the value of MPs as biomarkers of cardiovascular diseases.

Team 2 : Imaging of microcirculation

Name of team leader: Mr Olivier CLEMENT

Workforce

Team 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	5	6	6
N2: Permanent EPST or EPIC researchers and similar positions	0	0	0
N3: Other permanent staff (without research duties)	5	5	3
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	1
N6: Other contractual staff (without research duties)	1	1	0
TOTAL N1 to N6	**12**	**13**	**10**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	5	5

• Detailed assessments

Assessment of scientific quality and outputs

This research is mainly focused on methodological objectives employing in vivo imaging techniques to accurately characterize: 1) tissue angiogenesis and perfusion with MRI and optical imaging, 2) tissue metabolism with conventional and new PET tracers and 3) cell trafficking in cell therapy studies.

This research requires a multidisciplinary environment (biology, chemistry, physics, image processing) and is highly translational, involving clinical imaging, as well as imaging of various experimental models (tumor development, placenta, cell therapy). Therefore, this team is likely to interact with most of the other teams of the PARCC INSERM centre and it might have an important and strategic role in the centre's structure.

Such methodological research is mandatory for an accurate use and analysis of MRI functional imaging and of PET molecular imaging. Previous studies from this imaging team were definitely original and they were published in very high level journals of medical imaging – i.e.the highest ones regarding impact factors for medical imaging, such as Radiology (IF: 5.7, 9 publications in first or last authors), the Journal of Nuclear Medicine (IF: 6.4, 3 publications in first or last authors) and Magnetic Resonance in Medicine (IF: 3.4, 3 publications in first or last authors). Although it may be considered that this research did not lead to a real breakthrough in medical imaging, it is, however, very difficult to reach a breakthrough in such technological research fields. Moreover, the investigators from this team played an important role in a number of research studies from other teams thus contributing to major international publications (Circulation, Anesthesiology, Cell Transplantation..).

Assessment of the unit's academic reputation and appeal

There are 3 main investigators and all are opinion leaders at the international level in their respective research fields: contrast agents for MRI, tracers' kinetics analyses, radiotracers for metabolic PET imaging. All are frequently invited for lectures in international congresses, one of them is the head of an important European working group of the European Society of Radiology, and another one has built up and directed a very famous European master of medical imaging.

They were able to attract and recruit a high-level full-time researcher in metabolic PET imaging and, in the future, this should further enhance their own research projects, as well as the number of collaborative studies with other teams of the Unit.

The MRI/PET platform, which is directed by this team (as part of the university network "Descartes images", an IBISA platform), is very attractive for collaborations with private enterprises and other academic research teams.

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

There are numerous connections and collaborative studies with private enterprises working in the field of contrast agents, software for image analysis or radiotracers. Several private enterprises are already working on the MRI platform.

Their research has led to as many as 10 patents in the last years (mainly in the field of radiotracers of metabolic PET imaging) among which one has led to a license.

In addition, the research for new radiotracers of atheroma plaques (nanolipid contrast particles) could be greatly valorized in the future.

Assessment of the unit's organisation and life

This point is difficult to assess, especially for this small team where the organization will markedly change with the recent recruitment of a senior full-time researcher.

However, there are indirect signs that this organization works very well:

1) The two main investigators of the previous team are developing different, but highly connected projects, and they are co-authors in a large number of their published articles.

2) The recruitment of the new full-time researcher has been organized in order facilitate the connections with the other investigators. In particular, the PET-CT system, which will be mainly used by this new researcher, has been placed in close proximity to the MRI which was previously used by the other researchers. Methodological studies, combining MRI and PET imaging in the same animals, have been planned at a very short term.

Assessment of the unit's involvement in training through research

In spite of the low number of investigators, there are as many as 5 PhD students and a number of Master students.

This team, which provides high-level topics of pre-clinical and clinical imaging studies, is likely to be very attractive for the medical students working in the HEGP hospital.

One of the 3 main investigators is involved in the direction of a Master of Medical Imaging from the Descartes University. The newly recruited researcher was the head of a famous European Master of Medical Imaging when he was in the CEA at Saclay (he was at the origin of this master).

Assessment of the five-year plan and strategy

The project is definitely nice, original and innovative.

This project is well defined for the first years, especially for the methodological and technological studies, which are planned for analyzing cell trafficking, tissue angiogenesis and perfusion, and the new area of mixed PET/MRI analyses (perfusion with MRI vs. PET information regarding perfusion or hypoxia).

Interactions with other teams of the unit are less well described, especially regarding: 1) the actual participation to the research work planned in team 6 for cell therapy and 2) connection with the MRI cardiovascular projects, which are developed in team 7.

A potential problem is the lack of a real specialist of the imaging of heart and vessels, whereas this might greatly facilitate the connections with other teams. It may be pointed out that such a specialist has been recruited in team 7 (for clinical cardiovascular imaging) and this problem could therefore be simply solved by a higher collaboration level between teams 2 and 7.

Conclusion

- **Strengths and opportunities:**

Because of the multidisciplinary and translational nature of the research field, this team should play an important and strategic role in the centre's future structure.

This team involves high-level investigators, who work in complementary research fields, and the recent recruitment a full-time researcher will further enhance the projects (new areas of molecular PET imaging and of mixed PET/MRI analyses).

This team will have the opportunity to use a high level MRI/PET platform, which is very attractive for collaborations, not only with other teams from the PARCC unit, but also with other research teams and with private enterprises (a source of valorization for the overall INSERM centre).

- **Weaknesses and threats:**

The projects and organization of this relatively small research team will markedly change with the very recent recruitment of a senior full-time researcher. This is presumably the reason why the research projects were mainly described for the first years. Projects planned at a longer term should be at least partly described, especially regarding the actual participation to the research work planned in other teams such as the cell therapy studies from team 6 (the connection with the work planned by team 2 in cell trafficking imaging) and the clinical MRI cardiovascular projects from team 7.

There is a high number of research themes for this rather small team.

There is a need for a real specialist of the imaging of heart and vessels.

With the arrival of the new PET/CT system, it will be necessary to modify the organization of the platform and presumably also to enhance funding and personnel (engineers, technicians).

- **Recommendations:**

A more precise identification of the projects is needed for the long-term.

A priority could be given for research themes leading to interaction with the other centre's teams.

A specialist of the imaging of heart and vessels should be recruited (and this will surely further enhance the interaction with the other teams of the INSERM centre).

Specific funding and personnel dedicated to the new PET/CT system should be more clearly identified.

Team 3 : Genetics of rare arterial diseases

Name of team leader: Mr Xavier JEUNEMAITRE

Workforce

Team 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	3	4	4
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	2	2	2
N4: Other professors (PREM, ECC, etc.)	1	2	2
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	1	1
N6: Other contractual staff (without research duties)	2	2	1
TOTAL N1 to N6	**12**	**12**	**11**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	6	6

• Detailed assessments

Assessment of scientific quality and outputs

The main objective of the projects of team 3 is to identify new molecular mechanisms involved in the pathophysiology of rare forms of hypertension and vascular diseases. A second topic is vascular signalling in mendelian forms of hypertension. Although the search for molecular mechanisms of hypertension is a very competitive and busy field today, it remains very orginal mainly because of the new areas that are opened by the new discoveries including those published by the group of Jeunemaitre and collaborators. Indeed, the field has evolved from the investigation of humoral and hormonal parameters to cell signalling and intracellular pathways which would never have been considered 15 years ago. In this respect, the research proposed by this group represents a major paradigm shift in hypertension research. The opening of these researchs strategies towards rare vascular diseases is particular original as little is done for these sometimes debilitating diseases which can be considered as orphan diseases in terms of research.

In the last 10 years, huge progresses have been made in the identification of molecular mechanisms of hypertension but the precise role and importance of each of the mechanisms remain to be explored in animals and particularly in humans using translational research. This is actually a strength of this group which interacts very positively with the clinical research center.

The list of publications of this group is impressive and of very high impact demonstrating the ability of Jeunemaitre and his colleagues to produce high ranking research. In the last years they have published several highly referenced papers in the field. They published numerous articles in journals with an impact factor > 9 or >6.

The team leader has a very high international reputation for his research. He is member of numerous international societies and he and his colleagues participate in several international programs (FP7 projects, Leducq network…). Over the years he has created a very important network in hypertension research with many international contacts and collaborations. Moreover, within France, the unit is the reference center for rare vascular and hypertension diseases. This is a major advantage for conducting the proposed studies and the efficacy of this strategy has now been well demonstrated.

In summary, this group has reached a very high level of scientific quality and expertise in the field of genetics of hypertension and rare vascular diseases. Their publication output is outstanding and the impact of the group is major in all the domains they cover.

Assessment of the unit's academic reputation and appeal

As mentioned before, the team leader and his group have a very high international reputation in the field of genetics and hypertension and vascular diseases. The group has contributed in the past to several major discoveries in genetics for ex. on the role of renal transporters as a cause of monogenic forms of hypertension. The team leader is part and is also the leader of many international projects at the European and International level. Several other members of the group have international connections in their field. This group can be considered as a reknown leader in the field in France and worldwide.

The members of the team have given many conferences around the world and are regularly invited in main national and international meetings. In recent years, four of them have received distinctions for the quality of their research and presentations. They participate actively in many national and international societies in their field of expertise. The members of the group have organized international meetings in the context of fibromuscular Dysplasia, Ehlers Danlos disease and genetics demonstrating their impact on the topic. Moreover, the team is regurlary involved in the redaction of major reviews and texbook published in high ranking Journals (Hypertension, Circulation, Endocrinology, J Mol Med…).

In summary, the reputation of this research group is excellent both at the national and international level. Over the year, the leader of the group has demonstrated his ability to promote young researchers and to bring them to a very high standard of research. The group is very appealing for French students and post-docs and should attract more foreign researchers in the future.

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

The group has already demonstrated its ability to develop innovative methods in genetics and in the investigation of molecular mechanisms of hypertension and vascular diseases. They have also important collaboration with the clinical research as well as the animal facilities and imaging facilities enabling to conduct their project with the most updated techniques. The group is really at the top of the technologies in their research.

They have important collaboration with patients' organisations which is particularly important when dealing with rare disorders. The fact that they are respected as a reference center for physicians in the country and outside the country is of major interest and importance for the development of the projects. The research approaches they developed in the past are now appplied by several other groups, further emphasizing their impact.

Their collaboration with international partners which are also leaders in the field have lasted over many years and will probably continue as effectively as it has been so far. It is very likely that the proposed research will lead to the creation of new independent research groups in the future as it occurs previously with the renal and adrenal projects in genetics of hypertension.

Assessment of the unit's organisation and life

Due to the split-of leading to the creation of 3 new teams, this team is in organizational transition. Given the training track-record of the team leader, it is anticipated that this will occur swiftly without major problems.

Assessment of the unit's involvement in training through research

The impact of the team leader on academic careers is excellent as demonstrated by the proposition to create 3 new teams in the PARCC center based on the work of several of his previous team members. In this respect, the team leader has offered many possibilities to young researchers to develop their career and to become independent researchers.

The group has included many PhD students and post docs in its program. Looking at the list of students and post-docs, it seems that few of them are of foreign countries, a situation that could be improved providing the unit has sufficient means to engage foreign student and post docs. The group has the infrastructure and competence to host foreign researchers in the future.

Assessment of the five-year plan and strategy

The proposed project in hypertension and rare vascular diseases is original and is of little risk considering the preliminary data already obtained by the team. The team has direct access to the patient groups, they have the technology running in their laboratories, they have the internal collaboration with clinicians. So, all the conditions are gathered to perform their projects without signficant delays.

The group projects have been reassessed after the creation of three new subgroups from their team. The new project is well focused and coherent and goes in line with their previous work. The translational aspect of the project is very important and will create important links between the groups of PARCC center from basic science to clinical projects. The project will probably be the basis for several other projects in the domain and will certainly open new avenues for other non-vascular rare diseases.

The SWOT analysis of project is well balanced. The team recognizes that they need to be reinforced in vascular biology after the reorganization of the group and to establich new collaborations in imaging technologies. Looking at the CV of the actual members of the group, one can see some heterogeneity which will need to be equilibrated in the future in order to maintain the high level of research.

The five year plan is realistic and feasible.

Conclusion

- **Strengths and opportunities:**

The project of group 3 is an excellent, high standard, serious and well conceived research project based on excellent preliminary results, a longstanding experience in the domains, and high capacities to interact with other groups of the PARCC. It is a translational project that runs from basic science to clinical investigation and clinical studies. It may have a major impact on the development of new therapeutic strategies for rare vascular diseases

- **Weaknesses and threats:**

The project has only very few weaknesses which can be solved by external national or international collaborations (imaging) and by recruiting new researchers in the field of vascular biology. As usual, one threat is always the funding, but the high quality of the investigators make them very competitive for national and international grant proposals.

- **Recommendations:**

The team and its project are acceptable as presented.

Team 4 : Cardiovascular epidemiology and sudden death

Name of team leader: Mr Xavier JOUVEN

Workforce

Team 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	5	4	4
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	2	2	2
N4: Other professors (PREM, ECC, etc.)	1	2	2
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1	1
N6: Other contractual staff (without research duties)	3	3	1
TOTAL N1 to N6	**14**	**13**	**11**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	5	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	4	4

• Detailed assessments

Assessment of scientific quality and outputs

Team 4 focuses on four modules including sudden cardiac death, novel biomarkers of CVD, post-transplant arteriosclerosis and auto-immune mediated atherosclerosis. This team has been successful with important publications in each module. The team has set up and coordinated major new cohort studies (PPIII, CARTAGENE, and CADRE study). This field work alone is substantial, and should be taken into consideration when judging the publication track record. The international collaborations with CARTAGENE, with ERFC, with carotid IMT, and others are strong and focused. The leader has a proven track record of developing new networks (e.g. West Africa for CADRE study, e.g. professionals before during and after hospitalsiation with sudden death in CARTAGENE). He also demonstrates 'knowledge transfer / public engagement' by educating patients and the general public. The publication track record is definitely strong with 18 publications with IF>9, including NEJM, Lancet 3, and JAMA 2, Circulation 5 and 947 citations.

The research is original – the team has successfully identified, and addressed, important areas of scientific uncertainty which have previously had insufficient research endeavour. Each of the four areas - sudden death, 'newly neglected' diseases, biomarkers and immune mechanisms - have involved pioneering epidemiological research. Sometimes scientists are criticised for carrying out 'me too' research. The very opposite is the case here. This group should be congratulated on identifying where there have been important gaps in knowledge and carrying out high quality research to address these gaps.

Breakthroughs: For example there are scores of epidemiological research groups working on the biomarkers and cardiovascular disease: but here the team takes a substantive question: to what extent are specific disease phenotypes (stable angina, acute myocardial infarction, sudden cardiac death) associated with specific biomarker effects. The team has taken important steps to advance the recognition of the need to have a 'higher resolution' in disease phenotyping in large scale studies, in order to investigate where biomarker and genetic effects are homogenous, and where they are heterogeneous. This will only become more important as our ability to distinguish disease phenotypes at scale i.e. in ever larger studies becomes possible.

Scientific impact is high. The team appears to take the philosophy – which is a good one – that it is better to publish high quality papers (top journals, nearly a 1000 citations from their work in the review period), than to publish a higher volume of less good quality papers.

The team has an international and indeed global outlook. International working in collaboration with US on several studies (e.g. Roger, Mayo Clinic). Global in relation to the rheumatic heart disease work in Africa (rheumatic heart disease and sickle cell disease).

There are several publications in leading general medical (NEJM, JAMA, Lancet) and top cardiovascular (Circulation) journals.

Assessment of the unit's academic reputation and appeal

The team has developed and leads a network of cardiologists in several countries in West Africa.

The academic reputation is high.

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

The research of this team has strong impact on the clinical and public health environment. There are important implications of the research findings including: in African studies finding that the prevalence of rheumatic heart disease on echo is considerably higher than that based on auscultation has treatment implications: penicillin G. The antibody-mediated graft rejection publication had a Lancet editorial recommending a change in the way clinicians define rejection. The sudden death work has led to changes in the way that patients and professionals are educated.

Assessment of the unit's organisation and life

The team is very well organized, with complementary, strong leadership by two PIs, one with clinical and one with experimental expertise.

Assessment of the unit's involvement in training through research

There are 9 PhD students which are successfully integrated in the team, and have training opportunities in ED420 Doctoral Schools. 4 staff teach on masters programme.

Assessment of the five-year plan and strategy

The project plans are in four modules: 1. Sudden death (expertise center, sport related sudden death, long term prognosis after hospitalised arrest, and genetic determinants), 2. Paris prospective study (genetic determinants of arterial stiffness, echotracking carotid measurements, progression of IMT, and risk prediction in established CVD), 3. Newly neglected diseases (rheumatic heart diease and CADRE study in sickle cell) and 4. immuno-atherosclerosis (renal and heart transplant). These plans are (justifiably) ambitious, but feasible. They build on strong existing track records in these modules – which build well across teams in PARCC.

Conclusion

- **Strengths and opportunities:**

Internationally leading group which has made important contributions e.g. in sudden death and rheumatic heart disease and biomarkers. This team has not just contributed to knowledge, but the findings have also strong implications for treatment (e.g. kidney transplant antibody mediated rejection). The team has an impressive scientific agility: identifying interesting questions and hypotheses, addressing them and then moving on. There is not an automatic expectation of continuing in one project (e.g. the air pollution in JAMA meta-analysis, which was largely negative, was not then developed into a module).

One important opportunity is collaboration with large cohort studies with >100,000 participants. These include biobanked cohorts, and those based on linked electronic health records, and are increasingly 'open access'. The team is well placed to seize such opportunities.

- **Recommendations:**

The team is already highly successful and is set to continue being successful. A general question is how this epidemiology team may influence the vision of PARCC, and vice versa? Epidemiology may play an important, and expanded role potentially spanning PARCC research at multiple phases in the translational cycle: discovery, development and testing of interventions in trials, stratified approaches to medicine, quality of care and outcomes research, and health of whole populations.

Team 5 : Innate and adaptative immunity in vascular diseases

Name of team leader: Mr Ziad MALLAT / Mr Alain TEDGUI

Workforce

Team 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	5	3	3
N2: Permanent EPST or EPIC researchers and similar positions	3	4	4
N3: Other permanent staff (without research duties)	3	2	2
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	0	0
N6: Other contractual staff (without research duties)	1	1	
TOTAL N1 to N6	**15**	**10**	**9**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	3	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	6	4

• Detailed assessments

Assessment of scientific quality and outputs

This team has long-standing expertise in the field of atherosclerosis and the role of immune-inflammation therein, identifying crucial roles of B cells and Tregs in atherogenesis. Moreover, they developed expertise in the study of the pathophysiological mechanisms of Abdominal Aortic Aneurysms. Points of strength are:

- Major breakthroughs in the field of atherosclerosis with a good scale of progress, high originality and scope of research in the field.
- Created new theoretical breakthroughs and paradigm shifts, with interesting new investigation proposals.
- Very high quantity and quality of scientific production (21 with IP >9 from 2009) reaching the highest international standards.
- The entity is a leading reference in the field, with very good national and international recognition.

Assessment of the unit's academic reputation and appeal

- Team leaders and researchers are invited to communicate at leading international events.
- Great network of national collaboration on high scientific projects.
- Distinctions and awards to team leaders and collaborator.
- Lead partner in different network collaboration, communities and associations promoting projects, infrastructures or centers of scientific or technical interest, at international and national level.
- High-level foreign researchers (postdoctoral and students) recruited by the team.
- The team is leading several international program projects.
- Team leaders and collaborator are Editors of several journals, and members of scientific committees, reviewers of grants.
- Several patents issued by team leaders.

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

- Good collaboration with non-academic partners (industry), several patents.
- Excellent fund raising (around 106 Euro/year).
- Collaborations with other leaders in the field, innovative value with creation of start-up.
- Long duration of the partnership.
- This team interacts with several other partners within PARCC.
- Partnership with other institutes has attracted many young talented PhD students, who performed their thesis in this team.

Assessment of the unit's organisation and life

- Very well organized unit, great governance, with already a long-term impressive scientific track record. The field of research is very focused from the last years.
- Creation of several jobs position.
- The position of the team-leader#1 may be a limitation (50% UK – 50% PARCC).

Assessment of the unit's involvement in training through research

- Well-structured integration of students and post-doc in the scientific activities. The team is offering high-level, internationally recognized seminars.
- The team implemented strategies to monitor students and PhDs.
- The future supervision of PhDs is a little vague.

Assessment of the five-year plan and strategy

- The proposed project is excellent, innovative, and ambitious, with credible strategy and hypothesis, and clearly in the field and in continuation with previous work produced by this team.
- The project shows high feasibility in terms of resources (adequacy of goals and means).
- This team will benefit from important academic and non-academic partnerships.
- The team is likely to maintain its leading international position of the five-years plan.
- Already some successful translation from basic science investigation into clinical field (Il-17 projects).
- Question on the methods and potential clinical application of the immunization project?

Conclusion

- **Strengths and opportunities:**
  - Already long history of excellent track record in publications (quality and quantity).
  - Good quality of the project proposal.
  - High number of PhD theses performed and published in high impacted journals.
  - Collaboration with high-quality, well recognized academic partners.

- **Weaknesses and threats:**
  - The position and affiliation of the team-leader #1 (50% UK – 50% PARCC) raises questions on his presence and practical implication in the team's projects and life.
  - The first aim will be supervised by a PI, who is scheduled at only 50% of his time.
  - The publication and expertise in the field of abdominal aortic aneurysms does not reach the same high recommendations.

Team 6 : Regenerative therapies for cardiac and vascular diseases

Name of team leader: Mr Philippe MENASCHE /Mr Jean-Sébastien SILVESTRE

Workforce

Team 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	1	4	4
N2: Permanent EPST or EPIC researchers and similar positions	2	1	1
N3: Other permanent staff (without research duties)	3	2	2
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	4	4
N6: Other contractual staff (without research duties)	0	0	
TOTAL N1 to N6	**9**	**11**	**11**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	3	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	3	5

• Detailed assessments

Assessment of scientific quality and outputs

• The production of the 2 PIs focuses on therapeutic angiogenesis and stem cell therapy. They published relevant papers in specialist as well as general medicine journals, including JCI, JAMA, JACC, Circulation, Diabetes, ATVB, Stem cells etc. PI-1 has in total 105 PubMed publications (20 reviews) of which 39 since 2007. PI-2 has 394 publications (57 reviews) of which 65 since 2007. The PI-1 has a h-index of 34 and showed a constant publication rate during the last years. In general the production is original, employs advanced methodologies and has gained a very good reputation in the specialist field of vascular biology and regenerative medicine with extended readership through appropriate publication vehicles. The PI-2, who is a leader in the field of cell therapy for cardiovascular medicine being the first to use skeletal myoblasts for repair of ischemic heart, is now joining the group. This could open up new possibilities to translate the work of PI-1 into clinical results and publications.

• Of particular relevance is the contribution of PI-1 in unravelling the role of CHOP-10 in negatively influencing reparative angiogenesis (Circulation 2012), the influence of neuroadrenergic system and endothelial microparticles in the recruitment of vasculogenic cells into ischemic muscles (ATVB 2012 and Circulation 2009). Furthermore, multidisciplinarity and originality are highlighted by a series of publications on immunologic control of angiogenesis (ATVB 2012, Circulation 2009, Cardiovasc Res 2009). Finally, PI-1 is developing an original research on adiponectin and ephrin B2 as enhancers of angiogenesis and vasculogenesis with possible therapeutic application.

• PI-2's production is outstanding with a total of 299 publications prevalently as corresponding author, many of which on top cardiovascular journals like Circulation and comes with a plus but –although already embedded into the environment of PARCC- he was not formally part of it.

Assessment of the unit's academic reputation and appeal

• PI-1 is member of he Société Française d'Angiogenèse and of the American Heart Association. He is also associate editor of ATVB. In 2012, he has got a Junior chair at Paris-Descartes University (2012-2014) and his team has been labelled by the Fondation pour la Recherche Médicale (2012-2015) and, in 2010, received a Prime d'Excellence Scientifique (2010-2014). A leading role in international steering committees needs to be built in the future to strengthen the PI-1 visibility.

• Members of the team were invited as speakers in national congresses and to give 4 seminars in various scientific structures. Members of the team were invited as speakers in international congresses (European Society for Microcirculation, Munich, Germany; 4th International meeting on angiogenesis. Amsterdam, the Netherlands ; Hypoxianet meeting Dublin, Ireland ; 9th World Congress for microcirculation, Paris, France; Scientific meetings of the American Heart Association and Arteriosclerosis Thrombosis and Vascular Biology, USA ; Scientific meetings of European Society of Cardiology and European Society of Hypertension. The Unit has contributed to the education of a number of PhD students and postdoctoral fellows. The PIs are part of national and international projects involving external collaborators of high calibre.

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

There is a clear engagement with dissemination through scientific and also through vehicles to the non-experts of the field. They applied for several patents with perspectives of clinical exploitation.

Assessment of the unit's organisation and life

The team is going to experience a deep change due to the relocation of two PIs. This raises positive and risky issues. Although the two PIs seem very enthusisastic to work in collaboration, a clear plan on how this alliance will work was not presented, especially with regard to the evolution of PI-1 work into clinically relevant output. The leadership issue was also raised considering the different stages of the career of the 2 PIs. An effort to hire new investigators in the ascending phase of their career is necessary. In particular, PI-1 would need to have a clinical research assistant working directly with him. PI-1 should clarify his plan of future career inside the general environment and how this will evolve.

Assessment of the unit's involvement in training through research

The team is affiliated to the Doctoral School(s) « B2T» and includes 3 scientists entitled to direct research programs (HDR). The training seems excellent with successful completion of curricula and accreditation of masters and PhD courses. The subsequent success of students and post-doc was not reported, which attenuates the enthusiasm on this point.

Assessment of the five-year plan and strategy

The merging of 2 PI teams will eventually lead to the formation of an ideal platform of expertise and technical know-how, ranging from the basic features of cell injury, regeneration and remodeling to the clinical applications of cell-based therapies complying with the increasingly stringent regulatory requirements. Future activity consists of:

1. Investigate the mechanisms involved in circulating cell infiltration in ischemic areas and underscore the role of inflammatory cells, particularly that of B lymphocytes, in post-ischemic tissue remodelling,

2. Optimize the cardiac specification and subsequent sorting of embryonic stem cell-derived mesodermal progenitors as well as their delivery to the heart in combination with biomaterials,

3. Develop a biodegradable trileaflet tube conduit for replacement of the right ventricular outflow tract,

4. Combine the expertises of the two groups to investigate new modalities of cell therapy in chronic limb ischemia.

Although there are clear advantages from this collaborative plan, there is insufficient information on the master plan to lead the basic science from PI-1 to the clinic. This activity requires a high budget and the PIs should clarify how they plan to support this science. It is not clear which cell products will be delivered in the next years. They claim to be ready to use embryonic stem cells soon to support cardiac repair in a clinical trial, but evidence presented here was vague. The size and budget of the team is not sufficient at this stage for such an ambitious plan. This may delay the time for delivery.

Conclusion

- **Strengths and opportunities:**

Very good production and substantial contributions to the field. The group did an excellent job in training.

- **Weakness:**

In general, there is no weakness intrinsic to the scientific capability and organization of the group. The lack of senior researchers and the relocation of staff should be an opportunity to refocus on new challenges especially in view of the higher commitments of the PI in administrative and representative functions.

- **Recommendations:**

To apply for international grants at EU level and increase international collaborations. The design of a scientific master plan is absolutely necessary.

Team 7 : Physiology, pharmacology and imaging of large arteries

Name of team leader: Mr Stéphane LAURENT

Effectifs

Team 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	2	4	4
N2: Permanent EPST or EPIC researchers and similar positions	0	0	0
N3: Other permanent staff (without research duties)	2	2	2
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	0	0	0
N6: Other contractual staff (without research duties)	0	1	0
TOTAL N1 to N6	**4**	**7**	**6**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	0	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	2	3

• Detailed assessments

Assessment of scientific quality and outputs

Introduction : The main research field of team 7 is the clinical investigation of blood vessels, and large arteries in particular in relation to cardiovascular risk. This research includes clinical trials mainly in patients including hypertension, chronic kidney disease and genetic vascular diseases. The team is also largely involved in development of better imaging techniques for vascular investigation. Currently the team is broadening its research into cross-talks between the macrocirculation, the microcirculation and the heart.

Period 2009-2012

135 publications, 15 IF>8; 35 IF>6

Breakthroughs in research

1. Patients with Vascular Ehlers Danlos Syndrome are now treated with celiprolol (Lancet 2010)
2. Establishing normal and reference values for aortic stiffness (Eur Heart J 2010)
3. Establishing normal and reference values for carotid intima media thickness (Eur Heart J, in press)
4. Establishing normal and reference values for central blood pressure (submitted).

Pivotal studies

1. Chronic kidney disease (CKD) is associated with a hypotrophic remodeling of large arteries (*JASN 2011*)
2. Aortic stiffness (cfPWV), but not IMT, carotid wall stress, and central PP, have predictive value for CV events (*Hypertension, in press*)
3. An increased longitudinal bending strain of atherosclerotic plaque is associated with characteristics of unstable plaque and could play a role in plaque rupture (*JACC Imaging 2011*)
4. The hyper-IgE syndrome, accompanied by immunodeficiency linked to an abnormal STAT 3 pathway, is associated with a specific vascular disease (*Circ. Cardiovasc Genetics 2011*).

Ongoing pivotal research with breakthrough potential

1. SPARTE investigates improvement of clinical outcome by measuring aortic stiffness (*Hypertension 2012*)
2. Development of software to separate intima and media by ultrasound. To be validated.
3. Effect of omega3/omega6 fatty acids on endothelial function (in collaboration with Rouen)
4. Development of ultrafast ultrasound technique to assess in vivo arterial wall elasticity dynamics.

Assessment of the team's academic reputation and appeal

Members of the team have delivered more than 250 invited lectures during the last 5 years and are in the editorial board of 6 international peer-reviewed journals.

Members have received 5 (inter)national awards in the evaluated period.

The team has large collaborations within PARCC (with 4 other teams), national (11 centers in EXPLOR and 34 centers in SPARTE) and international collaborations.

The team leader is the coordinator of the European network for non-invasive investigation of large arteries gathering more than 50 expert centers in hypertension and cardiovascular research.

The team leader is past president of the ARTERY Society. Another team member is chair of the EUROCAM working group. A third team member is on the executive committee of ARTERY.

8 foreign doctoral and post-doctoral students have been trained.

The team has trained 6 PhD students and 4 master students.

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

The team members are actively involved in software development of devices, national and international guidelines/recommendation committees and have industrial partnerships/contacts with drug companies and (3) device manufacturers.

They are regularly interviewed on national professional media, TV networks and radio.

Assessment of the team's organisation and life

Team 7 has a coherent and logical scientific objective: large arteries and their interaction with heart and small arteries.

Team 7 is organized in 3 groups, each with an established researcher as group leader, and coordinated by the team leader:

- physics of ultrasound, rare vascular disease and clinical trials
- large and small arteries and kidney disease
- aortic disease, heart-vessel coupling.

Each group includes a research engineer and/or technician, and post-doc and PhD students.

The group consists of 7 permanent members, all appointed as hospital/university researchers, who also have other duties. There is no permanent INSERM position. The absence of permanent positions for engineers and/or technicians may be a threat for continuity of the research program.

Assessment of the team's involvement in training through research

Team 7 trained 8 foreign doctoral and post-doctoral students, 6 PhD students and 4 master students. In each subgroup, students are supervised and guided through the professional experience of the research group leaders. Team members participate as teachers in internationally renowned courses (e.g. ESH training courses).

Despite the fact that not all details are provided, it can be concluded that the successful training of many researchers is witnessing the quality of the training.

Strategy and project for the next 5 years

The ongoing and planned research has the potential to deliver many pivotal results and very likely also many breakthroughs in the next 5 years:

1. SPARTE investigates improvement of clinical outcome by measuring aortic stiffness (Hypertension 2012), which may tremendously influence current cardiovascular prevention and treatment,
2. Development of software to separate intima and media by ultrasound. This may substantially increase the predictive value of intima thickening for cardiovascular risk,
3. Normal and reference values for carotid stiffness,
4. Normal and reference values for carotid baroreflex sensitivity.

In addition the start of heart-vessel coupling research and the retinal artery research are assets and will deepen the understanding of the interaction between heart–macrocirculation-microcirculation.

Additional aims are to show that the carotid phenotype is a determinant of sudden death and to select carotid plaque mechanical parameters for further longitudinal study on stroke risk.

The program is in line with previous research, challenging, searching for breakthroughs and realistic.

The team has made an excellent SWOT analysis and shows the capacity to adapt to the evolution of research.

Conclusions

- **Strengths and opportunities:**

Team 7 has a strong and leading national and international research position in the field of arterial stiffness. It has built a large national and international research network and has a close collaboration with different departments of HEGP. This large collaborative network gives the opportunity to be more successful in attracting funding.

Other opportunities are to broaden the research field to interaction between heart- macro- and microcirculation, and the collaboration with other departments/units in developing new techniques/devices.

- **Weaknesses and threaths**

The competition in the research field has increased significantly in recent years. This makes it less easy to keep the leading position.

Team 7 had substantial funding from pharma industry and device manufacturers. This may limit its neutral scientific position by possible conflicts of interest. But also, funding from pharma industry is rapidly decreasing putting a threat on the research possibilities.

- **Recommendations**

The team leader is advised to help facilitate the start of the new project groups, in particular to pay attention to the integration of the MRI Imaging group within team 7 and to support the group leader of the 'large and small arteries and kidney disease' group in starting up/harmonizing (if needed) the subgroup, which hosts well-known established clinical researchers.

It is recommended to have a collaboration on MRI imaging with team 2.

It is recommended to attract a permanent position for engineer and/or technician to maintain the continuity in research know-how.

To decrease the threat on this internationally renowned team, the team should aim at attracting at least 1 permanent position from INSERM.

Team 8 :

GPCRs and tyrosine kinase receptors; role and interactions in development and disease

Name of team leader: Mr Eric CAMERER / Mr Pierre-Louis THARAUX

Workforce

Team 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	0	1	1
N2: Permanent EPST or EPIC researchers and similar positions	2	2	2
N3: Other permanent staff (without research duties)	0	0	0
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	5	5	3
N6: Other contractual staff (without research duties)	1	1	
TOTAL N1 to N6	**8**	**9**	**6**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	4	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	5	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	2

• Detailed assessments

Assessment of scientific quality and outputs

The work performed by members of the team is original and addresses important questions on the role of G-protein coupled receptors (GPCRs) and receptor tyrosine kinases (RTKs) in development and diseases, notably that arising secondary to glomerular capillary dysfunction with models ranging from cells to experimental models (mice) to humans.

Past findings have enabled major breakthroughs, and emergence of inventive concepts and tools as well, leading to excellent publications. The most innovative findings include: (1) the role of S1P (and mimetics) in modulating vascular leak, and the interest of other Gi-coupled receptors such as PAR2 for vascular protection (*JCI, 2009*); (2) an unexpected role for PARs and protease signalling in regulating neural tube closure in the mouse embryo (*Dev Cell, 2010*); (3) the role of a prostasin-matriptase cell surface protease cascade in early embryonic ectoderm formation, placental morphogenesis, and neural tube closure (*Plos Genetics, 2012*); (4) the implication of PAR2 as a potential mediator of pathologies linked to loss of serine protease regulation in skin, in addition to a methodological breakthrough (knock-in mouse line overexpressing Par2 in skin: *Nat Nanotechnol, 2009*); (5) the HB-EGF/EGFR pathway could be a suitable therapeutic target on top of current non specific immunosuppressive therapies in rapidly progressive glomerulonephritis (*Nat Med 2011*); (6) the identification of critical inflammatory and regulatory pathways in sickle cell disease.

The members of this new team altogether have published 20 original articles in excellent specialty and generalist journals, which underscores the high scientific impact: 1 Nat Nanotechnol, 1 Nat Med, 4 JCI, 1 Dev Cell, as first or last authors; 1 Science as co-author. The clinician joining the team is also credited a high number of papers (33 including 5 as last author) in very good clinical journals (Transplantation, Kidney International, Am. J. Transplant.). The targeted journals for publication of data have been privileged quality over quantity, although the quantity is quite substantial.

Assessment of the unit's academic reputation and appeal

The leading scientists have a well-established international visibility, as indicated by high citations of some of their papers, and invitations as speakers to national and international meetings. The quality of the work produced and of the current projects has been highlighted by the awarding of excellent and highly visible supports (competitive *Inserm Avenir* contract for one leader; prestigious *ERC starting grant* for the other leader). The team is also involved in international (2) and national networks, and had a high rate of success in getting funded (10 national grants and Marie Curie, EU). The two leaders of the team are members of national and international societies and serve as regular reviewers in top journals (Nature medicine, JCI, Circulation, Circ Res, Blood, ATVB, J Immunol., etc...).

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

The team has access to many original genetic models, with contribution to breakthrough innovation (e.g. a knock-in mouse line overexpressing Par2 in skin: *Nat Nanotechnol, 2009*) and they use relevant disease models. Four patents have been filed and there is a partnership with a couple of pharma (Gennentech, Eisai Pharmaceuticals). They have proficient local (within PARCC), national and international collaborations. They also collaborate with HEGP's departments and have interactions with non-profit organizations.

Assessment of the unit's organisation and life

Team 8 results from the merging of members of former team 8 and former team 5 . Previous collaboration and convergence of scientific interest has primarily driven this dynamic, which appears evident and timely. Notably, in addition to well-established links, the two leaders have a grant in common (ANR blanc), which should facilitate the scientific exchanges between members of this new team (mainly post-docs and PhD students in addition to the team leaders and one clinician). The scientific potential and the promises of valorisation are great, and should rapidly benefit to the team itself and to PARCC. The different projects and sectors are clearly defined in the project with complementary inputs, which should provide synergy.

Assessment of the unit's involvement in training through research

The team has trained 8 post-docs and 7 PhD students over the past years. There are currently 7 post-docs and and 3 PhD. One team leader has not the HDR yet, and it would be desirable that all senior scientists in this "small" team have this diploma to officially train PhDs. The leaders have successful access to different sources for Post-doc and PhD fundings. They are involved at various at different levels in teaching (local, 2 summer schools) and student supervision (M2, MD, PhD, Post-docs).

Assessment of the five-year plan and strategy

The current scientific objectives are derived from previous work and include: **1.** To further identify roles of GPCRs, protease and S1P signalling in development and disease; **2.** Identify critical switches in the pathogenesis of glomerular diseases with focus on GPCRs and RTKs; **3.** Explore pathogenesis of glomerular diseases. The project is characterized by simultaneous researches in developmental biology and disease models, which is likely to stimulate innovative concepts. There is a genuine effort to develop translational research, in particular from bedside (arrival in the team of one senior clinician from HEGP).

It should be noted that the quality of the overall project has been evaluated, at least in part, positively by INSERM (Avenir) and EU (ERC grant). Synergy and cross-fertilization is expected to result from the dynamic of this group. The merging will allow the new team to foster research within the field of GPCR signalling and renal vascular diseases. The goals for the next five years are quite reasonable with minimal risk. SWOT analysis was realistic. This young team has potential to progress and make it as a team.

Conclusion

- **Strengths and opportunities:**
  - Merging is timely, will foster new dynamic with better integration of clinical aspects. Cross-fertilization is expected to generate new ideas and concepts.
  - High level publications.
  - Leaders have a great potential recognized internationally (acknowledged by prestigious grants).
- **Weaknesses and threats:**
  - Need for technical support (1 technician).
  - Governance could be a threat and should be taken into account.
  - Despite a fair number of post-docs, the team identifies the recruitment of top level candidates as a weakness. The quality and number of grants obtained may help to achieve the goal.
- **Recommendations:**
  - Encourage strategies for recruitment of young researchers.
  - More interaction with University (recruitment of teachers to interface with students).

Team 9 : Pathogenesis of vascular infections

Name of team leader: Mr Guillaume DUMENIL

Workforce

Team 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	0	0	0
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2	2
N6: Other contractual staff (without research duties)	1	1	0
TOTAL N1 to N6	**5**	**5**	**3**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	0	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Introduction : This team evolved from an Avenir grant awarded on 2009 to the PI. The specific feature of this team is that there is only one permanent investigator (PI), together with 8 non-permanent collaborators (3 doctoral students, 3 post-doctoral scientists, 2 technical staff). The project focuses on the interaction between (human) host and *Neisseria meningitidis*.

Assessment of scientific quality and outputs

The strategy is fully multidisciplinary, including biophysics, protein structure, cell biology, in addition to methods currently used by bacteriologists.

The output is excellent : The leader went-on building a whole framework for understanding the pathogen strategy : after discovering the importance of shear flow heterogeneity in initial adhesion to blood vessels (J. Exp. Med 2006) and analyzing the mechanisms used to cross tight junctions in brain vessels (Science 2009), he discovered a molecular mechanisms involved in host invasion : post translational change of pili allows bacteria to detach from an aggregate on epithelial surface and generate systemic infection (Science 2011, last author). In addition, he analyzed host cell surface reorganization in contact with bacteria, resulting in important strengthening of attachment, as a requisite for colony formation (Plos Pathogens, last author). Altogether, the reports includes 7 original papers (including two that appeared in Science, two others in PLoS Pathog., Structure, Infect. Immunol) and 6 review papers (Methods Mol Biol, Embo Mol Med, Curr. Opinion Microbiol, all as first/last author). More recently, he developed a model of "humanized mice" to study human-restricted infection.

As a conclusion, within a few years, this young investigator secured a leading world position in the study of an important model of bacterial infection

Assessment of the unit's academic reputation and appeal

The principal investigator already obtained an outstanding recognition : in addition to an Avenir and ERC starting grant, he was awarded the excellence label for Inserm investigators ("prime d'excellence scientifique"). He was invited to participate in a Labex (emerging infection). He is coordinator of an ANR project (RPIB grant : recherches partenariales et innovations médicales).

He was also invited to present 11 talks in conferences (4 outside France,). In France, he was selected by the INSERM to present a talk at the 2011 meeting of research unit directors, as an example of a highly successful and promising researchers.

While these results already prove his international recognition as a researcher, he progressed by another step in academic recognition by acting as an editor of a special issue of "Current opinion in microbiology".

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

While the major breakthrough is about the basic mechanisms of infection, the work was used to generate a patent on methods for the screening of substances that may be useful for the prevention and treatment of infection.

Also, the Avenir team is co-funded by a major pharmaceutical group (Sanofi) providing a post-doc fellowship and participated in an ANR grant. The collaboration with industry is long lasting, since his projects involve another common project with Sanofi (development of high throughput tools for identification of molecular targets) together with a collaboration with Novartis for vaccine development.

In addition, the investigator obtained important research support from the region (CODDIM), thus testifying for the importance of addressed problems.

Assessment of the unit's organisation and life:

The research focus and strategy is perfectly clear. It must be emphasized that the present structure, with a single permanent investigator, imposes a particular burden.

Interaction between non-permanent young investigators of widely varying background (microbiology, cell-biology, biophysics) is based on regular group meetings together with individual discussion.

Assessment of the unit's involvement in training through research

The team is fully involved in student training : a thesis has recently been defended (the recipient is now in a research laboratory in UK), two others are scheduled, and a fourth doctoral student will follow.

In addition, the principal investigator organized a course on host-pathogen interaction (M2 level) and participated a cell biology course in Argentina. He also organized a young investigator meeting.

Thus, the participation in training is remarkable, in view of the youth and research activity of the principal investigator.

Assessment of the five-year plan and strategy

The scientific project is very clearly written and reveals a broad and multidisciplinary scope, including several scale/levels:

(1) at the molecular scale, the project includes a study of the bacterial components directly involved in their interaction with host cells, which has to be done, and will rely on standard approaches, and a more original (and risky) attempt at disclosing direct effect of bacterial components on lipid bilayer, in collaboration with a leading biophysics group (P. Bassereau).

(2) an in vivo approach will be used to assess the importance of inflammation in host-pathogen interactions. The project is fairly original : since Neisseria is specific for human tissue, the work will be based on a humanized animal approach, consisting of grafting human skin on immunodeficient (scid) mice. This will allow to study the importance of inflammation (particularly two cytokines : IL-6 and IL-8) and coagulation. A first paper presenting this approach has just been accepted by PLoS Pathogens (impact >9), as mentioned during the oral presentation.

(3) A major problem is the crossing of the blood-brain barrier. The projects includes two complementary approaches that are both quite original : *(i)* building an animal model by injecting mice with stem cells expected to colonize the vasculature (in collaboration with another team of PARCC), and *(ii)* building on recent technological progress to try and obtain biomimetic models for capillary vessels, in order to allow excellent monitoring of bacterium-microvasculature interaction. In both cases, one must be very cautious in assessing the physiological significance of results.

(4) the fourth part consists of developing therapeutic approaches, including a high throughput approach (based on 96-well plates) to identify molecular targets for manipulation of bacterium/edothelium interaction. This will be the basis for vaccine development that will take advantage of the mouse model.

Altogether, this project appears a a suitable blend of highly original and more conventional projects. The only problem is to assess the feasibility of maintaining all research lines simultaneously. This will involve collaboration with excellent neighbouring laboratories (Pasteur institute, Curie Institute). These collaborations have been initiated and pursued for years.

Some potential problems and limitations have been well identified by the principal investigator (as indicated in the SWOT analysis) :

- The project is very ambitious and the management of an increasing group of young doctoral and postdoctoral students may be increasing difficult.

- Is is emphasized that the choice to focus on Neisseria restricts the extrapolation of expected conclusions to many different types of infection. However, it is recognized that it might be difficult to apply this ambitious problem simultaneously to different pathogen models.

- The humanized model may have limited validity and needs more characterization/validation. The human relevance of this artificial model may be a problem. Models need to be consolidated by other models.

Conclusion

The principal investigator has demonstrated his capacity to associate a broad range of pluridisciplinary methods to dissect a complex problem (understanding the invasive strategy of a successful pathogen). This is a strong basis for both extending basic investigations and developing therapeutic tools.

The major challenge during the future years will be to manage the team expansion. It will be important to recruit a minimal permanent staff.

Another point, that may be important in a more distant future, is that it might be attempted to study several bacterial models to reach more general enlightment on bacterium-host interaction.

Team 10 : Immunotherapy and anti-angiogenic therapy in oncology

Name of team leader: Mr Eric TARTOUR

workforce

Team 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	5	8	8
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	0	0
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1	1
N6: Other contractual staff (without research duties)	3	4	3
TOTAL N1 to N6	**12**	**14**	**13**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	8	9

• Detailed assessments

Assessment of scientific quality and outputs

The studies of Team 10 in the last 5 years have been focused on three major and interconnected topics: i), analysis of head and neck tumor microenvironment; ii), optimization of cancer vaccines; and, iii), angiogenesis and immunity.

The research has generated original findings that have challenged the current dogmas in the field. Thus, they have found that soluble IL-15 receptor acts in vitro as a pro-inflammatory molecule (Cancer Research 2008), therefore suggesting its role in promoting tumor progression, and encouraging the use of anti-inflammatory drugs in these patients.

A second interesting and unexpected finding is that tumor infiltrating T cells expressing the PD-1 molecule associate with a good prognosis in HPV+ head and neck cancer (Cancer Research 2012).

They have also found that combining a cancer vaccine with small inhibitors of the interaction between CCR4 and the corresponding chemokines led to the induction of a more powerful anti-tumor immunity (Blood 2011).

Team 10 has found in an orthotopic mouse model of head and neck cancer that delivery of cancer vaccines by intranasal route induced a more potent anti-tumor immunity than vaccines delivered intramuscularly (Science Translational Medicine 2013).

They have also demonstrated the feasibility and efficacy of a lentivral based vaccine against telomerase (Blood 2011; Clinical Cancer Research 2011).

Finally, another innovative observation is that VEGF has a direct proliferative effect on regulatory T cells, therefore suggesting a previously ignored mechanism of action of anti-angiogenic molecules (Cancer Research 2012).

In the 2008-2012 period, Team 10 has published 48 papers and additional 4 papers are in press. The PI is corresponding author of 9 full papers, 8 reviews and 1 correspondence paper (Journal of Clinical Oncology). Members of the team are first/last authors in additional 10 papers. All together, the publications of Team 10 represent a substantial advancement in the field of cancer immunology and immunotherapy, with relevant impacts to the clinic. They have been published in highly ranked international journal within the field of expertise (e.g., New England Journal of Medicine, Lancet Oncology, Journal of Clinical Oncology, Blood, Cancer Research, Clinical Cancer Research, European Urology, Journal of Immunology, Science Translational Medicine). In addition, these results have been communicated at several top international meetings and reviewed together with the related publications in several review articles.

Assessment of the unit's academic reputation and appeal

The PI and his team members have very active national and international scientific interactions.

The PI has been participating in the organization of the REVIAC days (French vaccinology clinical network) since 2009. He is also co-organizer of the forthcoming International Symposium of Vaccinology 2013 at the Pasteur Institute. A member of the team has been involved in the organization of the European Congress of Immunology 2012. The PI and his team members have been invited at numerous and prestigious international meetings.

The PI is in the editorial board of OncoImmunology, and acts as ad hoc reviewer for several national and international scientific journals (e.g., Cancer Research, Clinical Cancer Research, Journal of Immunology, European Journal of Immunology).

The PI has been working as reviewer also for several national and international institutions and charities (e.g., ARC, ANR, INCA, Ligue, INSERM, A*Star Singapore, Wellcome Trust UK).

The PI was coordinator for a research project from INCA (2006-2008). He was also a member of a FP6 Cancer immunotherapy consortium. He is responsible for a regional research network gathering 6 labs and clinical teams founded by the Canceropole and Ile de France region. His lab is member of the labex-Immuno-oncology. A member of the team coordinates the FP7 program Predict.

Since 2007, the team has trained 6 PhD students, 12 M2 students and 5 M1 students. Several members of the team have several teaching responsibility both at the undergraduate and graduate levels. The team has also trained 4 post-docs.

In the 2008-2012 period, Team 10 has published 12 reviews in qualified international journals (e.g., Cancer Metastasis Reviews, Cancer Research, Cancer Microenvironment).

The PI and other members of the team are well-established scientists in their fields of research and the PI has been invited to several national and international meetings.

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

Team 10 is well integrated in both the academic and industrial communities. It has several collaborations, some of which long standing, with non-academic partners (e.g., Roche, Cytune Pharma, GSK, Merk). These interactions represent a substantial financial support for the team, but do not appear to imbalance the research activity of the group.

The PI is inventor in patents EP1938836 and EP11305959 that are focused on the adjuvant effects of B subunit of Shiga toxin. These patents have been licensed to STxB Pharma. An additional patent has been filed.

The team is fully engaged in teaching in udergraduate and graduate programs. The PI is also author of a videotape course available on-line, which is aimed at favoring international distant registration and remote teaching. This course is now included as a training course for PhD students.

Assessment of the unit's organisation and life:

The team is mainly composed of physicians who share their activities among hospital, research and teaching. Indeed, PARCC is attached to the Hopital Europeen Georges Pompidou. Thus the research developed by the team is mainly translational.

The team is organised in three subgroups that develop independent research projects yet linked to and cross-fertilized by each others. Each subgroup has its dedicated personnel, although the PI is also directly involved in the research of the subgroup leaded by another member of the team. In addition, some transversal projects are developed to optimise the combination between cancer vaccines and anti-angiogenic treatments, and to foster cohesion of the team. The team benefits from several distinct expertises that are shared among the subgroups.

A weekly meeting gathers all the staff of the team (physicians, reserachers, post-docs, techicians and students), in which ongoing research and future plans are presented and discussed either by senior scientists or by students. A journal club is helded once a month. Group leaders meet once a quarter.

Students benefit from in-house training (e.g., cytometry, cell culture), seminars, some of them dedicated to students, and they are encouraged and supported to actively participate at national and international meetings (at least 1-2 times during their PhD).

All financial support to the team is shared among the subgroups.

Assessment of the unit's involvement in training through research

The team is directly involved in teaching at the undergraduate and graduate levels. Since 2007, the team has trained 6 PhD students, 12 M2 students and 5 M1 students. The team has also trained 4 post-docs.

One member of the team obtained his PhD with the PI's supervision and has taken a professorship position at Besancon. Another member, after the PhD became the head of INCA.

Assessment of the five-year plan and strategy

Team 10 has two main objectives for the next five years: understanding the mechanisms by which mucosal priming favors an efficacious immune response against mucosal tumors, and the identification of molecular mechanisms at the basis of the effects of anti-angiogenic drugs on tumor-induced immunosuppressive mechanisms. More in details the future research projects of the team will be the following: 1. Mechanisms explaining why mucosal vaccination is required to cure mucosal tumors (e.g., lung and colon cancers). 2. Immunosuppression in the tumor microenvironment: role of hypoxia and tumor endothelial cells in modulation by anti-angiogenic molecules. 2.1. Demonstration of a direct relationship in vivo between hypoxic tumor area and immunosuppressive cell infiltration. 2.2. Role of endothelial cells in tumor immune suppression and modulation of their phenotype. 2.3. Vessel normalization by anti-angiogenic molecules: role in the reversal of immunosuppression.

Finally, a transversal project fully financed by the industry will implement all the information obtained by the projects described above to design novel combined treatment of cancer vaccines and anti-angiogenic drugs.

The projects are well-designed, require integration of multidisciplinary approaches and development of new technology (e.g. in situ multiparametric immunofluorescence and quantum dots technology in collaboration with Institut Cochin, and a vessel normalization index that combines vascular/permeability flow and microvessel volume measured by MRI and hypoxia measurement).

Although the issue of hypoxia and immune suppression is not novel (e.g., see Chouaib S. et al. Front Immunol 2012), the team has available models and expertise to generate a more comprehensive analysis of this event. In particular, in situ multiparametric immunofluorescence and quantum dots technology will help to directly link the characteristics of the immune cell infiltrate to hypoxic tumor areas.

The projects are in line with the research recently developed by the team, and will likely generate several deliverables: information necessary to develop more effective vaccines for mucosal tumors; information on the effects of anti-angiogenic drugs on the hypothesized immunsuppressive activity of tumor associated endothelial cells; new biomarkers of efficacy of anti-angiogenic drugs-

The projects will be developed by adequate figures of personnel with the necessary expertise. The projects are fully financed by a Canceropole and Region Ile de France grant, and from Labex Immuno-Onco. Other financial support comes from industry (Roche, Pfizer).

In summary, the projects are well-designed, aim at investigating basic biological problem with direct relationships with the clinic, and are strongly supported by the industry.

SWOT analysis is adequate. The team has shown to adpat to the evolution of the research in its field.

General feasibility is high.

Conclusion

- **Strengths and opportunities.**

Team 10 is a medium size research group well focused on translational research aimed at designing novel immunotherapeutic approaches against cancer. The PI is internationally well renowned for his continuous contribution in the field of cancer immunotherapy both at the preclinical and clinical levels. This guarantees a network of international collaborations and funding opportunities.

Transfer of his group from the Veterinary School to PARCC that is so close to the European Georges Pompidou hospital has substantially increased the opportunities of the team to rapidly transfer knowledge from the bench to the bedside of cancer patients. Indeed, the group has a strong component of physician scientists whose clinical responsabilities are critical for the conduction of studies in humans. The projects developed by the group have also a strong potential to generate patents.

PARCC is a unique environment for cutting hedge research in the field of cardiovascular research. Given the recent interest of the group in investigating the potential synergy between anti-angiogenic drugs and cancer vaccines, this is a unique opportunity for the team to take advantage of close collaboration of top scientists expert in this field. Two renowned experts in endothelial cell biology will join the group soon and reinforce the expertise of the team.

The team is also well qualified to train MD and PhD students.

- **Weaknesses and threats.**

The team has only one researcher and no permanent technician. This might endanger research continuity.

Tumor immunology is a rather peripheral research theme at PARCC. Without stronger collaborations between Team 10 and other teams at PARCC there is a risk for isolation.

- **Recommendations.**

The team would benefit from a technician with a permanent position to maintain the continuity in research. More collaborations between Team 10 and other teams of the PARCC should be fostered to take full advantage of the highly qualified scientific environment of PARCC.

Team 11 : Percutaneous arterial repair

Name of team leader: Mr Antoine LAFONT

Workforce

Team 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	6	8	8
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	2	2	2
N4: Other professors (PREM, ECC, etc.)	0	1	1
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	1
N6: Other contractual staff (without research duties)	1	1	0
TOTAL N1 to N6	**11**	**14**	**13**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	6	8

Detailed assessments

Assessment of scientific quality and outputs

This team focuses on the use of cell therapy for tissue repair and medical devices (stents, aortic valves) to treat cardiovascular diseases. The approaches range from the use of preclinical animal models (pigs, rabbits) to human applications.

- Heterogeneous projects with basic science and human in vivo device studies.
- Weak tract records in both basic science and device.
- Highly competitive field, with several prestigious institutes and industries as competitors.
- This team does not lead the field, and has a weak national or international recognition.

Assessment of the unit's academic reputation and appeal

- Poor invited communication at leading international events.
- No network or national collaboration.
- No distinctions and awards.
- Weak track record in grant funding.
- Several patents issued by team leader.

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

- Creation of start-up companies.
- Weak and vague interactions with other PARCC partners.
- The team does not attract young talented PhD students.

Assessment of the unit's organisation and life

- Poorly organized unit, many focused on devices.

Assessment of the unit's involvement in training through research

- Very vague information provided, weak impression.

Assessment of the five-year plan and strategy

- The proposed projects are very vague.
- The projects are largely related to devices (inadequacy of goals and means).
- Weak academic and non-academic partnerships.
- The team projects are unlikely to be successful within the five-year's period.

Conclusion

- **Strengths and opportunities:**
  - Mainly based on patents.
  - Collaboration with Team 5.
- **Weaknesses and threats:**
  - Project mainly based on mechanical devices.
  - Weak scientific production.
  - Weak international recognition.
  - Weak collaboration partners other than PARCC.
- **Recommendations:**
  - The abdominal aortic aneurysm project to be merged with Team5.
  - Device projects should be linked with, and financed by industry partnership.

Team 12 : Pathophysiology of the renal tubule, homeostasis and blood pressure

Name of team leader: Mr Dominique ELADARI

Workforce

Team 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	0	1	1
N2: Permanent EPST or EPIC researchers and similar positions	1	2	2
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	0	1	1
N6: Other contractual staff (without research duties)	0	0	
TOTAL N1 to N6	**2**	**5**	**4**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	0	
Theses defended	0	
Postdoctoral students having spent at least 12 months in the unit	Liste non trouvée	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

- This team is a new team made of the association of three excellent researchers : two of them who were already working together at the Centre de recherche des Cordeliers and one who was previously in team 3 at PARCC. They share a common interest for the study of integrated and molecular physiology of ion transport in the kidney. The team leader is a MD-PhD, and is internationally known in the field of kidney physiology. He has a position as physician (MCU-PH) at HEGP. One PI is CR1 INSERM and is expert in kidney function studies using very sophisticated methods such as microperfusion of isolated nephrons. In the past four years, one of the most important contributions of of these two PIs was the identification of a novel thiazide sensitive NaCl transport mechanism in collecting duct intercalated cells that seems to have a significant role in the control of salt balance and blood pressure. The third PI, CR1 INSERM, is expert in molecular biology and mouse genome engineering. Her main contribution was the study of the regulation of renal and vascular function by the kinases of the WNK family. WNK mutations are associated with Familial Hyperkalemic Hypertension (FHHT) in humans. Recently, this PI participated in the identification of KLHL3 as a new gene involved in that form of hypertension and she disclosed the role of the KLHL3 protein in the ubiquitination of distal renal transporters.

- The production of the team members in the last 5 years is very good, with 10 papers published in journals with IF>9 (1 Nat Genet, 2JCI, 1 Cell Metab, 4 PNAS, 1 EMBO Mol Med, 1 Annu. Rev) and more than 24 publications in journals with IF<9. In addition, 1 JCI, 1 PNAS are under review. In almost all the publications in high ranked journals, the team members are eitheir in first or last position.

- The team members have also been successful in getting financial supports, 4 ANR fundings (2007-10, 2010-13, 2012-15 and 2013-2015) for a total of more than 1 million € and several other fundings for about 200 000€.

- Team members participated together to a "Leducq Fundation Networks of Excellence (Transatlantic Network of Hypertension) during the period 2008-2012. They participated to 2 FP7 programs in the period 2008-2012. They also obtained a PICS financing travel costs for a collaboration with a laboratory in Moscow.

Assessment of the unit's academic reputation and appeal

- The team members' visibility is assessed by numerous invitations to international meetings (15 invitations) and organization of meetings (2). The team leader is president of the scientific council of the French Nephrology Society and member of several scientific councils. He is also member of the editorial boards of very important journals in the renal field (J. Nephrol, Am. J. Physiol. Renal Physiol. And Kidney International).

- The team leader is member of the CSS4 INSERM comittee.

- They have set a large number of national (5) and international collaborations (10) in basic science and also in clinical investigation, in particular with the departments of Human Physiology, of Genetic, of Nephrology-Vascular diseases-Hypertension and the Clinical Investigation Center at HEGP. International collaborations include collaborartions with higly renowned laboratories in Yale, New York, Rochester in the US or Berlin, Jena or Napoli in Europe.

- All the team PIs obtained the prime of scientific excellence during the last 5 years.

- One PI has been awarded the « prix de la Société de Néphrologie ».

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

- The PIs participated in large public events organized by INSERM (Ethics and Genetics….). There are no mentions of patents or indicators on the use of transferred knowledge.

Assessment of the unit's organisation and life

- The lab is well organized with 3 PIs having their own project but actively collaborating together. They have complementary skills and expertises. The merging of the 3 PIs is evident (they work together for several years) and the move timely. The team leader is clearly identified.

Assessment of the unit's involvement in training through research

- The team members supervised many bachelors and master students during the last 5 years (>30), 5 Ph.D students and 6 postdoctoral fellows and they also trained several foreign students.

- The team members also actively participate in teaching tasks (more than 100 hours a year).

Assessment of the five-year plan and strategy

The creation of this new team and its localization in the environment of HEGP will allow to develop an original project with far-reaching fundamental and translational implications in the understanding and treatment of hypertension.

The five-year plan and the strategy of the team is straightforward.

The project maintains the focus on regulation of distal renal transporters and implications on blood pressure. It proposes ambitious and original developments along three main lines : i) characterization of NaCl transport by intercalated cells and its regulation, ii) paracrine signalling controling blood pressure and iii) mechanisms linking blood pressure to K+ and acid-base homeostasis. In addition, a fourth line will be developped by the team to integrate human aspects in the basic research. This translational aspect between research and the clinic is somewhat the rule for all teams at PARCC and the position of the team leader as clinician at HEGP will favour this new development.

A very good and clever physiological approach taking advantage of genetically modified animal models will be developped to realize the projects. This functional approach will be implemented by biochemical, proteomic, phosphoproteomic large scale studies to analyse the dynamic network of WNK kinases and of the KLHL3-dependent ubiquitination in the distal nephron. For this issue, a very potent technique, the Complex Object Parametric Analyzer and Sorter (COPAS), will allow purifying DCT cells from transgenic mice expressing GFP in the collecting duct.

The 3 PIs have built efficient networks. They will take also adavantage of the hospital position of the team leader and of the location in the HEGP environment to develop a translational research.

The SWOT analysis is realistic: the team leader identified clearly the problems and proposes solutions.

This young team has a great potential to produce an excellent science in the coming years.

Conclusions

- **Strengths and opportunities**

  - Internationally known investigators who made important contribution in the field of kidney ion transport
  - The projects are funded with collaborations already in place.
  - With 3 permanent investigators, 3 postdocs and one technician, the team has the human ressources to realize ambitious projects.
  - The investigators have a solid experience in renal physiology and management of murine models allowing a continuum from genes to animal in vivo studies.
  - Translational research based on clinical activity of the team leader.
  - The team leader has the capacity to develop new collaborations with French and international researchers.

- **Weaknesses and threats**

  - As identified by the team researchers themselves, the crucial requirement for animal experimentation may be a serious limit in the coming years. Studies will become more and more expensive and animal handling more and more restricted.
  - Even though kidney function is crucial for the control of blood pressure and also for maintaining the body homeostasis, studying kidney physiology is not really fashionable these days. The discipline declines and this fact may limit the publications in high-impact journals and the opportunities for funding. However, the team presents a really modern approach of this physiology that remains crucial to public health. It is important that good teams like this one continue to keep alive this field.

- **Recommendations**

  - It is important to consider developing projects without or with less animal experimentation.
  - If the general environment is excellent at PARCC, the kidney environment itself is probably less efficient than it could be at the Institut des Cordeliers from where two PIs are coming. It is important for them to keep close collaborations with people in their previous institute.

Team 13 : Pheochromocytomas and paragangliomas: from genetics to molecular targeted therapies

Name of team leader: Ms Anne-Paule GIMENEZ-ROQUEPLO

Workforce

Team 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	2	2	2
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	0
N4: Other professors (PREM, ECC, etc.)	0	3	3
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	0	0
N6: Other contractual staff (without research duties)	0	0	
TOTAL N1 to N6	**5**	**7**	**6**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	3	2

• Detailed assessments

Assessment of scientific quality and outputs

During the previous 4-yr contract, the PI was managing a small research group focusing on the genetics of pheochromocytomas (PCC) and paragangliomas (PGL) within team 3. Following the recommendations of the Scientific Advisory Board of PARCC, the PI is now applying for an independent research team within the PARCC. The PI is Professor of Genetics (PU-PH) affiliated to Hôpital Européen Georges Pompidou who benefits since 10 years of a "Contrat d'Interface INSERM pour Hospitaliers" which allows her to spend less time on clinics and more time on research. Her group is composed of 1 full-time INSERM researcher, 4 clinicians, 2 technicians, 4 PhD and Master students and 1-3 post-docs. During the last five years (2008-2012), this group has published 29 original articles, mostly in top journals of endocrinology and genetics. These include 5 articles as first or last author in J. Clin Endocrinol. Metab., 3 in Hum. Mol. Genet. and 1 in Lancet Oncol. In 2009, the group identified a novel susceptibility gene for PCC/PGL, namely SDHA encoding succinate dehydrogenase A, that is mutated in 3% of the cases. The team also lead a large multicentric study (1694 patients, 17 referral centers) in Europe that allowed to show for the first time that, besides the germinal mutations, somatic mutations in the VHL, RET or NF1 genes are found in 35% of sporadic PCC/PGL tumors. The group has also put a strong effort on the generation of transgenic animal models and could establish that double heterozygous KO mice for Sdhb and Pten develop early and metastatic PCC/PGL. This paves the way for evaluating targeted therapies on these cancers.

Assessment of the unit's academic reputation and appeal

As a chairman of the French PGL-Net clinical network and as a coordinator of the PCC/PGL working group of the european clinical network ENS@T, the PI has gained a strong international recognition from her peers and is in a favorable position for coordinating multicentric european studies.

The team's contributions to the field of PCC/PGL are well recognized as major breakthroughs with strong clinical implications in the diagnosis of patients. The PI and team members were Invited 9 times to give lectures at international meetings, including one at the International Congress of Endocrinology in Kyoto, Japan (March 2010). Pr Gimenez-Roqueplo also received the The Endocrine Society-Pfizer international award for the Excellence in opublished clinical research in the Journal of Clinical Endocrinology and Metabolism, which was given to her during the 2010 Endocrine Society Meeting in San Diego (USA).

The PI and team members organized the Third International Symposium on Pheochromocytomas and Paragangliomas (ISP 2011) in September 2011 in Paris. This meeting gathered 213 participants from 28 countries.

The team has published several reviews in endocrinology journals (J Clin Endocrinol Metab, Endocr Pathol, Horm Metab Res, Best Practice & Res Clin Endocrinol & Metab).

The team particpates in a European network research program on adrenocortical tumors (ENS@T-Cancer, FP7).

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

The team is strongly linked to the clinical Departments of Hypertension and Genetics of the Euopean Hospital Georges Pompidou (HEGP). This allows a priviledged access to the patients suffering from PCC or PGL since the PI has set up a specific multidisciplinary consultation for oncogenetic counsel to PCC/PGL families (150-200 patients/yr). This allows also to very rapidly translate the results from basic research of susceptibility genes into an adapted clinical practice.

Through the COMETE network set up by a member of the team, the team has contributed to build the largest and best characterized collection of adrenal tumors worldwide, including a large collection of PCC. It has therefore a priviledged access to this tumor bank.

Assessment of the unit's organisation and life

The team is headed by a clinician (the PI), but relies also on the expertise in angiogenesis of a dynamlc young INSERM researcher. This tandem seems to work well and to be extremely complementary. The team lacks some permanent technical support that would greatly help for the studies on the animal models.

Assessment of the unit's involvement in training through research

Only 2 (MD)PhD students during the last 5yr-contract. Both published well. Both stayed in the team. Formation of PhD students and participation to teaching activities should be improved.

Assessment of the five-year plan and strategy

The project has two main goals: to pursue the genetic analyses of the germinal and somatic mutations responsible for PCC/PGL and to improve the basic understanding of the biology of these diseases. The first objective will benefit from the combined analysis of different omics-based sudies of the human tumor collections from the COMETE and ENS@T networks (transcriptome, exome sequencing, methylome). The second objective will be favored by the recent development of an animal model (double heterozygous mutants SDH-B/PTEN) of SDH-B-mutated PCCs. The resulting progress in the genetic classification and in the understanding of the biology of the different tumor subtypes will also allow to evaluate some targeted therapies. The project is therefore original, well positioned in the international oompetition, and realistic. The team has raised funding from several agencies (CIT program from the Ligue contre le Cancer, ANR-Genopat, FP7 EU program, ANR Jeune Chercheur) that secures the feasibility of the project.

Conclusion

- **Strengths and opportunities:**

A well-focused team devoted to the study of pheochromocytomas/paragangliomas.

Privileged access to the largest and best annotated collection of these tumors via the COMETE network.

Leadership position in European networks.

Publication of some breakthrough papers in the field: first description of SDH-A mutations, first description of somatic mutation.

Large use of different omics to decipher the genetic alterations of these tumors.

Recent development of a mouse model for pheochromocytomas.

Original hypothesis to explain the biology of SDH-B mutated (the most aggressive form) pheochromocytomas (pseudo-hypoxia).

Opportunity to evaluate personalized (mutation-dependent) targeted therapies.

Good complementarity in the leadership of the team between a clinician (geneticist) and a young basic scientist.

Good integration in PARCC.

Strong funding.

Excellent translational activity (the lab-bench discoveries are rapidly translated into modified medical practice).

- **Weaknesses and threats:**

Limited support by permanent technical staff.

Few PhD students formed during the last 5yr-contract.

Insufficient implication in teaching activities.

Risk of considering the recently developed animal model as the sole start point for future research. Although this mouse model required a time- and energy-consuming effort and represents a real achievement, it may still not be the most appropriate one and the team should not close the door to analyzing other combinations of gene deletions in the future.

On the long term (beyond the 2014-2018 contract), the study of the PCC/PGL may become a too narrow field as the major discoveries will have been made. So, the team should start thinking about how they could diversify their centers of interest.

- **Recommendations:**

Recruit a permanent technician.

Put an effort on the formation of PhD students.

Get more involved in teaching activities.

Keep developing new animal models of PCC/PGL based on the increasing knowledge of the genetic alterations observed in human tumors/patients.

Start thinking about alternate research domains to the PCC/PGL field.

Team 14 : Genetics mechanisms of aldosterone-related disorders

Name of team leader: Ms Maria-Christina ZENNARO

Workforce

Team 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	0	0	0
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	2	2	1
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	2	2
N6: Other contractual staff (without research duties)	1	0	
TOTAL N1 to N6	**7**	**5**	**4**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

Since the separation as an independent team from team 3 in 2008, the group has developed nicely to become internationally renowned in the field of aldosterone research.

The major breakthroughs concern: 1) the identification of a mutation in the mineralocorticoid receptor (MR) as cause of pseudohyperaldosteronism-1 (PHA-1) (JCEM 2003); 2) the identification of the prevalence of mutations in the KCNJ5 potassium channel in the large collection of aldosterone-producing adenoma casuing human primary aldosteronism (PA) made available by the ENSAT network (lHypertension 2012).

Overall the scientific quality is good-to-excellent, particularly in the field of PHA-1, where this group has been one of the leader worldwide with the highest record of publications (n=19) in peer-reviewed journals.

In the field of PA the team proposed a large omics approach and has the potential to be successful, although it is not clear what will happen afterward in case candidate gene(s) will be pinpointed and how the data will be analysed. The chances for success depend much on collaboration with clinicians and existing networks, the degree of interactions with which, particularly at the level of phenotypic characterization, appears to be satisfactorily developed.

The PI has 10 publications in peer-reviewed journals with an IF>4 in 2011 and 2012; in 4 of them the PI was last author (Endocrinology, Hypertension (2), JCEM). From 2007 to 2102 the PI had 20 publications in 8 of which as last author. However, it has to be noted that the evaluation of this team, as compared to the other teams at PARCC by common bibliometric indexes is hampered by the fact that this type of research, with regard to very rare diseases, is targeted to niche or subspecialty journals that do not have a high IF.

Assessment of the unit's academic reputation and appeal

The standing of the group in terms of international reputation, quotations, and visibility is excellent.

The PI has successfully managed research project at the european level within the ENSAT network and is also involved in a number of national research projects.

The PI obtained the Prix René Descartes young investigators award in 2007, has chaired two international conferences (the US Aldosterone Conference and the European Section of Aldosterone Council) and has been in the scientific committee of 8 congresses. She is in the Editorial Board of Endocrinology, and acts as referee for the JCEM, Hypertension, and J. Mol Endocrinology. She has also published some invited review articles including 3 recent ones in Hypertension, Circulation Research, and Endocrinology. The lecturing reputation is well established as testified by invitation to lecturing at seven international conferences.

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

The methods proposed are original and have the potential to generate novel knowledge and products for diagnosis and treatment of disorders related to MR signalling, including primary aldosteronism. At present, there seem to be no joint ventures with non-academic partners, but there are obvious strong long-standing collaborations with other leading groups worldwide for PHA-1 and in Europe for PA. The identification of the novel mechanisms of PHA-1 has the potential of generating new research issues for the unit and for the scientific community at large in this very rare disease.

The laboratory is said to be the only one in Europe for the genetic testing of patients with PHA-1, which makes this team valuable for the community at large in Europe. The potential for accreditation and/or certification of procedures implemented by the unit (ISO standards) is good.

Assessment of the unit's organisation and life

The team is organised with coherent and logical scientific objectives in mind. The collaborations with clinical units at Hopital GP involved in the phenotyping of patients suspected to have PHA-1 and with the hypertension unit are major assets in this proposal, as is the integration in large networks for the collection of PA cases as ENSAT and COMETE.

The premises for the team's scientific activities and staff needs are appropriate. However, the team is undersized for the proposed goals: besides the PI there are 2 post-doc and 1 technician for the PHA-1 projects and 6 post-doc in the PA projects.

Assessment of the unit's involvement in training through research

The team is effective in student guidance and supervision. However, it was unable to raise any younger investigators to a tenure position thus far, likely because of its only recent branching from a previous team. Recruitment of further staff is to be recommended in the future and there seems to be plans in this direction.

There is a consistent internal auditing and discussion of the on-going research within and outside the team and PARCC that is likely to lead to identify recent scientific progress to be included in teaching.

The team has clearly been involved in disseminating novel knowledge in the field of MR biology and of PA through conferences at the national and international level. The degree of involvement and responsibility in international training networks is excellent.

Assessment of the five-year plan and strategy

The current proposal entails four scientific projects:

- two on PHA-1:

  - i) identification of new genes and signalling pathway in PHA-1;
  - ii) mechanistic determinants of transcriptioanl remodeling by MR variants).

- two on PA:

  - i) integrated genetic and genomic analysis of PA;
  - ii) regulation of K channels by ubiquitination.

The theoretical basis for the study proposed is sound and the proposed and methodological approach is based on state-of the-art technologies. The integration of clinical and basic research renders this project appealing and competitive at the international level, particularly as compared with the US research. However, it is not entirely clear how the project will develop into patients' care, thus entailing an example of true translational medicine.

The general feasibility of the proposed five-year plan is reasonable, but an expansion of the currently limited human resources, which entail only the PI as an established investigator, should be pursued. Currently, the available resources are planned to be devoted to 4 different projects, all of which are very time-consuming and demanding. For example, even by relying on collaborations, conducting GWAS, miRnomics, SNParrays and transcriptome data in a huge number of familial and sporadic forms of primary aldosteronism is a challenging task, both in terms of data generation and analysis. In the likely case that candidate genes will be identified, the work to prove their functional role will be a very demanding and time-consuming task. However, the PI has full capacity for adaptation and change in strategic direction in response to results of ongoing research, and the team is well inserted in an efficient netword of collaborations either within the PARCC and externally.

The quality of the SWOT analysis is reasonable and denotes a clear understaning of the potential and limitations of the project.

All together, the series of projects are original and innovative, and reasonably feasible within the 5 yr timeframe. Major risks identified in the project include the lack of strong preliminary data on the ubiquitination project and the strong international competition.

Conclusion

- **Strengths and opportunities:**

Overall the team and the proposed research appear to be excellent. Strengths are represented by 1) a cutting edge research in the field of PHA-1 and the dissection of mineralocorticoid receptor biology, where the team has a recognized leadership; 2) the access to necessary technology and to a large collection of primary aldosteronism patients.

Weaknesses relate to the limited manpower in relation to the ambitious work proposed.

- **Weaknesses and threats:**

Potential threats are represented by the tight completion in this field, which might cause some of the goals to be out dated when they will be reached, and by the tapering investment of the pharma industry in the field of cardiovascular diseases in general, and even more so in the field of MR antagonists, which will decrease the chances of getting partnerships and external funding.

- **Recommendations:**

A tight integration with the clinical collaborators is advised and the recruitment of other established investigators would be instrumental for success.

5 • Conduct of the visit

Visit dates: 15-16 january 2013

Start : 15 january 2013 à 08:00

End : 16 january 2013 à 17:15

Institution : UMR_S970, PARCC-INSERM U970, 56, rue Leblanc, 75015 Paris

Specific premises visited: Centre du PARCC

Conduct or programme of visit:

Tuesday, January 15, 2013

8:00 – 8:30	Welcome
8:30 – 9:00	Private AERES Committee Meeting (closed for AERES members only)
9:00 – 10:00	PARCC 2009-2012 Achievements and 2014-2018 Project Mr Alain TEDGUI

I. Angiogenesis & Microcirculation

10:00 – 10:45	Mr Philippe MENASCHE/Mr Jean-Sébastien SILVESTRE
10:45 – 11:30	Mr Olivier CLEMENT
11:30 – 11:45	Coffee Break
11:45 – 12:30	Ms Anne-Paule GIMENEZ-ROQUEPLO
12:30 – 13:15	Mr Eric TARTOUR
13:15 – 14:00	Lunch

II. Kidney & Hypertension

14:00 – 14:45	Dominique ELADARI
14:45 – 15:30	Ms Maria-Christina ZENNARO
15:30 – 16:15	Mr Eric CAMERER/Mr Pierre-Louis THARAUX
16:15 – 16:30	Coffee Break

III. Biomarkers & Epidemiology

16:30 – 17:15	Mr Stéphane LAURENT
17:15 – 18:00	Mr Xavier JOUVEN
18:00	Return to hotel

Wednesday, January 16, 2013

8:00 – 8:15	Arrive at the PARCC
IV. Arterial Diseases	
8:30 – 9:15	Mr Ziad MALLAT/Mr Alain TEDGUI
9:15 – 10:00	Ms Chantal BOULANGER
10:00 – 10:45	Mr Xavier JEUNEMAITRE
10:45 – 11:00	Coffee Break
11:00 – 11:45	Mr Guillaume DUMENIL
11:45 – 12:30	Mr Antoine LAFONT
12:30 – 13:30	LUNCH
13:30 – 14:15	Meeting of AERES Members with ITA (room A)
	Meeting with PhD Students/Post-docs (room B)
14:15 – 15:45	Meeting of AERES members with INSERM and University Paris Descartes representatives
14:45 – 17:15	Private AERES Committee Meeting (closed for AERES members only)

Specific points to be mentioned:

Absence de Mr Michel BURNIER, Lausanne, Suisse lors de la visite.

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

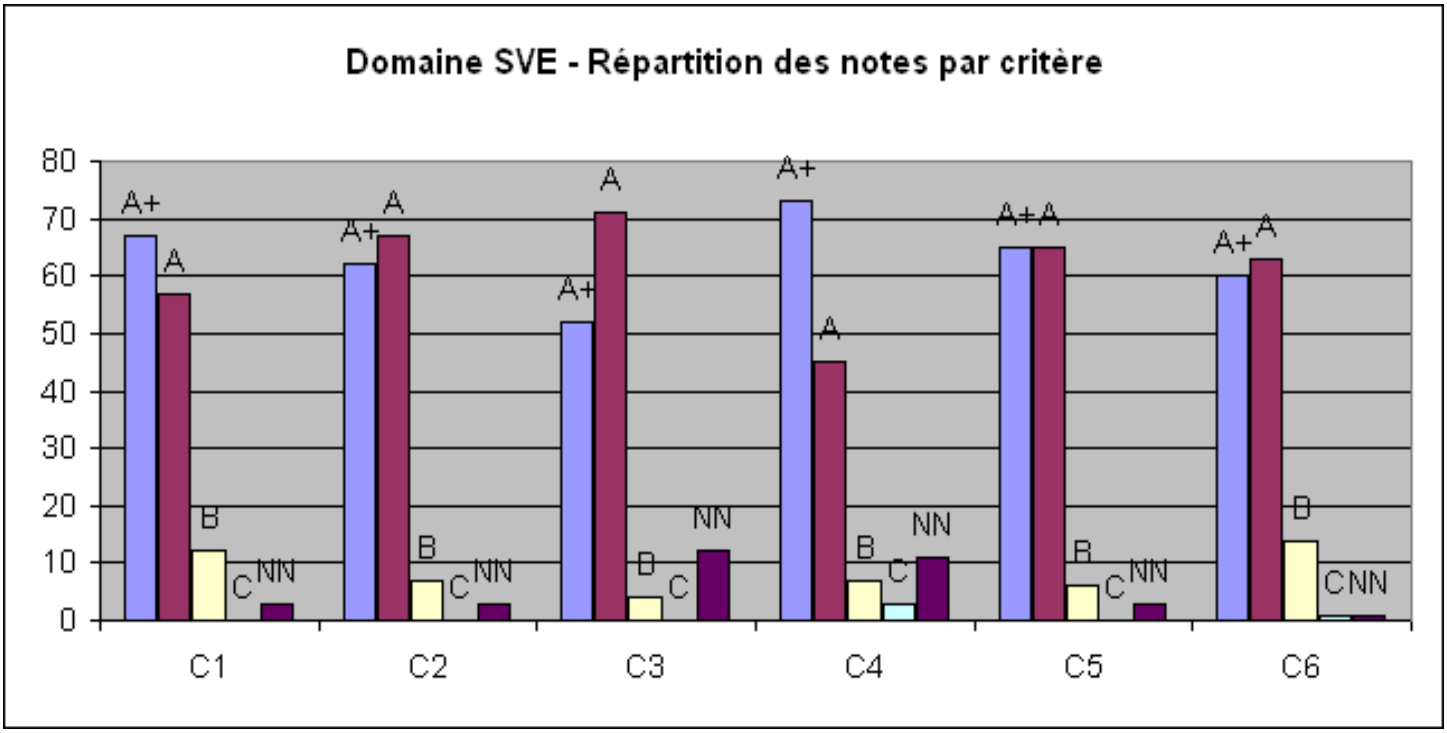
Grades

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



7 • Supervising bodies' general comments

UNIVERSITÉ PARIS DESCARTES

Vice Président du Conseil Scientifique

Paris le 16.04.2013

Vos ref : S2PUR140006223 – Paris
Centre de Recherche
Cardiovasculaire- 0751721N

Monsieur Pierre GLAUDES
Directeur de la section des unités de recherche
Agence d'Evaluation de la Recherche et de l'Enseignement Supérieur
20, rue Vivienne
75002 PARIS

Monsieur le Directeur

Je vous adresse mes remerciements pour la qualité du rapport d'évaluation fourni à l'issue de la visite du comité d'expertise concernant l'unité « Paris Centre de recherche Cardiovasculaire »

Vous trouverez ci-joint les réponses du Directeur du Centre, Alain TEDGUI, auxquelles le Président et moi-même n'avons aucune remarque particulière à rajouter.

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

Le Vice Président du Conseil Scientifique

Stefano Marullo, DM, DesSci

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Réponses au rapport AERES concernant le Paris-Cardiovascular research Center (PARCC) – INSERM UMR_S970

2. Observations de portée générale

Fait à Paris le 12 avril 2013

Alain Tedgui

AERES report on team 10: Immunotherapy and anti-angiogenic therapy in oncology
Name of team leader: Prof. Eric TARTOUR

I firstly would like to thank the committee for the report with which I fully agree.
The committee recommends the "recruitment of a technician with permanent position to maintain the continuity in research". I would like to mention that a position for a permanent technician has just be opened by the Paris Descartes Medical Faculty for my team with effect from September 2013.
I am aware that stronger collaboration is important for a good integration of my team in the PARCC. Since my arrival in PARCC in 2010, three joint publications with other teams have been published (Sandoval et al Sci Transl Med 2013, Korpershoek E et al J Clin Endoc Metab 2011, Seguier et al Plos One in revision). Two collaborations recently started with team 5 and 8 in order to generate preliminary results before submitting applications for funding of these projects.

AERES report on team 11: Percutaneous arterial repair
Name of team leader: Prof. Antoine LAFONT

Suite au rapport de l'AERES réalisé en 2013 pour le Centre de Recherche U970, je tiens à utiliser le droit de réponse, en tant que responsable de l'équipe n°10 « réparation artérielle », car je considère ce rapport trop négatif par rapport à notre activité et un peu surprenant quand il est comparé à celui réalisé en 2011 par la même agence AERES et qui avait abouti à la recréation de notre équipe en 2012 selon les recommandations du conseil scientifique de l'INSERM, confirmée par le Directeur Général de l'INSERM, avec l'avis favorable de l'ITMO « technologies pour la santé » et du Président de l'Université Paris Descartes.

Les arguments suivants me semblent devoir être mentionnés :

1-le comité de l'AERES 2013 ne comprenait pas d'expert véritable pour juger nos travaux:
Le comité qui nous a expertisé était composé d'experts de renommée internationale sur le plan fondamental, mais il n'y avait pas d'experts orientés sur la valorisation et l'innovation technologique. Il n'y avait pas non plus de représentant de l'ITMO « technologies pour la santé » (nous sommes la seule équipe appartenant à cette ITMO). Le Pr François Mach qui nous a évalué, n'avait pas à mon avis l'expertise requise dans le domaine de la technologie en cardiologie interventionnelle:
-De manière générale, il ne conçoit pas l'innovation comme prioritaire et a manifesté un mépris d'emblée lors de l'audition.
-Il n'a pas considéré que la conception d'un stent biorésorbable devait être développée à l'INSERM, pas plus qu'une nouvelle valve aortique percutanée, que la recherche institutionnelle ne devait pas participer au développement industriel, que nous n'étions pas en mesure de lutter contre la concurrence internationale : nous étions selon lui hors-sujet. Pourtant, depuis 2011, nous avons pu démontrer l'originalité de notre stent biorésorbable, et obtenir de l'ANSM l'autorisation d'un essai chez l'homme, actuellement en cours dans 5 centres français. Cette compétitivité, nous avons pu l'avoir grâce à la création de la startup ART (que nous avons créée via nos institutions), lever 15 millions € en 8 ans, et développer un prototype selon nos propres critères, en s'affranchissant de l'influence de tout grand groupe industriel international. Les données précliniques ont suscité une collaboration avec le Pr Abdul Barakat (Ecole Polytechnique), sur le comportement mécanique du stent au cours du temps, avec un projet en cours, et une thèse en cotutelle.
-Le rapporteur a considéré de plus qu' il n y avait pas d'innovation car à son avis, ce produit était déjà en vente depuis longtemps ; il a reconnu qu'il confondait stent en polymère biorésorbable et stent métallique actif recouvert d'un revêtement biorésorbable, et que ce n'était pas de sa compétence…
-L'approche thérapie cellulaire a été occultée par le rapporteur, alors qu'elle se situe au cœur de notre activité au PARCC. Pas de commentaire, pas de question. Celle-ci est pourtant soutenue par 3 ANR consécutifs, dont un en cours, en collaboration avec le Collège de de France.
En bref, il semblait qu'il n'y ait pas à ses yeux, de place pour la technologie de la santé dans une unité INSERM.

2-Discordances avec le comité de l'AERES 2011, le Scientific Advisory Board, et le DHU cardiovasculaire:
En 2011, l'AERES a clairement identifié nos faiblesses, nos forces, les menaces et les opportunités et nous a classé A (qualité scientifique et production: A ; rayonnement & attractivité : A ; stratégie, gouvernance : B, appréciation du projet : A). Cette approche d'innovation technologique transversale non prise en compte par le rapporteur en 2013 a été reconnue et encouragée par le

conseil scientifique de l'INSERM en 2011 et nous a reconduit au sein de l'U970 où nous apportons cette spécificité, en ligne avec une recherche transversale forte vers l'HEGP (pôle clinique cardiovasculaire). L'environnement du PARCC a été, et continue d'être un atout majeur pour progresser, tant au niveau de l'aide reçue, que de son excellence scientifique. Il est surprenant que l'AERES tire des conclusions opposées en 2013.
Nous avons eu 4 évaluations depuis 2006. Lorsque le comité d'évaluation était sélectionné spécifiquement sur notre thématique, l'avis de l'INSERM a toujours été favorable (2006 et 2011). Lorsque nous étions évalués par le comité sélectionné de façon plus générale pour l'U970 (sans experts dans notre spécificité) nous avons eu un avis défavorable (2008 et 2013). L'effort lié à ces multiples évaluations a été certes bénéfique pour nous améliorer, mais, compte tenu de la taille de l'équipe, a représenté un travail considérable qui a clairement limité notre capacité à publier, paralysé le recrutement de doctorants, de postdocs, et de chercheurs statutaires. Depuis notre recréation en 2012, nous avons recommencé à recruter deux doctorants (un premier a commencé), déposé des projets, inclus les chirurgiens cardiaques et les radiologues interventionnels de l'HEGP et de Necker (cardiopédiatrie), et suivi l'orientation donnée par le Conseil Scientifique de l'INSERM et du Scientific Advisory Board (SAB) de l'U970. Nous avons eu deux visites du SAB ; notre équipe a été reconnue comme « the most translational of all groups; fits well in the PARCC ». Ils ont encouragé l'effort d'innovation et mentionné le nombre de brevets sous licence.
Pour être en phase avec les autres équipes, nous avons participé à l'évaluation 2013.
A titre personnel, j'ai pris les dispositions suivantes afin de me consacrer plus à mon équipe: j'ai quitté en 2012 mes fonctions de Directeur du plateau technique interventionnel à l'Hôpital Européen Georges Pompidou, et toutes fonctions au sein de la société Européenne de Cardiologie.
Enfin, nous sommes hors sujet pour l'AERES en 2013, et pourtant notre thématique sur le stent biorésorbable représente une des innovations incluses (work package 3) dans le projet du DHU cardiovasculaire « pathologies artérielles rares et communes » présenté par le Pr Menasché à l'appel d'offres et sélectionné début 2013 pour un contrat de 5 ans par un jury international sous l'égide de l'APHP et de l'INSERM.

Tout en reconnaissant un manque de publications, mais pas d'innovations et de brevets, je souhaiterais que la Commission Spécialisée n°8/l'ITMO « technologies pour la santé » auxquels je suis rattaché puisse prendre connaissance de mes réponses afin d'éclairer le Conseil Scientifique au mieux sur la décision de création ou de non-création de mon équipe de recherche.

A Lafont

AERES report on team 14: Genetic mechanisms of aldosterone-related disorders
Name of team leader: Dr. Maria-Christina ZENNARO

Answers to the report:
The team leader thanks the committee for the evaluation. For completeness, a few minor comments and corrections are listed below:

Assessment of scientific quality and output:
The major breakthrough since 2009, in addition to those mentioned by the reviewer, concern: 1) the identification of the first case of severe autosomal recessive pseudohypoaldosteronism (PHA-1) linked to mutations in the mineralocorticoid receptor (MR) (*J Am Soc Nephrol 2011*); 2) The discovery of two new genes mutated in 7% of aldosterone producing adenoma (*Nat Genet 2013*; accepted in December 2012 and presented at the AERES visit).
Concerning the publications in 2011 and 2012, the PI was last author in 6 publications (*Endocrinology* (2 – one co-last authorship), *Hypertension* (2), *J Clin Endocrinol Metab*, *J Am Soc Nephrol*). One additional publication in *Nat Genet* was accepted in December 2012 and presented at the AERES visit. From 2007-2012, the PI had 21 publications, with 9 publications as last author.

Assessment of the unit's academic reputation and appeal:
The PI is head of the "aldosterone producing adenoma" working group of the European network for the study of adrenal tumors (ENS@T, elected in 2011), member of the executive committee of the International Aldosterone Conference (since 2012) and president of ESAC (European Section of Aldosterone Council) France. She has not obtained the Prix René Descartes, but is in the scientific committee of the Congrès des jeunes Chercheurs en Biologie – Prix René Descartes and has organized the annual congress in 2012. She has been invited to lecturing at 14 international conferences since 2009.

Assessment of the unit's organization and life:
One senior non-tenured researcher, Sheerazed Boulkroun, is currently applying for a tenured position at INSERM as indicated in the application. Two clinicians, Laurence Amar (Hypertension unit) and Tchao Meatchi (Pathology department) are also part of the team.

Assessment of the unit's involvement in training and research:
One senior non-tenured researcher is applying for a tenured position at INSERM as indicated in the application.

Assessment of the five-year plan and strategy:
In contrast to what indicated by the expert in his report, the genomic high throughput data on which the project on primary aldosteronism relies on have already been acquired. Primary data analyses have already been performed, thus rendering the indicated objectives feasible. Translation to clinical practice will be achieved through the clinical activity of the PI at the Genetics department of the HEGP and that of other members of the team (L. Amar, T. Meatchi), and established collaborations with the Genetics department, the Hypertension unit, and the Clinical Investigation Center at the HEGP. Examples of such translational research include the transfer (which is unique in Europe) of the genetic testing for *KCNJ5* mutations in patients with familial hyperaldosteronism type 3 to the Genetics department within one year after the discovery of gene mutations.