

EVALUATION REPORT OF THE UNIT
PARCC – Paris centre de recherche
cardiovasculaire

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Université Paris Cité,
Institut national de la santé et de la recherche
médicale – Inserm

EVALUATION CAMPAIGN 2023-2024
GROUP D

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In the name of the expert committee¹ :

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For the Hcéres² :

Stéphane Le Bouler, acting president

Pursuant to Articles R. 114-15 and R. 114-10 of the French Research Code, evaluation reports drawn up by expert committees are signed by the chairmen of these committees and countersigned by the President of Hcéres.

To make the document easier to read, the names used in this report to designate functions, professions or responsibilities (expert, researcher, teacher-researcher, professor, lecturer, engineer, technician, director, doctoral student, etc.) are used in a generic sense and have a neutral value.

This report is the result of the unit's evaluation by the expert committee, the composition of which is specified below. The appreciations it contains are the expression of the independent and collegial deliberation of this committee. The numbers in this report are the certified exact data extracted from the deposited files by the supervising body on behalf of the unit.

MEMBERS OF THE EXPERT COMMITTEE

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CHARACTERISATION OF THE UNIT

- Name: Paris Centre de Recherche Cardiovasculaire
- Acronym: PARCC
- Label and number: UMR 970
- Composition of the executive team: Chantal Boulanger

SCIENTIFIC PANELS OF THE UNIT

SVE3 / CSS3 Sciences du vivant et environnement

SVE6 / CSS6 Physiologie et physiopathologie humaine, vieillissement

THEMES OF THE UNIT

The Unit declares that it has four main research areas: 1) Vascular disease; 2) Cardiac Disease; 3) Kidney disease; and 4) Hypertension. All Teams contribute to one or more of these research areas. Additionally, the Teams also contribute to cross-cutting research programs such as Immunity and Inflammation; Prevention and Biomarkers; and Imaging.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The Paris Cardiovascular Research Center (PARCC) –UMRS 970 at the Georges-Pompidou European Hospital was established on January 1, 2009. Originally, the Unit comprised six Teams (Ms Chantal Boulanger, Mr Olivier Clément, Mr Xavier Jeunemaitre, Mr Xavier Jouven, Mr Ziad Mallat, Mr Jean-Sébastien Silvestre) and an AVENIR Team (Mr Eric Camerer). This structure received approval from INSERM and the University of Paris-Descartes for a five-year term (2009–2013). During this period, four additional Teams joined PARCC (Mr Stéphane Laurent, Mr Eric Tartour, Mr Guillaume Duménil — AVENIR team, Mr Antoine Lafont). From 2014 to 2019, the Unit expanded to include thirteen Teams due to the division of one Team (Mr Xavier Jeunemaitre) into four individual Teams (Mr Xavier Jeunemaitre, Mr Dominique Eladari, Ms Anne-Paule Gimenez-Roqueplo, Ms Maria-Christina Zennaro). Additionally, one Team (Ms Ann Eichmann) joined the unit, while two Teams (Mr Guillaume Duménil, Mr Dominique Eladari) departed for other units. Finally, a new AVENIR Team was created (Mr Alexandre Loupy), and one Team (Mr Jean-Sébastien Hulot) relocated from La Pitié Hospital to PARCC.

The Unit occupies 4,200 square metres of office space, laboratories, and core facilities conveniently located at the Georges-Pompidou European Hospital. This single location offers numerous advantages in terms of organisation and opportunities for interaction. Additionally, dedicated shared equipment in the core facilities fosters a favourable research environment.

RESEARCH ENVIRONMENT OF THE UNIT

PARCC is situated at the Georges-Pompidou European Hospital and is affiliated with Université Paris Cité, which has earned the 'Initiatives of Excellence' (IdEx) label, affirming the institution's standing as a significant hub for higher education and research in France and Europe. As part of IdEx, Université Paris Cité implements innovative programs in research and training, international affairs, and technology transfer.

In 2021, PARCC took the lead in establishing the Institute of Cardiovascular Sciences (Institut Hors Mur, Faculté de Santé, Université Paris Cité), led by Mr Jean-Sébastien Silvestre, and comprising 33 teams dedicated to cardiovascular research in Paris. Notably, this initiative has led to the creation of the Graduate School in Cardiovascular Sciences, offering educational programs. This effort is closely coordinated with the Graduate School in Innovative Cancer Therapies.

Team members are also actively involved in founding other research institutes, such as the Institute of Immunology and Immunopathology and the Paris Institute for Transplantation & Organ Regeneration.

PARCC teams actively participate in LabExs programs that unite research teams with international recognition, including LabEx REVIVE (Stem Cells in Regenerative Biology and Medicine), LabEx GREX (Biogenesis and Pathologies of the Red Blood Cell), and LabEx ImmunoOnco. PARCC also coordinates the future investment program RHU 'Kidney Transplant Diagnostics Innovation'.

PARCC is a leader in imaging techniques through its core facilities (MRI, High-resolution X-ray scanners, PET, luminescence and fluorescence, photoacoustic imaging, etc.).

PARCC members have strong interactions with the clinical divisions at the Georges-Pompidou European Hospital, covering cardiology, cardiovascular prevention, hypertension, nephrology, internal medicine, genetics, cardiac and vascular surgery, and more. Fifty percent of PARCC Team leaders are regularly involved in clinical research activities at the Georges-Pompidou European Hospital.

UNIT WORKFORCE: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	42
Maîtres de conférences et assimilés	19
Directeurs de recherche et assimilés	11
Chargés de recherche et assimilés	9
Personnels d'appui à la recherche	61
Sous-total personnels permanents en activité	142
Enseignants-chercheurs et chercheurs non permanents et assimilés	17
Personnels d'appui non permanents	50
Post-doctorants	27
Doctorants	54
Sous-total personnels non permanents en activité	148
Total personnels	290

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons at 31/12/2022. Non-tutorship employers are grouped under the heading 'autres'.

Nom de l'employeur	EC	C	PAR
UNIVERSITÉ PARIS-CITÉ	71	0	19
INSERM	0	23	49
AUTRES	7	2	34
Total personnels	78	25	102

GLOBAL ASSESSMENT

The Paris Cardiovascular Research Center (PARCC) – UMRS 970 at Georges-Pompidou European Hospital is an outstanding unit. All metrics confirm the very high quality of the science developed at PARCC. The scientific productivity is exceptional. Moreover, while all teams develop excellent to outstanding research programs, a couple of teams go even beyond, proposing truly disruptive approaches that are gradually adopted by the scientific community worldwide. The unit is therefore widely acknowledged in the cardiovascular research community as a leading European center. This contributes to making PARCC extremely attractive for researchers, PhD students, and postdocs.

PARCC members publish their findings in leading journals within their specialities (such as *Circulation*, *Circulation Research*, *European Heart Journal*, and others), as well as in top journals with a broader readership (such as *The New England Journal of Medicine*, *The Lancet*, *Nature Medicine*, *Nature Genetics*, *Nature Communications*, *Science*, *Cell Reports*, and others). In five years, PARCC members have published over 1200 original papers and reviews. Key discoveries include 1) the coordination of the first meta-analysis of six genome-wide association studies, demonstrating the highly polygenic nature of fibromuscular dysplasia with five predisposing genes, and 2) the development of MRI imaging of meningeal lymphatic vessels following the discovery of new cerebrospinal fluid drainage pathways, paving the way for the use of MRI in patients with neurological diseases. PARCC is coordinating a multi-center Phase III randomised clinical trial to evaluate a therapeutic approach developed in the laboratory for patients suffering from vasculitis and kidney damage (PHRC, 128 patients over four years). A PARCC team has developed and validated the world's most robust system for predicting kidney graft loss, through the creation of an 'lbox scoring system', validated by the European Medicines Agency with a major media impact that has changed transplantation practices in the United States.

Science at PARCC is supported by the remarkable ability of the team and group leaders to attract external funding. Over the past five years, PARCC members have been successful in calls from European (three ERC (consolidator, proof-of-concept, advanced), six H2020 as coordinator, three Leducq foundations (2 as European coordinator)) and French agencies (as PI, 28ANR, eight teams labelled by FRM and three teams labelled by 'Ligue nationale pour le cancer'), resulting in numerous fellowships and grants totalling 45 million Euros. This amount represents approximately 90% of the total budget of the unit. The unit is, therefore, highly dependent on its capacity to raise this kind of money, considering that the annual endowment by INSERM/University of Paris-Cité represents 'only' five million Euros over five years/excluding salaries. This is an inherent fragility, as most of the funding is, by definition, not sustainable.

The center will benefit from an optimal and performant administrative and technical staff in order to deal successfully with duties and that will help researchers to focus on their work.

The unit declares that it has four main research areas: 1) Vascular Disease; 2) Cardiac Disease; 3) Kidney Disease; and 4) Hypertension. All teams contribute to one or more of these research areas. Additionally, the teams also contribute to cross-cutting research programs such as Immunity and Inflammation; Prevention and Biomarkers; and Imaging. The organisation results from a deliberate decision to work in a flexible environment, with no particular constraints that would prevent team leaders from developing innovative research. While this soft management style from the Director has been successful in the past, it may pose a risk that each team works somewhat in isolation.

In terms of functioning, the unit has well-defined internal regulations approved by regulatory authorities, featuring various committees such as the steering committee and the laboratory council to ensure effective unit management. However, some issues were raised by PARCC personnel about the implementation and communication policy. It seems, in particular, that communication within the team by team leaders is sometimes not adequate and should, therefore, be improved. The center benefits from five technological platforms and five technological services (metabolic and physiological phenotyping, microsurgery, IPS cell culture) and bioinformatics support for omics data and 'big data' processing.

Members of the unit are involved in educational roles within Université Paris Cité, including undergraduate teaching and master's courses. The unit supervised 149 PhD students, including 97 defended theses and welcomed 67 and post-docs of 23 different nationalities. The team's members are frequently invited to international meetings (European Society of Cardiology; American Heart Association; Keystone Symposia; Gordon Conferences; EMBO; etc.). They actively participate in international consortia (FP7-HEALTH ENS@T-Cancer; H2020 ENS@T-HT, ENS@T PPGL; COST Action VascAgeNet; etc.), scientific councils, scientific advisory boards, recommendation committees (international imaging societies), research networks,

Additionally, they participate in public outreach events and collaborate with schools and colleges for communication and mentoring activities. However, this latter aspect could be improved. Finally, PARCC maintains regular communication with INSERM-Transfer, contributing to the formation of biotech companies. The unit filed 43 patents in the past five years. Four of them were licensed to companies (two to Polygon Therapeutic, one to Cytune Pharma, one to Cibiltech, and one to Annexin Pharma). Notably, Polygon is a spin-off from PARCC and PARCC team members serve as consultants for the pharmaceutical industry (AstraZeneca, Alnylam, Bayer, JAZZ Pharma, BIOPROJET, ACER Therapeutic) and small companies (Bioserenity, Withings, Axelife). The unit obtained eleven CIFRE contracts for PhD students.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

During the previous evaluation, several recommendations have been made. They are listed below, together with the responses/comments by the Unit. Overall, the Unit was able to satisfactorily address the concerns raised by the previous evaluation committee.

1. Recommendations on scientific production and activities

a. Ensure continuity in scientific production

The Unit has maintained high-level activities as exemplified by original publications, invited reviews and editorials and position papers in highly recognised international journals such as New England Journal of Medicine, Lancet, Nature Medicine, Nature Genetics, Nature Communications, Nature Review Cardiology, Science, Cell Reports, Cell Stem Cell, Circulation, Circulation Research, European Heart Journal, Hypertension, Kidney International, and others.

b. Work on better defining the Unit's identity

No specific response here but, clearly, working on the other aspects of the recommendations, contributed to advertising the Unit's activities, and support its visibility. In particular, achieving scientific excellence is the most effective means of sustaining the Unit's reputation.

c. Improve communication with external entities.

To develop its communication, the Unit has improved its presence on social networks, and tried to better communicate with funding bodies/foundations that support the Unit financially. However, the Unit recognises the need to better disseminate its research. Communication with researchers, clinicians, patients, pharmaceutical industry, and the general public still needs to be better worked out.

2. Recommendations on the unit's organisation and life

a. Connect the Unit to other research centers; work on improving internal and external network activities.

The Unit has participated in establishing three institutes and two graduate schools. This created opportunities to meet with pairs and improved networking. This is in particular the case for young researchers. The Unit organises scientific retreats for improving interaction and cohesion within the Unit. Finally, the Unit has supported the creation of an Early Career Researcher Association (approx. 60 members).

b. Clarify the internal promotion system for technicians

An internal working group in charge of the promotions has been established to better prepare individual candidacies. The results are encouraging with 42% of the technicians/administrative personnel in the Unit that received a promotion in the last evaluation period.

c. Take advantage of the internal working groups with dedicated missions to foster a favourable environment for research.

All the teams should comply with the guidelines edited by INSERM, University of Paris-Cité and PARCC for managing human resources, providing a safe environment, and promoting ethical behaviour. The Unit promotes scientific integrity, for instance, via the mandatory use of an electronic lab notebook system. However, an internal system to prevent and address scientific fraud and plagiarism still needs to be established. Clear procedures for data management also need to be implemented. Clear rules for preventing discrimination and harassment at work must be established. These points are well taken and the Unit is currently working at solving these issues.

3. Recommendations on scientific strategy and projects

a. Maintain a multidisciplinary approach.

Scientific strategies are discussed among all team leaders at the monthly steering committee. Over time, the Unit has been able to maintain multidisciplinary basic and translational research. In this regard, the core facilities offer multidisciplinary platforms that help bring different research lines together. Overall, there is a delicate balance between leveraging the various expertise within the Unit and managing heterogeneity and dispersion.

b. Support spin-off activities

The Unit supports spin-off activities. One start-up has been created, Polygon, based on research developed at the Unit. Interactions are facilitated since the start-up occupied laboratories within the Unit. This is a significant achievement.

c. Work on better managing big data.

The Unit should also establish clear procedures for data archiving, storage and sharing, and provide training and support to all members of the Unit on the important aspect of research. This is supposed to take place within the next evaluation period.

B – EVALUATION AREAS

Considering the references defined in the unit's evaluation guidelines, the committee ensures that a distinction is made on the outstanding elements for strengths or weaknesses. Each point is documented by observable facts including the elements from the portfolio. The committee assesses if the unit's results are consistent with its activity profile.

EVALUATION AREA 1: PROFILE, RESOURCES AND ORGANISATION OF THE UNIT

Assessment on the scientific objectives of the unit

The scientific objectives of the unit are excellent. All Teams contribute to one or more of these research areas. Additionally, the Teams also contribute to cross-cutting research programs such as Immunity and Inflammation; Prevention and Biomarkers; and Imaging. This matrix organisation encourages interactions and, therefore, makes sense. However, the Unit does not specifically define its objectives, which may only be defined at the team level. This is clearly an apparent element. Simply stating that the unit works to understand disease processes and to produce innovation in basic and translational science seems quite superficial. Objectives could be explicitly stated, and the teams could have the possibility to position themselves within this context to achieve the unit's goals. Having said this, the management of the unit is fully aware of the situation. The organisation results from a deliberate decision to work in a flexible environment, with no particular constraints that would prevent team leaders from developing innovative research. There is no doubt that the science is excellent, but at this point, there is a risk that each team works in isolation.

Assessment on the unit's resources

The Unit is doing an outstanding work for supporting its members and creating favourable conditions for research. The Unit comprises thirteen teams, at the Georges-Pompidou European Hospital (HEGP), all in a single location equipped with laboratories, office space, and core facilities. Several technical platforms are on-site, providing valuable scientific expertise, particularly in imaging techniques. The Unit has been able to secure very significant external funding, i.e. 299 research contracts for approx. 45 million Euros over the evaluation period (2017–2022) with an annual endowment of approx. one million Euros is received from the University of Paris – Cité and INSERM.

Assessment on the functioning of the unit

The functioning of the Unit is excellent and complies with the guidelines edited by INSERM and the University of Paris-Cité for human resources, ethical conduct, safety, and data management. PARCC has a policy promoting gender equality and non-discrimination.

The Unit has well-defined internal regulations approved by regulatory authorities, featuring various committees such as the management committee and the laboratory council to ensure effective Unit management. Additionally, core facilities have their own committees dedicated to day-to-day operations and technical guidance. A risk prevention officer is on-site every day and is a part of the psychosocial risk committee established within the Unit.

Overall, the system has been well thought out.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The Unit outlines its activities at the intersection of vascular disease, cardiac disease, hypertension, and kidney disease. Transversal expertise in immunity and inflammation, prevention and biomarkers, and imaging techniques offers additional opportunities for interaction among the thirteen Teams comprising the Unit. The research fields are therefore well-defined.

Weaknesses and risks linked to the context

Surprisingly, the self-assessment document lacks listing objectives, which is a clear omission. Furthermore, one would expect the primary objectives to be structured into specific aims. These specific aims could possibly align with the individual Teams' objectives. This aspect is inadequately described and gives the impression that each Team operates independently. This is regardless of the excellent quality of science produced by each Team.

2/ The unit has resources that are suited to its activity profile and research environment and mobilises them.

Strengths and possibilities linked to the context

Resources include human personnel, space, equipment, and funding. The Unit is a large entity with thirteen Teams, totalling approximately 90 researchers. Additionally, around 30 technicians/engineers work in the core facilities, bringing the total Unit membership to 120 individuals. This level of personnel makes the Unit one of the large centers in the cardiovascular field in Europe. This provides the conditions necessary for conducting research across the whole range of basic, preclinical, translational, and clinical research. The Unit occupies 4,200 square metres of office space, laboratories, and core facilities conveniently located at the Georges-Pompidou European Hospital. This single location offers numerous advantages in terms of organisation and opportunities for interaction. Additionally, dedicated shared equipment in the core facilities fosters a favourable research environment. Last but not least, the Unit has the ability to attract significant funding from various external sources. An impressive sum of 45 million Euros has been generated through research contracts during the evaluation period. This amount is in addition to the recurring annual endowment of one million Euros received from the University of Paris-Cité and INSERM. Overall, the Unit's organisation and the dedication of its members make PARCC a robust cardiovascular center, providing ample opportunities for the development of high-quality research.

Weaknesses and risks linked to the context

The primary challenge that the Unit will encounter in the future is sustaining success in securing external funding. This is critical for their capacity to hire personnel and conduct top-notch research. Furthermore, this occurs in a context where INSERM is reducing its endowment.

3/ The unit's practices comply with the rules and directives laid down by its supervisory bodies in terms of human resources management, safety, environment, ethical protocols and protection of data and scientific heritage.

Strengths and possibilities linked to the context

The Unit has well-defined internal regulations approved by regulatory authorities, featuring various committees such as the management committee and the laboratory council to ensure effective Unit management. The Unit complies with the guidelines edited by INSERM and the University of Paris-Cité for human resources, ethical conduct, safety, and data management. Additionally, core facilities have their own committees dedicated to day-to-day operations and technical guidance. PARCC has a policy promoting gender equality and non-discrimination. In total, 55% of staff members are women. Four out of five core facilities are managed by women. PhD students and postdoctoral fellows come from 23 different countries, which is estimable. However, it is not mentioned whether group leaders and staff members have diverse origins beyond France. A risk prevention officer is on-site every day and is a part of the psychosocial risk committee established within the Unit. Cultural diversity can be an asset and should be actively encouraged. To this end, PARCC has established a working group to address inequalities and foster collective and inclusive behaviour. Its objectives include

creating conditions for equal access to responsibilities and promotions, enhancing support for work-life balance, and combating racism, sexism, and sexual misconduct.

The Unit recognises its responsibility in promoting a safer and more environmentally friendly setting. An environmental officer has been designated for this purpose. His responsibilities encompass tasks such as implementing recycling policies, implementing energy-saving measures, and working on enhancing biodiversity in outdoor green spaces. The Unit also encourages its members to use public transportation or to commute by bicycle.

The protection of scientific assets and activities is guaranteed through the Business Continuity Plan (BCP), which is a contingency plan that continuously assesses potential threats to the Unit's operations. These threats include natural disasters, pandemics, power outages, equipment failures, and cyberattacks, among others. The Unit has backup solutions in place for critical scientific equipment, computers, and data storage systems. The biobank facility and the freezers are connected to an alarm system. A communication plan is in effect to ensure that all personnel receive timely updates in case of disruptions. Additionally, as part of the HEGP site, the Unit benefits from a Flood Risk Management Plan.

In summary, the aspects related to the Unit's operations seem to have been carefully considered to ensure a safe research environment for all personnel.

Weaknesses and risks linked to the context

As is frequently observed, only 30% of women hold leadership positions at the highest level of the hierarchy (group leaders). There is one notable exception: the Unit director is a woman, who will nonetheless step down for the next evaluation period.

The Unit believes that it lacks adequate financial support for administrative requirements and organisational initiatives.

However, during interviews, staff members raised issues about the implementation and communication of this policy. Communication needs to be improved at the team level. It is the responsibility of the team leaders to implement this, and the responsibility of the director to make sure this is happening. It seems, in particular, that communication within the team by team leaders is sometimes not adequate. Decision-making should also be improved since several group leaders and other personnel seem not to be involved in the process.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The Unit is widely acknowledged in the cardiovascular research community as a leading European center and the attractiveness is outstanding. This recognition is built upon an exceptional level of scientific output, making PARCC highly appealing to researchers and students. Success in obtaining competitive grants: 36 ANR (24 as coordinator), nine teams labelled by FRM, Coordinator in H2020 European programs), European coordinator of 2twoLeducq grants, three ERC) also contributes to this recognition.

The Unit places significant focus on staff promotion opportunities and the recruitment of new researchers (five CRCN) and post-docs. They have the ability to fund post-doc positions using their own team's resources through project and funding contracts 150 PhD s students defended their thesis. Recognition of its members is further demonstrated by frequent invitations to major national and international conferences: Gordon, Keystone, ...

The Unit provides a comprehensive array of services through dedicated core facilities, covering everything from small and large animal research to molecular and imaging analyses.

- 1/ *The unit has an attractive scientific reputation and is part of the European research area.*
- 2/ *The unit is attractive because for the quality of its staff support policy.*
- 3/ *The unit is attractive through its success in competitive calls for projects.*
- 4/ *The unit is attractive for the quality of its major equipment and technical skills.*

Strengths and possibilities linked to the context for the four references above

1/ The unit has an attractive scientific reputation and is part of the European research area.

The team's members are frequently invited to international meetings (European Society of Cardiology; American Heart Association; Keystone Symposia; Gordon Conferences; EMBO; etc.). They actively participate in international consortia (FP7-HEALTH ENS@T-Cancer; H2020 ENS@T-HT, ENS@T PPGL; COST Action VascAgeNet; etc.), scientific councils, scientific advisory boards, recommendation committees (international imaging societies), research networks, and more. They play a significant role in peer review processes, evaluating grants for various national and international funding agencies and serving as reviewers for top international journals. Additionally, several members hold editorial positions in prestigious journals (Ms C. Boulanger: associate editor for Arteriosclerosis Thrombosis Vascular Biology; Mr Z. Mallat: co-editor for Atherosclerosis; Mr J. S. Hulot is associate editor for Journal American College Cardiology; A. Eichmann: associate editor for Physiology; Mr P.-L. Tharaux: associate editor for Kidney International; etc.). Over the past few years, multiple team members have been recognised with national and international awards for their contributions to cardiovascular research (Ms C. Boulanger: Lucie and Olga Fradiss Award, and Jean-Paul Binet Award; Mr H. Ait-Oufella : Alain Castaigne Award, Outstanding Achievement Award, Robert Debré Award, and the national prize of the French Academy of Medicine; Mr Z. Mallat was elected Fellow of the Academy of Medical Sciences, UK; Ms S. Taleb: Lucie and Olga Fradiss Award; Mr J. S. Silvestre : Jeanne-Philippe Beziat Award; etc.). All of these activities have established PARCC as a highly respected unit within the cardiovascular community.

2/ The unit is attractive because for the quality of its staff support policy.

The Unit is an attractive research center for both PhD students and postdoctoral fellows. Over the past five years, 150 PhD students conducted their research at PARCC for 94 HDR, with 97 successfully defending their theses. Additionally, 64 postdoctoral fellows were recruited to join one of the Unit's teams. These PhD students and postdocs come from various countries, representing 23 different nationalities (Lebanon, Singapore, Spain, Korea, ...), highlighting the Unit's global reputation. Notably, the Unit has recruited five new tenured staff members as CRCN Inserm, along with seven other personnel, including engineers, technicians, and administrators. Between 2017 and 2022, PARCC also hosted four visiting scientists (Australia; India, Scotland). Overall, there is a well-

balanced composition of personnel across all categories, including members. The Unit has established a support and preparation group for staff members looking to advance in their careers, and it has been highly successful, resulting in a 42% promotion rate for the entire staff during the last evaluation period. The Unit's management has been a strong advocate for the creation of an Early Career Researcher (ECR) association, providing financial support. This ECR association assists young researchers in networking activities and hosts various events to help them in their career development.

3/ The unit is attractive through its success in competitive calls for projects.

The Unit has been highly successful in attracting external funding through competitive national and international grants (36 ANR Grants; 24 as coordinator). During the evaluation period, a total of 45 million Euros were secured across all teams. This includes six projects funded by European sources (coordinated by PARCC), three European Research Council (ERC) grants (ERC Starting Grant, ERC Proof of Concept, ERC Advanced Grant), and three networks of excellence funded by the Leducq Foundation (Mr E. Camerer: Sphingosine 1-Phosphate in Neurovascular Biology and Disease); Ms A. Eichmann: Arterial flow as attractor for endothelial cell migration; Mr J.-S. Hulot: Towards Precision Medicine with Human iPSCs for Cardiac Channelopathies. PhD students have received a significant number of fellowships covering their own salaries, while postdoctoral fellow salaries are typically supported by individual grants within the teams, such as ANR, FRM (nine teams labelled), and European contracts. Lastly, the Unit has received support from the French government through funding from the 'Programmes d'Investissements d'Avenir'. Several Teams developed specific research projects and received financial supports through this governmental program.

4/ The unit is attractive for the quality of its major equipment and technical skills.

Over the years, the Unit has established a variety of core facilities aimed at providing specialised services for its members. These technical platforms offer a wide range of expertise in various areas, particularly biological sample preparation and analysis, flow cytometry, histology, and data analysis (bioinformatics). These platforms were developed with financial support from various foundations and research programs within INSERM, including Leducq and Sesame.

Weaknesses and risks linked to the context for the four references above

Teams frequently mention in the self-assessment document, the use of transcriptomic approaches, including advanced methods such as single-cell RNA-Sequencing and spatial transcriptomics. However, it is not entirely clear how the Unit organises this critical research activity. It appears that each Team manages its own needs through collaboration or by using platforms established in other Units. Given the size of PARCC, this approach is somewhat surprising. Additionally, it seems that the responsibility for bioinformatics assessment lies with the individual Teams rather than the Unit as a whole. There appears to be a lack of clear organisation in this regard. It would likely benefit everyone if an omics and bioinformatics platform were established, staffed with dedicated technicians and bioinformaticians.

The success in competitive grant applications is truly impressive, but, as is often the case, it results in a dependency on external funding. An estimated 90% of the financial resources come from non-sustainable sources. If these vital sources were to diminish in the future, a substantial portion of PARCC's activities could be in jeopardy. In addition, the decrease in institutional funding is undermining the unit's training, career advancement, and core support programs. While a portion of the endowments is allocated to facilities, the teams are critical of the ongoing high maintenance costs.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific output at PARCC is truly impressive (approx. 1200 publications) and outstanding. The number of publications with main authorship is exceptional. Unit members publish their research in highly regarded cardiovascular research journals such as *Circulation*, *Circulation Research*, *European Heart Journal*, and others. They contribute to top scientific journals with a broader readership, including *The New England Journal of Medicine*, *The Lancet*, *Nature Medicine*, *Nature Genetics*, *Nature Communications*, *Science*, *Cell Reports*,

- 1/ *The scientific production of the unit meets quality criteria.*
- 2/ *The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.*
- 3/ *The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.*

Strengths and possibilities linked to the context for the three references above

- 1/ *The scientific production of the unit meets quality criteria.*

The Unit regularly publishes its research in highly respected journals within its scientific field and in journals aimed at a wider readership. The scientific output, based solely on this criterion, is truly exceptional, as evidenced by various evaluation criteria. First, the quantity and quality of scientific papers published in the past five years are remarkable. Unit members consistently publish their research in highly regarded cardiovascular research journals such as *Circulation*, *Circulation Research*, *European Heart Journal*, *Hypertension*, *Kidney International*, and more. Additionally, they contribute to top scientific journals with a broader readership, including *The New England Journal of Medicine*, *The Lancet*, *Nature Medicine*, *Nature Genetics*, *Nature Communications*, *Science*, *Cell Reports*, *Cell Stem Cell*, and others. In total, the Unit has made significant contributions, with approximately 1,200 original papers, around 250 reviews, and approximately 450 other publications, including book chapters and meeting abstracts. A detailed description of the team's contributions can be found in the team assessment section below.

- 2/ *The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.*

The scientific production reveals a balanced distribution among all Teams. There are some variations in the number of publications between high-producing Teams and those with a more moderate scientific output. However, this appears to be proportional to the number of personnel in the teams and does not indicate a lack of quality in the research of the less productive Teams. In addition, the Unit organises seminars with external speakers, internal seminars for the entire Unit to attend, master classes, and other events. This certainly helps spread the research conducted at PARCC throughout the entire scientific community of the Unit.

- 3/ *The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.*

PARCC has established rules to ensure scientific integrity. Members of PARCC use the INSERM-certified electronic laboratory notebook. All personnel follow standardised operating procedures under the guidance of staff members, and data are subject to review and validation by senior staff members. Additionally, the Unit has ethical guidelines and complies with regulations and guidelines for human research. All activities in these areas are overseen by institutional, national, and international committees. PARCC is committed to Open Access (OA)

practices and is dedicated to making data available to everyone by depositing data and manuscripts in appropriate repositories before publication. Authorship is determined by individual contributions to the work, and the responsibility for publication lies with each team.

Weaknesses and risks linked to the context for the three references above

The Unit needs to further improve its sharing and open access practices.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

Assessment on the inclusion of the unit's research in society

Members of the Unit are involved in educational roles within Université Paris Cité, including undergraduate teaching and Master's courses. The Unit also enrolls students funded by industry grants, which facilitates partnership development. The unit filed 43 patents in the past five years. Four of them were licensed to companies (two to Polygon Therapeutic, one to Cytune Pharma, one to Cibiltech, and one to Annexin Pharma).

Additionally, they participate in public outreach events and collaborate with schools and colleges for communication and mentoring activities, such as 'Fête de la Science,'. PARCC members actively engage in societal debates, including discussions about women's health.

The Unit demonstrated its adaptability during the COVID-19 pandemic, with staff volunteers stepping in to support hospital teams.

In conclusion, the contribution of the unit to research activity to society is excellent.

- 1/ The unit stands out for the quality and the amount of its interactions with the non-academic world.*
- 2/ The unit develops products for the cultural, economic and social world.*
- 3/ The unit shares its knowledge with the general public and takes part in debates in society.*

Strengths and possibilities linked to the context for the three references above

1/ The unit stands out for the quality and the amount of its interactions with the non-academic world.

There's no doubt that PARCC is deeply involved in teaching and mentoring activities for the benefit of university students, PhD students, and academic personnel. However, its engagement with the non-academic world is less evident. It is possible that this point has been misunderstood in the self-assessment document, and it would be helpful to provide examples of specific interactions with non-academic entities. For example, collaborating with patient associations would be a positive step. Nevertheless, the response to the COVID-19 pandemic serves as an example of how PARCC has demonstrated its ability to address a social crisis. Despite a challenging situation, the Unit not only continued its scientific activities but also adapted its objectives to provide society with crucial information about COVID and its implications for cardiovascular disease. This research resulted in the publication of a substantial number of papers assessing various therapeutic approaches for the benefit of both the academic world and society.

2/ The unit develops products for the cultural, economic and social world.

The Unit takes the valorisation of research very seriously. To illustrate, 43 patents have been filed in the past five years, with four of them licensed to companies (two to Polygon Therapeutic, one to Cytune Pharma, one to Cibiltech, and one to Annexin Pharma). Notably, Polygon is a spin-off from PARCC. These achievements are significant, but given the Unit's size, there is room to further enhance this aspect of PARCC's activities. Additionally, PARCC team members serve as consultants for the pharmaceutical industry (AstraZeneca, Alnylam, Bayer, JAZZ Pharma, BIOPROJET, ACER Therapeutic) and small companies (Bioserenity, Withings, Axelife).

3/ The unit shares its knowledge with the general public and takes part in debates in society.

PARCC is engaged in research dissemination through various channels, including annual reports, social networks, and press releases. The Unit has a policy of sharing knowledge with the general public. This includes participation in specific events designed for a wider audience, such as 'Fête de la Science,' special events in high schools for minority students, and events organised by the Fondation pour la Recherche Médicale. PARCC members also take part in societal debates, including discussions on women's health. Interactions with politicians can also occur on these occasions. Additionally, the Unit collaborates with non-academic institutions like the Red Cross to educate the public about emergency procedures. In summary, the Unit actively engages in various initiatives that benefit society.

Weaknesses and risks linked to the context for the three references above

The Unit's engagement with the non-academic world is less evident. It would be helpful to provide examples of specific interactions with non-academic entities. For example, collaborating with patient associations would be a positive step.

ANALYSIS OF THE UNIT'S TRAJECTORY

In the future, PARCC will continue its activities in four major physiopathological fields: 1) micro and macrovascular diseases, 2) heart failure and sudden cardiac death, 3) hypertension, and 4) kidney diseases and transplantation. Within these areas, the Unit has outlined three primary research axes: 1) gene and molecular signalling, 2) immunity and metabolism, 3) predictive models and multidimensional approaches.

The main stated objectives are to leverage cutting-edge technologies to unravel the mechanisms of cardiovascular diseases and translate this knowledge into new therapies for enhancing patient outcomes. PARCC's overall policy aligns with the missions and goals established by INSERM and Université Paris Cité, with the aspiration to promote cross-disciplinary basic and translational biomedical sciences, foster disruptive approaches, and support training and mentorship.

PARCC has initiated a robust policy to back young researchers and attract new talents through various fellowship programs. This initiative will receive further support in the future to ensure the maintenance of the Unit's expertise and workforce.

PARCC will actively promote the economic development of its research, particularly by collaborating with start-ups that have spun off from PARCC. Subsequently, PARCC will forge strategic partnerships with companies drawn to its technical platforms, which should generate revenue.

In terms of organisation, the current PARCC Director, Ms Chantal Boulanger, has stepped down from her managerial position end of October 2023. Mr Jean-Sébastien Silvestre has been elected as the Director for the next evaluation period and has started since October 2023. Several teams will restructure to better align with the Unit's research objectives. Some teams will merge, others will be divided, and some will leave the Unit, while an additional team will join. Ultimately, the new organisation should enable PARCC to focus efficiently on cardiovascular disease and reduce heterogeneity in its research programs.

In this context, the team led by Mr David Smadja at the Faculty of Pharmacy in Paris will be moving to PARCC to strengthen expertise in micro- and macro-vascular disease, following a suggestion by the Scientific Advisory Board. It is certain that the expertise of the new team in endotheliopathy and hemostasis disorders represents a great addition for the unit. The research program on endothelialization of artificial organs, such as the heart and the lung, is truly exciting. Mr David Smadja is already integrated into the Hospital Georges Pompidou for his clinical activities, ensuring a smooth transition.

PARCC has also restructured its technical facilities, bringing them under common governance to increase their utilisation and visibility, and to establish an investment plan necessary for renewing equipment and investing in future technologies.

PARCC will continue its efforts to support early career researchers by funding and providing guidance to the established early career researcher association. Additionally, PARCC will develop a scientific integrity program that includes measures to prevent and address scientific fraud and plagiarism.

PARCC acknowledges the need to develop a program addressing work-related psychosocial risks, gender bias, health and safety. This program will encompass measures to prevent and address harassment, discrimination, and other forms of unacceptable behaviour, while also supporting employees in maintaining a healthy work-life balance.

RECOMMENDATIONS TO THE UNIT

Recommendations regarding the Evaluation Area 1: Profile, Resources and Organisation of the Unit

The unit's director should ensure that team leaders communicate with their respective teams and involve all team members in discussions.

The unit's director should ensure that team leaders comply with existing management rules, including following dedicated advanced courses if needed.

The unit's director should organise a survey about communication issues and hold at least one event involving everyone to address communication issues.

For core facilities, the platforms should be encouraged to apply for iBISA certification.

Recommendations regarding the Evaluation Area 2: Attractiveness

Within the constraints of the French system, the unit is very attractive. However, it could improve its visibility by working to enhance its website, making it more appealing to international researchers. Success stories from PARCC should be advertised on the website.

PARCC should also work on attracting talented individuals from INSERM to strengthen existing lines of research.

Recommendations regarding Evaluation Area 3: Scientific Production

PARCC should do whatever is possible to maintain its outstanding level of research and productivity.

Recommendations regarding Evaluation Area 4: Contribution of Research Activities to Society

PARCC has some activities aimed at the general public. However, the unit could improve its public outreach.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Endothelial pathophysiology and extracellular vesicles
 Name of the supervisor: Ms Chantal BOULANGER

THEMES OF THE TEAM

The themes of the team are dedicated to the field of extracellular vesicles in cardiovascular diseases with two scientific aims: 1) deciphering the deleterious effect of atheroprone blood flow and circulating extracellular vesicles on endothelial function and 2) understanding how extracellular vesicles released within the infarcted myocardium regulate inflammatory responses and cardiac repairs.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In reference to the previous evaluation report, the team put successful efforts in maintaining high levels of productivity, recognition, and integration within the rapidly evolving fields of extracellular vesicles and cardiovascular biomarkers.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	6
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	2
Total personnels	8

EVALUATION

Overall assessment of the team

The team has generated 44 publications in leading position, including original articles, letters, reviews, and editorials, which have been highly cited and quoted in the field of extracellular vesicles (Proc Nat Acad Sci USA, 2xCirc Res), 2xHepatol, Nat Rev Cardiol...). This underscores the team's capability to contribute across various facets of this discipline.

Throughout the evaluation period, the team successfully secured sixteen national grants. Notably, senior members of Team 01 spearheaded eleven of these grants, including prestigious ones from ANR, FRM, and the Fondation de France. This underscores their adeptness at attracting research funding and effectively managing intricate research projects. It's crucial to note, however, that the number of grants has decreased over time from 2017 to 2022, and it is significant to highlight the comparatively lower success rate in European and international grants.

The team has demonstrated innovation by filing three patents during the evaluation period. The acquisition of two patents and extensions in the USA showcases their commitment to translating research findings into practical applications. Furthermore, the team's patents have garnered interest from Annexin Pharma Biotech, indicating the potential for real-world applications and commercialisation.

In summary, the team exhibits an overall excellence in their research endeavours and achievements.

Strengths and possibilities linked to the context

Attractiveness

The team benefits from diverse expertise in the field of extracellular vesicles in cardiovascular diseases, enhancing their ability to approach research questions from different perspectives. Collaborative efforts among senior team members in publications reflect an interdisciplinary and cooperative approach to research. Two young researchers obtained a three-year ANR grant for young researchers.

One member obtained his HDR during the last mandate meaning that four scientists have HDR to supervise PhD students. The team successfully supervised eight PhD and post-doc students, of six nationalities (France, Senegal, India, Singapore, Algeria, Morocco) with a high rate of thesis completion (seven, meaning a ratio of two PhD/HDR for the last mandate). The team actively involves students in thesis and post-doctoral positions as first authors in publications, showcasing their commitment to mentoring and knowledge transfer.

One junior scientist obtained a professor position and an Atip/Avenir team and moved to the Center for research on Inflammation in 2019.

Ms Chantal Boulanger was promoted 'Directeur de Recherche Inserm Classe exceptionnelle' in 2020. One Inserm assistant engineer was promoted 'Ingenieur d'études' in 2022.

Team 01 is a co-founder of the IVETH platform which received competitive funding from the National Plan for Future Investments in 2021.

Continuous and substantial investments in state-of-the-art equipment (high-sensitive flow cytometry, ...) have enabled the Team to maintain its position as a leader in the technological analysis of extracellular vesicles.

Recognition

The team actively involves students in thesis (n=8) and post-doctoral positions (n=2) as first authors in publications, showcasing their commitment to mentoring and knowledge transfer. The team successfully supervised a diverse group of PhD and post-doc students, with a high rate of thesis completion.

The team has successfully secured sixteen national grants for a total of €2,000,000 during the period 2017–2022. Senior members of Team 01 coordinate eleven of these grants, including prestigious ones from ANR (three as coordinators, one co-fund with German agency Deutsch DFG), labelisation of the team by Fondation pour la Recherche médicale (FRM) (2021–2024), and the Fondation de France, demonstrating their ability to attract research funding and manage complex research projects effectively. One member of the team has a European grant from European Foundation for the study of chronic liver failure (300 K€).

The head of the team received the Lucie and Olga Fradiss award from the French society of Cardiologie (2017) and Jean-Paul Binet prize from FRM (2019). Two members of the team participated to the Board of French Society of extracellular vesicles.

Ms Chantal Boulanger was the vice-president ((2020–2022) and is the president of the scientific board of FRM (2022–2024). She was also senior associate editor of ATVB Journal, American Heart Association (2010–2022).

Team 01 actively participates in international conferences and scientific meetings, presenting oral and poster communications. This demonstrates their commitment to share their research findings with the scientific community. They were invited to give state-of-the-art lecture at the International Society of Extracellular vesicles (ISEV) meeting in 2021 and lectures at the British Society of Cardiovascular Research (2018) and the European Society of Cardiology (2019).

Ms Chantal Boulanger is now the director of 'Institut thématique MultiOrganismes Physiopathologie, Métabolisme Nutrition (ITMI PMN) since 2023.

Scientific production

Team 01 has demonstrated a significant strength in research productivity, with a total of 85 publications over the 2017–2022 periods with 52% (44) of which as first/last/corresponding (PDC) authorship. This includes a diverse range of publication types, such as original articles (47, 19 as PDC), letters (4), reviews (24), and editorials, showcasing the team's ability to contribute to various aspects of their field. They published as PDC in high visibility journals such as Proc Nat Acad Sci USA (2017), Circ Res (2018, 2019), Hepatol (2018, 2019), Cardiovasc Res (2019), Eur Heart J (2019).

As an example, the team has decrypted the atheroprotective role of endothelial autophagy in response to shear stress (J Hepatol), the deleterious effect of circulating extracellular vesicles (EV) on endothelial function (Blood, JCI) and that cardiac EV regulate local inflammation if myocardial infarction (Circ res).

The fact that team members have been invited to contribute reviews and editorials as PDC in high impact journal like Nat Rev Cardiol, Circulation Research, and others highlights their expertise and recognition in their respective topics in the field of extracellular vesicles.

Team 01 has demonstrated a strong culture of collaboration within the team, with 30% of their 85 publications being co-authored by at least two senior authors and 6% co-authored by three or more senior authors and 64% of the total numbers of publications are in open access.

Contribution of research activities to society

Team 01 has shown innovation by filing three new patents (2017, 2019, 2021) during the evaluation period. The acquisition of patents and extensions in the USA for two other patents ((2018, 2022) reflects their commitment to translating their research findings into practical applications. Additionally, their patents have attracted interest

from Annexin Pharma Biotech, indicating the potential for real-world applications and commercialisation. They also received funding from pharmaceutical industries Hoffman La Roche (45 K€), Sanofi (31K€). One member received the SATT INNOV prize in 2017.

The team has participated to 'Fête de la Science', communications actions aimed at the general public (French television (2017), magazine (2019))

Weaknesses and risks linked to the context

Although the team has successfully secured sixteen national grants, it's important to note that most of these grants are primarily at the national level, with a lack of major European or international grants.

The extensive involvement of the team leader in various roles and organisations may raise concerns about over-commitment. Moreover, given her leadership roles, there should be a consideration for succession planning to ensure the sustainability of these roles and responsibilities in the long term.

There is high recurrent cost for equipment maintenance.

There are only a few actions towards the General Public.

Analysis of the team's trajectory

Team Boulanger has dedicated itself to deciphering the deleterious effects of atherosclerosis-prone blood flow and circulating extracellular vesicles on the endothelial function, a barometer of vascular health, to identify therapeutic targets. Publications in high-impact journals can be reported that document that this is a highly interesting and topical pursuit. However, for the next term, the team will not seek renewal as the current team leader retires. Sensibly, the team will be split into two groups where the individual members will be in an environment conducive to their own research effort and where this prior success has a high likelihood of being repeated. This makes total sense.

The current Team will split into two groups: – Mr Olivier Blanc-Brude will join the CNRS laboratory of Ms Florence Gazeau (Sts Pères campus, UPC) and maintain its general orientation, continuing the study of circulating EVs in the context of intravascular hemolysis and vascular injury.

—The group of Ms Chantal Boulanger will join the future PARCC Team led by Mr Jean-Sebastien Silvestre and Mr Jean-Sébastien Hulot.

RECOMMENDATIONS TO THE TEAM

It is very important for PARCC not to waste the experience and skills that the Chantal Boulanger's team has acquired over these years. It is crucial that the integration into the new group clearly expresses the intention to continue research in the field of Extracellular vesicles, which indeed represents a unique niche for PARCC.

Team 2: Imageries of the living
 Name of the supervisor: Mr Bernard TAVITIAN

THEMES OF THE TEAM

Team 02 focuses on and translational live in vivo imaging research ranging from methodological imaging development to image feature extraction using AI. Clinicians, scientists, and engineers build a team that is very well equipped to address related tasks. Elucidating the link between cardiovascular disease and cancer therapy is highly topical and timely, while PET-CT & US provide unique and novel opportunities to study atherosclerosis, another highly topical research pursuit. Simultaneously, detecting biomarkers predictive of future cardiovascular events among patients with FDG-PET for oncological clinical indications ideally completes this portfolio.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The prior report asked for the team to further strengthen interactions with other teams and a ratio of close to 50% of common publications documents that this has been achieved but begs the question if a further increase might be beneficial or detrimental to the research effort. They also note that innovative imaging technologies are not available in other teams and that could be leveraged for common research, a point that is valid. They compensate for that deficiency by entering sensible external collaborations.

As for hiring full-time researchers, this remains a critical point that could unfortunately not successfully be addressed. Nevertheless, the recruitment of Mr Fabien Hyafil with a considerable international reputation for the team is considered highly positive and ought to be commended.

The critique that costly equipment should be more supported financially by the unit has been faced head-on and a laudable effort for pooled funding has been undertaken to finance a complete renewal of the 4.7T MRI electronics.

Set up of a dedicated radiochemistry facility is not feasible but collaboration – and contractual arrangements with outside entities account for this relative shortcoming.

Generally, the team has responded very well to the prior critiques.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	10
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	7
Sous-total personnels permanents en activité	19
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	8
Sous-total personnels non permanents en activité	12
Total personnels	31

EVALUATION

Overall assessment of the team

The team exhibits exceptional strength, boasting an interdisciplinary, diverse, and remarkably efficient approach across all facets. Their consistent publication in top-tier journals such as Nature Commun, Lancet Oncology, and even beyond (Am J Pathol, Eur Radiol, Hypertension, Theranostics,...), attests to their exceptional productivity and outstanding track record in disseminating findings. The mentoring program stands as outstanding, also evident in the numerous grants (Fondation des maladies rares, FONDATION MR — KHEN, Fondation Lefoulon Delalande) awarded to junior researchers. Overall, the team's track record in securing grant funding is considered excellent SESAME grant (1436 K€), three ANR as PI and they obtained a HORIZON-EIC-2022-PATHFINDEROPEN-01 starting September 2023 but can be improved by leveraging the team's outstanding preliminary studies.

The team has obtained 24 grants for clinical studies managed by AP-HP and four start-ups were created by the PIs and mostly received funding from public innovation funds (4,632 K€) and they obtained a CIFRE from FEALINX.

Given the above, the global assessment of this team falls between excellent and outstanding.

Strengths and possibilities linked to the context

Attractiveness

Clearly, the team has set itself relevant standards as the goals pertain to preclinical and clinical research with translational potential covering a very broad spectrum of topics that include oncology, cardiology, nuclear medicine, interventional, and vascular medicine. And these are covered using a multidisciplinary approach that includes clinicians, scientists, and engineers. These are predominantly located on the same campus which is an additional asset.

The team has supervised 27 PhD thesis from nine different nationalities for nine HDR and all the students have found a position. Judging by the new recruitment of three staff members as PU-PH, MCU-PH and three engineers and the promotion of four PU-PH and two engineers, it can be deduced that the team must be attractive. Looking at the infrastructure, the personnel, and the highly topical research areas covered, there is an excellent match between the resources adapted to the activity profile of the multidisciplinary team and the platform. The addition of AI as part of a 'retro-translational' effort demonstrates a dynamic adaptation to the needs at this present time and demonstrates flexibility in resource allocation.

The team has state-of-the-art equipment that has been renewed in part and the combined, multi-pronged efforts to renew the 4.7 T MRI through securing multiple sources of funding ought to be commended. The PET-CT Us system is unique and obviously offers new avenues of research. The state-of-the-art equipment of the team supports their chosen avenues of research very well. Not only does this make the team attractive because of the overall infrastructure, but also for the culture and the spirit that prevails.

The team functioning complies with the rules and directives defined by its supervisors on human resources management, safety, environment, ethical protocols, and data as well as scientific heritage protection.

Recognition

There is objective documentation for the international reputation and notoriety of the team's leader and members of the team. This is obviously paired with the attractiveness of the state-of-the-art equipment of the team.

Attractiveness may also be supported by the international stature and recognition of the team leaders. Mr Tavitian was named an honorary member of the European society for molecular imaging (2021).

One member obtained the 'Chaire de l'Institut 3IA PRAIRIE' (2019–2029). One member was awarded Cum Laude – CIRSE 2017.

They have organised every year a European conference (TOPIM Winter Conference of the European Society for Molecular Imaging (2017, 2018, 2019, 2020).

The future leader is a member of Regulatory Affairs Committee – European Society of Cardiology (2017-present). The actual leader was in the European Research Commission: panel member of LS7 Starting grants Committee (2017–2021) and the future leader is Expert, Medical Device for the European Medical Agency (2020 present).

The team has been successful in securing grant money and has been awarded ten research grants for more than 2 million euros (participation in RHU AS-STOP), INRA GIS IBISA 2020 as PI. The major grants are a SESAME grant (1436 K€), three ANR as PI and they obtained a HORIZON-EIC-2022-PATHFINDEROPEN-01 starting September 2023. This unequivocally demonstrates recognition.

Of note, an impressive number of young team members have also secured recognition through extramural funding (Fondation des maladies rares, FONDATION MR — KHEN, Fondation Lefoulon Delalande), which, yet again, points to excellent mentorship and sustainability within the program that should further add to its attractiveness and legacy.

Scientific production

The scientific production of the team is outstanding with 224 publications including sixteen reviews or editorials and 104 research articles. A further aspect concerns scientific production by junior members of the team with half of the articles having junior first authorship, which documents a working mentorship program. The productivity is considered outstanding as well. Visibility in a large number of leading journals such as Nature Comm (2017), Lancet Oncology (2017) and in speciality journals with high visibility Cardiovascular Engineering and technology (2022), Am J Pathol (2022), Eur Radiol (2022, 2021, 2020), Hypertension (2021, 2019), Theranostics (2021, 2020, 2017), J Thromb Haemost S (2021), JACC-Cardiovasc Imaging (2020, 2019), Phys Med Biol (2020), Am J Physiol-Heart Circ Physiol (2020), Circulation (2021) documents outstanding scientific production. They have also published in collaboration in Lancet Oncology (2022), Diabetes & Metabl (2021), and Circulation (2017). Their initiative to revamp the imaging infrastructure has notably enhanced the competitiveness of their research program with their expertise in cardiac 4D flow measurements using MRI. Moreover, their adaptability to embrace new research directions showcases a flexibility that greatly contributes to the program's success. Notably, certain elements within both imaging (PET-US) and therapy (HIFU valve treatment) hold transformative potential. They have developed open-source software for quantitative analysis of succinate MR spectroscopy, machine-based learning-based measurement of fibrosis in tissue sections and methodological innovations in the evaluation of radiomics results.

Contribution of research activities to society

The team has obtained 24 grants for clinical studies managed by AP-HP for approximately 2092 K€. They have also secured support from GE MEDICAL SYSTEMS 2018-262 and CARDIAWAVE 2018-246 CT PREST° AC SPÉ 4. They also conducted the first-in-man international multicentre trial of non-invasive ultrasound therapy in patients with severe asymptomatic aortic valve stenosis.

The support garnered by the creation of start-ups is impressive. Four start-ups were created by the PIs and mostly received funding from public innovation funds (4,632 K€) and they obtained a CIFRE from FEALINX.

Weaknesses and risks linked to the context

The team may consider sacrificing breadth for depth. Especially in the domain of the development of new and own imaging strategies there may be quite some untapped opportunity.

For pushing the envelope even further, the identified research areas are perfectly well chosen and so is the infrastructure. To take it to the next level, a more technical focus where new technology is developed in-house may be useful. However, it is acknowledged that building up such a team is an endeavour that takes its time and mandates the recruitment of additional talent that can ensure growth, sustainability, and stability, and which can attract new talent. A large number of publications are not open access – almost half of 230 since 2017.

While the 4.7T system is most certainly adequate to perform the research proposed, the potential for a direct translation of the knowledge gained to the human setting is more complex as a result. If there was research access to a human 3T system, the tempo of translation could be increased. As for the strong observed diversity, it seems as if women are still in a minority.

It seems that many team members can only devote about half of their time to research. From an outside perspective, this may affect successful recruitment of scientists. Also, if only 50% are available for research and much of the remainder must be spent writing grants, how is this sustainable? As stated above, attracting full-time permanent Inserm researchers would be of paramount importance.

To this reviewer it is a bit unclear whether the Teams work together in a sense where they are better in combination than they would be alone. I may have missed that metric and while this is outstanding in Team 02 alone it begs the question how the different teams cross-fertilise each other.

Analysis of the team's trajectory

As for Team with Mr Tavitian as leader, they propose to pursue three major axes that include the development of new imaging methodology, the development and validation of innovative technologies, and the pursuit of image processing supported by AI. All these axes will build on prior expertise and success and are considered a most worthwhile investment. However, 'new' imaging methodologies and 'innovative technologies' critically hinge on the support of basic researchers in the engineering domain, one of the major deficiencies – if not the major deficiency, which has been identified. Without improvement in that domain, the pursuit of these axes is considered worthwhile yet fraught with considerable risk.

The new organisation of the team including the co-leadership of Mr Hyafil is well thought out.

RECOMMENDATIONS TO THE TEAM

First of all, the team ought to be commended for the depth, breadth, and quality of the research they have conducted and that has reached international visibility.

This provides a substrate and a culture that can be built upon to expand what exists and taking this successful business to the next level. In order to get there, I see two major roadblocks.

The first pertains to the hiring of basic science talent. And this cannot be accomplished by hiring one 100% engineer. This needs a dedicated effort to build a team where a culture is developed that guarantees sustainability and continued cutting-edge innovation in the best interest of the general research goals that will remain highly important for the foreseeable future. Attracting full-time scientists to the team remains a shortcoming and needs to be addressed to take this to the next level. But this would be extremely enabling and would further build on the excellent substrate that already exists.

The second relates to translation, a declared goal of the general research. At least for MRI, without having the infrastructure to translate 4.7T innovation from the bench to the bedside, there exists a significant limitation that affects the potential impact. Developmental research on human MRI systems is therefore highly recommended.

Finally, the team may want to consider increasing their extramural grant funding leveraging both their outstanding preliminary results and international collaborations.

Team 3: Genetics to Understand Arterial Disease
 Name of the supervisor: Ms Nabila Bouatia-Naji

THEMES OF THE TEAM

Team 3 study the genetics of monogenic disorders including familial hyperkalemic hypertension (FHH) and Ehlers-Danlos syndrome (vEDS) and the complex cardiovascular conditions of mitral valvulopathies (MVP), fibromuscular dysplasia (FMD) and spontaneous coronary artery dissection (SCAD). The team focus on genetic discoveries, downstream dissection of disease mechanisms and translational research.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous committee had recommended the group maintain their high levels of productivity, and recognition of their work internationally and for the two groups to reinforce their existing collaborations.

The team have followed the recommendations and in the report they highlight their continuing and new roles in international leadership positions in their disease areas (genetic investigation of vascular Ehlers-Danlos Syndrome, mitral valvulopathies, fibromuscular dysplasia and spontaneous coronary artery dissection) and their productivity has been maintained alongside publications of their work in leading general science and cardiovascular journals. The report did not provide a narrative of how the two groups work together except mention there is sharing of authorship for publications relating to the ERC grant ROSALIND. The group, however, do demonstrate evidence working with other teams in the unit from shared publications.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	6
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	5
Total personnels	11

EVALUATION

Overall assessment of the team

The team is outstanding. The team leaders are world experts in their fields, with international standing and have delivered 113 publications (68 original publications as PI) across all of the diseases they work with many high visibility journals such as (Science Transl Med, J Clin Invest, Nature Commun, ...) and received several invitations to international meetings (European Society of human genetics, European Society of Cardiology) in addition to guest invitations by international and prestigious research centers (Mayo clinic, Cleveland clinics, USA, RIKEN institute, Japan).

The team has recruited one former post-doctoral fellow as CRCN Inserm. They had strong funding in the period >2.8M Euros from national such as FFC, fondation Coeur et recherche et one ANR as partner, European (one ERC starter award) and smaller amounts from international funding bodies and the team was also labelled FRM. Training of the PhD students and team was excellent (six postdocs and eight PhD students), with one post doc transitioning to an ECR associate in 2022.

One PhD student was granted by a CIFRE funding (Servier-Inserm) and one post-doc is data scientist freelance – Sanofi.

The team has also demonstrated excellence in outreach activities – both national and international.

Strengths and possibilities linked to the context

Profile, resources & team organisation

The team has a common goal of understanding the pathophysiology of arterial diseases, rare (Mr Jeunemaitre) and common (Ms Bouatia-Naji). There is synergy with both groups leading efforts in disease gene discovery to follow through studies on understanding molecular and cellular mechanisms to translational and preclinical research. The PIs are leaders in their fields and demonstrate collaborative practices with sharing of expertise and senior authorship on several publications.

The team has ten permanent staff, six post-docs, eight PhD students and nine supporting staff on fixed term contracts. The team was successful in attracting two young ECRs, and currently comprises 26 women and thirteen men.

Attractiveness

The team has leading researchers across their disease areas and over the past five years have increased visibility of the research they do on the international stage. One member of the team (co-leader) was appointed dean of the newly created Faculty of Health at Université Paris Cité. The leader of the team is an ERC starting awardee (2017–2022). She is invited to international meetings (European Society of human genetics, European Society of Cardiology) in addition to guest invitations by international and prestigious research centers (Mayo clinic, Cleveland clinics, USA, RIKEN institute, Japan).

The team leader was appointed to define the scientific content of the American Heart Association Scientific Meetings (2020–2022). She was also the chair of Early Career Committee of the Genomic and Precision Medicine (2021–2022) and she is also associate editor at the journal of this council (Circulation: Genomic and Precision Medicine).

It is noted that early career researchers are the fulcrum of the team – with opportunities for their training highlighted at both national and international levels, one post-doctoral fellow who was highly productive has now been appointed a permanent member of the team (CRCN Inserm since 2022) and others will join the group. The team for the last mandate has hired six postdocs (most from France and one from Denmark). The team has also recruited a permanent position as an engineer at the university and a senior analyst in bioinformatics.

The groups have strong funding and from different sources (National, European and International) to support their team. Over the last five years, substantial funding was National and European, with funding over the five-year period (>2.8M Euros), with substantial funds coming from an ERC starting grant to Ms Bouatia-Naji for 1.5M Euros, this money contributed to funding many of the staff and students. The team has supervised eight PhD students (two were defended and the others are ongoing) for seven HDR. The majority of the grants for the larger amounts were from French funders, with limited funds from overseas funders co-PI from NIH, Chinese Scientific Council). The team has benefited from ANR as collaborator (2017–2021), and as PI from Fondation pour la recherche médicale (FRM) (team labelled FRM 2014–2018), Federation française de Cardiologie).

The team is attractive for the quality of its major equipment and technological skills. There are good facilities to deliver the work packages and the team uses platforms and equipment available at PARCC. The team benefits from the new iPSC facility and imaging and flow cytometry. For the 'omics perspectives, the team has access to local (Cochin platform) and resources and also to facilities (European platform of genotyping at CNIO, Madrid).

Scientific Production

The research productivity of this team is highly impressive, there are continuous high-profile papers from the teams each year in an individual's area of interest, and across collaborative projects too. There were 113 publications – 87 original articles and 11 reviews. They are leading (first, last and corresponding) authors for 68 publications in general high visibility journals (Science Transl Med, J Clin Invest, Nature Commun, ...) and also in high levels of specialist journals (J Am Coll Cardiol, Circ Res, Cardiovas J, Circ Genom Prec Med, Plos Genetics, Eur J Hum Genet). The reviews indicate the prestige of the lead researchers, as this is a large amount in such a short time period. The group published 25 abstracts, thus illustrating how the team is promoting junior researchers to present their work.

The team leaders have shared authored papers, seventeen are mentioned since 2017 and across the team of six post-doc fellows and eight PhD students over the period – 80% of the students have now defended their thesis. There is a strong supportive community for sharing publications, as each post-doc has a first author paper, a few people many more, with students also doing well in public dissemination of their findings.

As an example, their publications reported follow-up of studies of their genetic investigation in mitral valve prolapse describing novel genetic risk loci (EJH, Science Trans Med). They provided functional exploration of the genomic organisation of gene regulation in mitral valves (JCI). One of the major achievements was the conduction of the largest genetic investigation for fibromuscular dysplasia (Nat Commun).

The team is compliant with scientific integrity, ethics and open science, the electronic lab book is being used and there is sharing of protocols/analysis plans and the team has 80% success in publishing in open access journals.

Contributions of research activities to society

One PhD student was granted by a CIFRE funding (Servier-Inserm) and one post-doc is a data scientist freelance – Sanofi. The team leader over the past five years has developed an excellent profile in promoting women in science, with contributions to mid and high school activities, mentoring and early career training thus promoting the activities of the unit and looks to be the public face.

The team is promoting the research of the team, with interactions with leadership of FMD Society of America to disseminate research findings, similarly also preparing videos of their research across FMD and SCAD and engaging with patient families for increasing awareness of the conditions, these activities are really outreach to the wider community.

There is the promotion of the team sharing knowledge with the general public and in debates with one of the main contributors, really impressive number of contributions across many areas. I am in agreement with the self-evaluation in that it is outstanding.

Weaknesses and risks linked to the context

An observation is that the team currently has more women than men, double, it was not mentioned or ways in this would be addressed going forward.

The team indicates difficulties in recruitment and costs of omics work – investment and training in this area seem a necessity for competitiveness in the genomics and omics field.

The makeup of the research team is primarily ECRs and the pathway for permanent contracts is not clear and whether the unit could benefit from two or three more permanent members who could help to expand the programme's activities.

The team indicates a high burden on time for training to junior members of the staff – English not being a primary language, there is no mention of this being an issue across the Institute and what processes are in place to support.

Analysis of the team's trajectory

Over the past five years, the team excelled in delivery of their goals and addressed previous recommendations. The team going forward will be led by Ms Bouatia-Naji with the focus being advancing knowledge about 'arterial health and disease in women'. There are two new team leaders joining the group Mr Bruno and Mr Boutouyerie and there are two further permanent members of staff. There will be a focus on three research topics. 1. Leader: Ms Bouatia-Naji: Genetics of SCAD, FMD and related arterial diseases, 2. Leaders: Mr Bruno and Mr Boutouyerie: improving cardiovascular risk stratification and treatment in women, 3. Leaders: Ms Bouatia-Naji and Mr Georges: molecular and biological translation of genomic loci involved in SCAD and FMD. In the presentation and report details of the different topics were articulated, and it is an ambitious package of work where new funding is required to build up the team of post-docs and students. Grants are submitted and in preparation, and new paper. The team have exciting results to follow up and new ideas, and the goals if

delivered will maintain the international leadership in FMD and SCAD and a move into risk stratification is very complimentary.

RECOMMENDATIONS TO THE TEAM

The team is in flux with new team members and a refocus. How they integrate and work together will be interesting to see and how many collaborative papers will result. The current genetics results provide huge opportunities, so it would be expected to prime further high-profile publications and funding. Short to medium term delivery of some tools for risk stratification for FMD and SCAD would be a good translational outcome. With there being so many target genes, a focus on a set of particular genes and pathways may be advantageous, so early therapeutic targets could be identified.

Team 4: Integrative Epidemiology of Cardiovascular Diseases

Name of the supervisor: Mr Xavier Jouven (& Mr Jean-Philippe Empana)

THEMES OF THE TEAM

Team 04 has specialised in Integrative Epidemiology, combining various medical fields to investigate CVD and beyond, such as renal graft rejection and sickle cell diseases. Their 2017–2022 strategy included research on sudden cardiac death (SCD), AI in healthcare analysis, vascular aging, primordial prevention for CVD, and global health efforts in Africa. They also studied COVID-19's impact on out-of-hospital cardiac arrests and collaborated on acute rejection in renal transplants.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Team 04 seems to have addressed most of the previous evaluation's recommendations for the 2012–2016 period, but some open questions remain.

1. Team 04 was challenged with respect to the novelty of their biomarkers, it is not clear what was their strategy to address this.
2. More information would be needed on new or enriched cohort data and samples strategy as well as a long-term strategy for a high-level sustainable research infrastructure attached to the team.
3. To which extend results from other teams impact the research line of Team 04 could be further detailed as well to describe the translational aspect of the work and the interactions with other PARCC teams.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	6
Maîtres de conférences et assimilés	7
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	9
Sous-total personnels permanents en activité	23
Enseignants-chercheurs et chercheurs non permanents et assimilés	5
Personnels d'appui non permanents	13
Post-doctorants	3
Doctorants	6
Sous-total personnels non permanents en activité	27
Total personnels	50

EVALUATION

Overall assessment of the team

Team 04 has made strides in integrative Epidemiology of cardiovascular diseases, combining various specialities and focusing on areas like sudden cardiac death, vascular aging or primordial prevention. They have secured 23 out of 26 grants as coordinators for a total amount of 3,100 K€, with large national such as one IDEX grants, two ANR grants including a binational (with Switzerland) and international grants such as one H2020 and expanded their research activities to include other chronic diseases or renal graft rejection, and participated in global health initiatives. Recommendations include further enriching unique cohort studies and improving engineering support to prepare the team for the future challenges on digital technologies and AI.

The team has published more than 300 articles in generalist journals with high visibility as first, and last position (NEJM, JAMA, Nature Med) and specialist journals with high visibility (Lancet Haematol, Lancet Public Health 2020, 3 J Am Coll Cardiol, Eur Heart J, Circulation, Circ Res).

The team has four PHRC managed by APHP and has established contracts with industry such as Sanofi/Bioiterativ for and two CIFRE PhD contracts have been established with the start-up Cibiltech.

Overall, Team 04 has produced outstanding research.

Strengths and possibilities linked to the context

Attractiveness

The objectives of the team, highlights the focus on Integrative Epidemiology of CVD, the investigation of chronic diseases, and the impact of the COVID-19 pandemic. The scientific strategy involves work on major topics like sudden cardiac death (SCD) research, AI in health data, vascular aging, and primordial prevention. Staff members place emphasis on expertise dissemination and collaboration. Economic and societal impacts include contributions to public policy, both locally. Interestingly, they also obtained Dutch (705 K€) and Australian (860 K€) grants. Collaborations feature innovative projects on SCD prevention. Human Resources Management emphasises supervision, diversity, gender balance, and remote work, with a strict adherence to guidelines on human resources management, safety, and ethics.

The team supervised twenty PhD students for sixteen HDR with fourteen PhD thesis defended and 6 post-docs. There are four nationalities among postdocs and PhD students (The Netherlands, Australia, Togo and Egypt). Four new HDR have been successfully defended totalling ten senior HDR researchers. The profile of the team has been enriched by engineer researchers (coming from engineering schools: Polytechnic, ENSAE) to increase their expertise in AI. Women account for half of the staff members.

Recognition

The team has global recognition through international invitations to conferences and meetings (European Society of Cardiology, European Rhythm Society, ...) and participated in research steering committees (Lancet commission on sudden cardiac death, on ischaemic heart disease or members of epidemiology

Funding achievements are marked by the effective utilisation and securing of 23 out of 26 grants as coordinators for a total amount of 3,100 K€ such as one H2020, 6 ANR grants (2 as collaborator) including a binational (with Switzerland), one IDEX grant. The team's influence in the scientific community is evidenced through organisational roles, awards, and memberships, as well as participation in European networks and projects, enhancing scientific influence. Supervision of diverse talent and a nurturing environment for junior researchers demonstrates the growth and trajectory. Success in obtaining various grants (International Research Project Inserm, and the effective use of funds for specific research (the team was labelled FRM (2021–2024), coupled with expertise in diverse medical and technical areas, is notable (ex the Sudden Death Expertise Centre (n=50000), the PARIS prospective study III (n=10157).

The presence of significant research platforms and efficient operations in technical management further strengthens this area.

One member belongs to Institut Universitaire de France and is EHRA: Scientific Initiatives Group Member (2020). The leader is coordinating the International summer school of Global Health under the framework of the European Circle U project.

Scientific Production

The team has published more than 300 articles and is marked by strong publications in generalist journals with high visibility as first, and last position (1 NEJM 2019, 2 JAMA 2018, 1 Nature Med 2020) and specialist journals with high visibility (1 Lancet Haematol, A Lancet Public Health 2020, 3 J Am Coll Cardiol 2022, Eur J Heart J (2018, 2022), one Circulation 2019, one Circ Res 2020, ...).

This remarkable scientific production underlines focused research. There's a well-defined publication expectation and support structure for junior researchers with a minimum of 2–3 publications at high levels for post-docs and a minimum of two publications expected for PhD students), with an unwavering commitment to scientific integrity, ethics, open science, and a focus on reproducibility. All the scripts written for statistical analyses are saved on the PARCC servers and can be shared.

They have addressed the epidemiology of sports related to sudden cardiac death and the sex disparities. They have described how the cardiovascular health score changed overtime and how this change was related to an incident cardiovascular event. They are also dedicated to global health via the African Research Network gathering the team and researchers from twenty sub-saharian African countries through the studies addressing the burden of uncontrolled blood pressure as examples.

Contributions of research activities to society

The team has established contracts with the industry. The Sanofi/Bioiterativ grant permitted the launch of a programme on the genetics of sickle diseases in Africa. Two CIFRE PhD contracts have been established with the start-up Cibiltech. The team has four PHRC managed by APHP (1,050 K€). The creation of the Sudden death Expertise Centre (started in 2011) allowed tight interaction with healthcare actors (ARS, CNAM). Involvement in funding and education in cardiovascular epidemiology is significant. Activities include drafting care standards, expert participation in the CVD field, collaboration with renowned organisations (Fondation Coeur et artères, Fondation Global Heart Watch), organisation of public events, active engagement with patient associations, contributions to public policy, and wide media coverage (organisation of an annual of sudden cardiac death day dedicated to the general population), showcasing a multifaceted approach to cardiovascular epidemiology. Economic and societal impacts include contributions to public policy, both locally and globally,

Weaknesses and risks linked to the context

The evaluators felt a lack of clarity in how interactions between different research axes within the team are fostered (cross-pollination). It also pinpoints a need for the team to consider hiring or training more engineers, particularly in areas that require technical expertise like AI, to support large-scale efforts. The evaluation further suggests that the team should explore additional strategic interdisciplinary collaborations and partnerships (both public and private) to enrich the research programs and leverage external expertise.

The need to offer continuous training and development opportunities to staff and students is also emphasised to foster growth and innovation within the team.

The team needs to expand interdisciplinary research or collaboration. This area also indicates room to develop more interdisciplinary and high-risk high-gain research projects, in particular in the field of primordial prevention. It underlines the need for additional support mechanisms or alternative pathways for junior researchers, and points out a lack of institutional funds to realise the team's full potential. Suggestions also include the need for new strategies for publishing and communicating emerging fields like AI, as well as measuring Team 04's impact beyond the impact factor of a journal, and improving strategies to communicate complex and novel research to general audiences, possibly through increased public engagement.

The team needs for further exploration of collaboration opportunities and tracking the effectiveness of nonacademic interactions. It also observes limited communication materials (e.g. infographics, social media) to reach a wider non-specialised audience. There is a call for the expansion of research products and an explanation of how the work contributes to economic and social advancement. Additional public-private partnerships would be welcomed reaching clinical and societal impact faster, especially for AI-driven research in the future, assuming easy access to external administrative support to facilitate public-private partnerships. Finally, there is a need for increased efforts in disseminating information and developing communication strategies to connect with non-specialised audiences.

Analysis of the team's trajectory

Team 04 has exhibited a very impressive trajectory, maintaining a high level of scientific quality. The integration of different scientific expertise and international contexts has allowed them to provide a more holistic view of CVD epidemiology, leading to novel insights into complex medical challenges. Their work on sudden cardiac death, vascular aging, and primordial prevention has demonstrated creativity and innovation. Collaborations with external organisations and the effective utilisation of funding have enabled them to maintain this upward momentum. The strong record of publications in top journals, along with their involvement in cutting-edge projects and global health initiatives, underscores their continued commitment to excellence and influence in the scientific community. Their remarkable achievements in areas such as SCD research, supervision of diverse researchers, and public policy contributions reflect a team that continues to thrive and lead in their field.

RECOMMENDATIONS TO THE TEAM

The following recommendations seek to support the ongoing progress of the research team. There is encouragement to continue building and expanding partnerships, both public and private, to cultivate research growth. While innovative and productive, Team 04 could enhance internal cohesion through increased cross-pollination between research domains in the team and also with other PARCC teams, as well as highlight more their societal impact, beyond their high-level publications.

Clarity in communicating strategies, enhancing and expanding new data collection and cohort studies is essential for Team 04 to be future ready. Recommendations include further enriching unique cohort studies and improving engineering support to prepare the team for the future challenges on digital technologies and AI. Opportunities to integrate digital technologies, but not restricted to AI, could be explored further, perhaps by relying on specialised platforms or support systems (internally or at the PARCC level) and preparing the team for the significant impact these technologies may have. Developing specific metrics to assess real-world impact, such as societal benefits and policy influence, would add value beyond traditional scientific outputs. Considering centralised management could facilitate cohesive integration and prevent dispersion among different research themes. Finally, an enhancement in efforts to promote Open Access and Open Science aligns well with broader trends in transparent and accessible scientific research.

Team 5: Immuno-metabolic mechanisms of cardiovascular diseases
 Name of the supervisor: Mr Hafid Ait-Oufella (& Mr Ziad Mallat)

THEMES OF THE TEAM

The research focus of Team 5 is the study of immunometabolic mechanisms underlying atherosclerosis and post-myocardial infarction remodelling, in order to propose therapeutic interventions aimed at modulating immuno-inflammation. The impact of inflammation/high-fat diet on the immune response to tumour growth and the development of atherosclerotic plaque is no longer a research focus since the departure of one junior researcher. An emerging line of research led by another member investigates the link between the immune system and cardiometabolic diseases.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

One recommendation relating to scientific strategy and projects was to avoid the risk of diluting strengths and to strengthen PARCC's internal collaborations on the 'oncology-heart and vessels' axis. Cancer as a risk factor is no longer presented as a research focus, but rather obesity and microbiota as a co-morbidity. Interactions between the team's PIs are good and synergistic. The time allocation of certain PIs with shared activities is not particularly explicit, but the results obtained and the efficient running of the team demonstrate that the current organisation is effective.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	7
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	1
Post-doctorants	3
Doctorants	3
Sous-total personnels non permanents en activité	8
Total personnels	15

EVALUATION

Overall assessment of the team

The team's track record over the period in question is outstanding, with excellent scientific output, fund-raising capacity (for a total of €3.7 million) and national (labellisation by FRM (X2), eight ANR with six as PI...) and international visibility (one H2020 as PI, two ERA-CVD with one as coordinator).

There has also been a good transfer of knowledge to the general population, with efforts made to popularise the team's work, and value added through six patents, the creation of a start-up (Polygon therapeutics) and the coordination of a horizon H2020 (RITA-MI2) which is a phase IIb trial. Despite the moderate size of the team, scientific output is remarkable, and research training for students and young PhDs is excellent. The team's synergy between the various PI is also clear, and the direction taken towards clinical applications is very promising.

Strengths and possibilities linked to the context

Attractiveness

Despite the moderate size of the team, their ability to raise funds is more than excellent (a total of €3.7 million), with twenty grants acquired during the period as project leaders, whether from ANR (n=8, 6 as coordinator), European funds (2 ERA-Net CVD, 1 as coordinator and one Horizon H2020 as coordinator, another starts in 2023) or foundations (team labelled by Fondation pour la Recherche Medicale (FRM) (2017-2020, 2021-2024), Fondation de France, Fédération Française de Cardiologie (total of 3.7M€).

The team has played a major role in setting up and promoting the center's cross-disciplinary platforms. The team has access to well-phenotyped biological collections from the acute phase of myocardial infarction and atherosclerosis, thanks to valuable collaborations (Ms T. Simon, Mr G. Paterkamp).

The team pays particular attention to the career progression of its technical staff and to the future of its PhD students (supervision of 11 PhD students for seven HDR with eight PhD thesis defended and 3 ongoing), almost all of whom are either on post-doctoral research training or have been recruited by the private or public research sector. All PhD students published articles as first author except two who's the work is currently submitted. They also welcomed seven post-doc fellows. The team has welcomed fellows from eight different countries (Algeria, Lebanon, Morocco, China, France, and Germany). One Inserm engineer has obtained her PhD supervised by a member of the team in 2018.

Recognition

The national and international visibility of team members is revealed by invitations to international meetings (Gordon Research conference (2017, 2019), Keystone Symposia 2018, plenary lectures at ATVB 2019, ...) and the organisation of master classes and international congresses (Advanced courses of the European Atherosclerosis Society, Fusion Conference 2017, 2020, 2022)). They also participate in European consortia. They also have an excellent track record of scientific evaluation in various national and international agencies, as well as reviewing scientific articles for prestigious journals, for which they are also involved on the editorial board). Finally, the team's recognition is reflected in the various awards its members have received (prize ARDRM (2021) as well PhD students (International Bernd R Binder prize, young investigator award from the European Atherosclerosis society).

Scientific Production

The team has published 87 articles with 49 original, 38 reviews or editorial. Scientific output is excellent, with original articles published in generalist journals with high visibility as dominant position (two Nat Med (2017, 2018), five Nat Commun (2 × 2017, 2021, 2 × 2022)), one J Clin Invest (2021) and the best journals in the cardiovascular field (two Circulation (2019, 2021), two J Am Coll Cardiol 52,018, 2022), two Cardiovasc Res (2017, 2021), three Circ Res (2017, 2 × 2018).

They have developed innovative research based on immune therapies (e.g. monoclonal antibodies, recombinant cytokines) targeting B cells (Nat Med, J Exp Med, Nat Commun) and they also investigate the mechanisms involved in metabolic diseases and interplay between gut microbiota and systemic immune responses (Nat Med,...).

Contributions of research activities to society

Two PhD students have been funded by a CIFRE contract (Servier and ScarCell).

Members of the team are very active in clinical research with 6 patents (human studies and creation of a start-up (Polygon therapeutics).

The team coordinated a horizon H2020 (RITA-MI2) which is a phase IIb trial.

The leader has obtained two highly competitive grants from Inserm transfert for proof-of-concept study.

The team participates and supports PARCC's policy for sharing knowledge with the general public and in particular with school populations (fête de la science,...). Team member organise meetings with FRM donors.

Weaknesses and risks linked to the context

One weakness highlighted by the team is the potential for analysis of the large amount of data generated, in particular by approaches to studying the microbiota and single cell analysis, which will probably need to be strengthened.

Particular attention should be paid to recruit junior researchers who can interface with PIs and PhD/post-doctoral students, given the very high level of involvement of the team's managers in national and international proceedings, with a very time-consuming administrative workload.

Analysis of the team's trajectory

The team has extensive historical expertise in the development of pre-clinical models to investigate the processes of atherosclerosis, abdominal aortic aneurysms and post-myocardial infarction remodelling. Significant efforts are being made to apply some of their discoveries to human therapies. Indeed, a start-up has

been created and several clinical studies aimed at depleting certain lymphocyte populations and modulating immuno-inflammation with interleukin two have been initiated in various human atherosclerosis settings.

In terms of its trajectory, the team will continue in the same direction, with the pursuit of three main objectives:

- The mechanistic aspects of the development of atherosclerosis, with a particular focus on the impact of inflammatory cells on vascular and cardiac cells
- the impact of metabolic factors on the immune response, and how these comorbidities influence atherogenesis and post-infarctus remodelling
- the development of immunomodulatory therapies to combat cardiovascular disease.

The project is structured around five axes involving the three research directors, with collaborative translational axes, in particular that relating to trained immunity in cardiometabolic diseases. In addition, each researcher has his or her own clearly identified thematic and therapeutic focus, with well-defined clinical applications.

RECOMMENDATIONS TO THE TEAM

The first recommendation would be to maintain the team's current level of excellence. To achieve this, it will be necessary to encourage the recruitment of researchers to act as the interface between PIs and students/post-docs, either through competitive recruitment, or through mobility within the university system or Inserm. The development and use of technologies generating large amounts of Big Data will also require the support of bioinformaticians and data managers, who will need to be included in future funding applications. Ensure that the microbiota theme is well integrated with the team's other research areas.

Team 6: Regenerative therapies for cardiac and vascular diseases
 Name of the supervisor: Mr Jean Sébastien Silvestre

THEMES OF THE TEAM

The Team addresses two major topics, namely signalling pathways involved in post-ischemic tissue remodelling and cardiac regeneration by both cellular and non-cell-based approaches (EVs and secretome).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations were to maintain the same level of scientific production, synergistic exchange, outreach activities and collaborations with other teams, such as Team 1 for EV biology but also Team 7 for cell therapy.

Most of the recommendations have been taken into account. How the two groups synergise with each other and other Teams at PARCC remain not totally clear.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	8
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	6
Sous-total personnels non permanents en activité	7
Total personnels	15

EVALUATION

Overall assessment of the team

Overall, the performance of the team has been excellent in terms of both scientific production and grants, with 96 publications including 44 original articles such as *Circulation*, *J Am Coll Cardiol*, *European Heart Journal*, *Circ Res*, *Theranostics*, 39 reviews or editorials and thirteen clinical research articles, and having obtained thirteen grants for a total amount of 4.7 million euros from both national (five ANR with four as coordinator) and international granting agencies (one Horizon-RIA as a coordinator).

Both PIs are regularly invited as speakers at important international conferences (AHA 2019, 2021, 2022; European Society of Cardiology, 2017, 2018), which is an additional indication of worldwide scientific reputation.

They also produced three patents, which demonstrate tech transfer capacity and vision. While the two groups appear to be leader in their respective fields, their synergy remained somehow unclear in the report.

Two PhD students have been funded by a CIFRE contract (Gecko Biomedical, Poietis). The team has been funded by the Ministry of Solidarity and Health to support and coordinate a national clinical research hospital program. Social engagement is evident and concrete.

Strengths and possibilities linked to the context

Attractiveness

The team builds on the collaboration between two groups, which focus on basic (Mr Silvestre) and translational (Mr Menasche) research in the field of cardiac repair and regeneration. This is a relevant scientific goal, considering the epidemic of cardiovascular disorders and the need to bring new therapeutic approaches (and biotherapeutics in particular) into the clinics. The team has adopted state-of-the-art methodology and standards in its research, as documented by excellent and joint publications (seven joint publications since 2017).

The team has obtained thirteen grants for a total amount of 4.7 million euros from both national (five ANR with four as coordinator) and international granting agencies (1 Horizon-RIA REGerNA as a coordinator), in which the synergy between the two PIs has been successfully leveraged. Examples of joined grants are by the Deutsch DFG/French Research National Agency and the Fondation pour la Recherche Médicale (FRM, labellisation of the team (2016–2019), thus mainly national. These funds are allowed to keep high scientific level and reputation and to cover the salary of non-permanent staff.

The team entails seven permanent staff and seventeen researchers with non-permanent position, out of which three and fourteen are women, respectively. Thus, the team is overall gender balanced. The team has supervised fifteen PhD students (10 were already defended) and three post-doc from three different nationalities (France, Brazil, China).

The team has recruited as permanent CRCN Inserm researcher in 2021, a former post-doc in the team supported by a Marie Skłodowska-Curie action. Significant effort is spent by the team in ensuring a smooth and successful career to its young researchers, ensuring them publications and awards, participation to high quality meetings and helping them find their next job, with all PhD students having found a position to pursue their career.

The team can benefit from numerous facilities available at PARCC, as well as from external equipment and expertise, thanks to their own collaborations. Team members have been instrumental to acquire new instruments and pioneer novel technologies in the institute.

Recognition

The scientific reputation of the team is excellent by the inclusion of PIs in reviewing boards by granting agencies (European Research Council consolidator grant, Netherland Heart foundation, Science Foundation Ireland) and journals (Nat Med, J Clin Invest, Circulation, Circ Res). Both PIs are regularly invited as speakers at important international conferences (AHA 2019, 2021, 2022; European Society of Cardiology 2017, 2018), which is an additional indication of worldwide scientific reputation. They also took part in the coordination of European calls (ERA-NET scientific advisor), which is a significant contribution to the progress of European research.

The team leader has participated in the writing of a review describing the cardiovascular landscape in France (Circ Res 2018) and the co-leader has participated in the writing of several guidelines and position papers by international societies (Cardiovasc Res 2022, ESC Heart Fail 2021) and is a member of the working group on regenerative therapies of the European Society of Cardiology.

Team members received grants and awards for their scientific activity, such as Victor and Erminia Mesclé (2017) and Jeanne-Philippe Beziat (2017) awards from FRM.

Scientific production

The team kept being highly productive, with relevant publications in the two main fields of investigation, the role of immune cells in cardiac repair and regeneration and cell/secretome therapy with 96 publications including 44 original articles, 39 reviews or editorials and thirteen clinical research articles. The team should be commended for their capacity to publish high quality pre-clinical and clinical research, as documented by excellent joint publications (7 joint publications since 2017) in high standard international journals, such as Circulation (2019), J Am Coll Cardiol (2018, 2022), European Heart Journal (2018), Circ Res (2018) Theranostics (2021), etc. Several publications show the collaboration with other Teams.

The scientific production is well proportionate and distributed among members of the team.

As already highlighted in the previous evaluation, the team has pioneered the use of electronic books and it keeps promoting its use to enhance scientific integrity. Publications are largely in Open Access (67% of the publications). The team is also very experienced and active.

As an example, they have decrypted the importance of the interaction between different cellular components of innate and adaptative immunity and cardiac hemostasis (Circulation, Circ Res) and developed cellular and acellular-based therapeutic approaches for patients with cardiac diseases (J Am Coll Cardiol, Cardiovasc Res, Eur Heart J).

Contribution of research activities to society

Non-academic interactions of the team are in place with companies producing medical solutions, which is in line with the major scientific objectives of the team.

Two PhD students have been or are funded by a CIFRE contract (Gecko Biomedical, Poietis).

One of the co-leaders of the team is member of the advisory board of pharmaceutical companies (Astra Zeneca, FujifilmCDI). He chairs the Medical and Scientific Committee of the Agency of Biomedicine and the steering committee on the use of CAR-T cells (AP-HP).

The scientific products developed by the team have been the subject of three patents. The team has been funded by the Ministry of Solidarity and Health to support and coordinate a national clinical research hospital program (PHRC, SECRET-HF, 620 K€, 2019–2922). Social engagement is evident and concrete. The team has been very active in engaging the public, with particular attention to schools and younger generations, which are the most relevant target for dissemination of their research activities.

Weaknesses and risks linked to the context

As acknowledged by the PIs, the field of cardiac repair and regeneration is extremely competitive, and requires increasing resources. A slight decrease in the number of academic research grants was noticed compared to the previous evaluation (30), despite similar human resources. Eventually, the amount of funds secured to manage the team is still very high.

As often happens, women are more represented among students as in leading positions.

Most post-doc come from either France or Belgium, with not many people from other countries.

The PIs have not obtained highly competitive awards, such as ERC grants or personal grants.

The number of published papers has slightly decreased compared to the previous evaluation period and some publications are in specialised journals.

The capacity of the team to exploit their patents was not very clear in the report, some concrete examples have been shown during the on-site visit.

Specific actions could be taken to increase public acceptance and confidence towards ATMPs in general, given the reputation and the expertise of the team.

Analysis of the team's trajectory

The team has produced excellent science in the field of post-ischemic recovery and cell and cell-free therapies for heart regeneration. They also secured and coordinated competitive grants in this field, establishing themselves as leaders in their respective field. Joint publications, also with members of other Teams, prove their efforts in collaborating and leveraging existing expertise at PARCC. The future trajectory was less clear in the report, particularly how the two groups intend to maximise their synergy to co-exist within the same group. The presentation made during the evaluation clarified most aspects and demonstrates a promising trajectory for the whole team, indicating a fusion of Teams 6, 1 and 7, with two leaders, Mr Silvestre and Mr Hulot, who will co-lead the team.

RECOMMENDATIONS TO THE TEAM

The team is expected to maintain the level of its scientific production and capacity to secure funds at international level. Also, outreach activities and industrial vision should be kept at high levels. In view of the nomination of Mr Silvestre as the new Director of the Center, roles and responsibilities of the other leader (Mr Hulot) as well as permanent staff in the team could be reshaped for future activities, together with the definition of a few, clear and measurable objectives for the years to come. Synergy between Team members should be maximised, as their role/contribution to ongoing projects led by other Teams at PARCC. With such a large team and such a large number of ongoing projects, a risk for defocusing can arise, but the Team shows full awareness of its capacity and possibilities.

Team 7: Biology and pharmacology of heart failure
 Name of the supervisor: Mr Jean-Sébastien Hulot

THEMES OF THE TEAM

The team is interested in a particular situation observed in heart failure in which the left ventricular ejection fraction is preserved. The research is focused on the mechanisms of myocardial and arterial stiffening and their implication in heart failure with a translational approach.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has generally followed the recommendations of the previous evaluation (1- to maintain excellence and 2- to increase collaboration with other PARCC teams).

In particular, the team maintained its level of scientific production despite the merge of three groups and the shutdown of activity during the COVID.

They have conducted a significant number of collaborations with other PARCC teams (illustrated by high-level collaborative publications). The creation of a platform (iPS Cell technology) within PARCC has significantly contributed to these new collaborations.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	6
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	8
Post-doctorants	5
Doctorants	3
Sous-total personnels non permanents en activité	18
Total personnels	24

EVALUATION

Overall assessment of the team

The team led by Mr Hulot was created at the beginning of this evaluation period (based on the recommendations of scientific supervisory authorities). During this last four years, this team was able to bring together the skills from the three original groups to build and carry out a research project on heart failure in accordance with the evolution of this field of research including high-level technical tool development in validation (e.g. hiPSC platform).

This is evidenced by the quality (e.g. International Leducq Network grant one as PI and one as partner)) and number of grants obtained (19 significant grants for more than 4 million euros) such as three ANR grants as PI and the team was labelled by FRM). The team's publication record is of excellent level (134 original publications directly related to the team research axis in leading journals including New England Journal of Medicine (2021), Circulation (2017, 2022), J Am Coll Cardiol (2017), Eur Heart J (2022) in dominant positions (1st or last author). In addition there is a significant number of doctoral students (n = 12) and post-doctoral students (n=12) present over the period. The team has filed three patents, obtained two CIFRE grants with a big Pharma (Servier) and demonstrated its ability to obtain funding from private companies in three collaborative research programs. Moreover national collaborative projects (SME Company, France) and international (Pliant therapeutics, USA)

To conclude the overall assessment of the team is excellent.

Strengths and possibilities linked to the context

Attractiveness

The pooling of complementary skills from three pre-existing teams at the origin of this team allowed this team to determine its scientific objectives in a relevant manner in a context of change in the landscape of heart failure and its manifestations in patients. The team's interdisciplinary project on the importance of the involvement of cardiac and arterial stiffening in heart failure is therefore a relevant objective and the combination of molecular, cellular and integrated mechanisms approaches used by the team allows them to envisage significant contributions to the knowledge of this subject.

Beside a recurring financial support from INSERM, the PARCC unit provided the space necessary for the team to settle in upon their arrival (including the space necessary for the iPS Cells platform).

Furthermore, over the period the team obtained nineteen significant grants for more than four million euros illustrated by the coordination of three ANR grants and one Leducq Transatlantic Network of Excellence and another as partner. They are also partners in five European Union grants (three H2020, one ERA-NET CVD, one COST action). The team was labelled by foundation pour la Recherche Médicale (2020–2023). This makes it possible to maintain a good scientific level but also to cover the non-permanent staff (including post doc) and PhD salaries. The team has supervised twelve PhD thesis (nine were defended) for seven HDR and welcomed twelve post-docs of eight different nationalities (Italy, Pakistan, Portugal, Canada, Lebanon, Japan, Tunisia, India). Moreover the team is overall gender balanced with three out of six permanent positions and eighteen out of 24 PhD (and Post-doc) occupied by women.

Many efforts are made by the team to ensure this quality of the staff hosting policy. As an example, the integration of foreign students is facilitated by daily use of English.

The team chose to comply with the guidelines edited by INSERM, the University of Paris Cité and the PARCC concerning the quality of life at work, training specific to scientific equipment, manipulation of biohazard, management and protection of data (acquisition of local storage server).

Furthermore, the publication strategy giving important places to doctoral and post-doctoral students and including technical staff contributes to this attractiveness. The recruitment as a study engineer (INSERM) of two initially non-permanent technicians also reflects the team's particular attention to professional promotion.

The team undertakes to use the electronic lab book from INSERM and to use standardised protocols previously validated by supervisors and engineering staff.

The team respects all the rules relating to clinical research, in particular by ensuring that the regulatory training of its members is complete.

Recognition

The scientific reputation of the team is attested by numerous invitations to conferences and congresses (European Society of Cardiology (2017–2021), AHA 2021, German Society of cardiology (2018, 2021), European Society of hypertension (2022)). Furthermore, there is a real contribution to the construction of the European research Area through regular participations but also involvements in the organisation (e.g. European Days of the French Society of Cardiology, ARTERY meeting) of national and European events. The team members are also involved in editing (e.g. associate editor in JACC).

One member was president of the artery society (2018–2021).

The team manages all activities and equipment related to iPSC (human pluripotent cells). This platform is used by the entire PARCC (four other teams). Furthermore, the team has also developed an in vitro tissue model platform. It led to national and international expertises which have contributed to the recruitment of post-doctoral fellows and of two PhDs. This is clearly illustrating the attractiveness associated with those equipment and technological skills.

Scientific production

The team was very productive (227 publications, including relevant 134 original publications (directly related to the axis research on heart failure in a translational approach) in leading journals (e.g. New England Journal of Medicine (2021), Circulation (2017, 2022), J Am Coll Cardiol (2017), Eur Heart J (2022)) in dominant positions (1st or last author). The involvement in collaborative projects has also given rise to co-authorship positions in high-level journals (e.g. Nature, Nature Comm, Cell Metab).

As mentioned in various previous sections, the team has produced a significant number of publications related to their research theme. They strive to place doctoral and post-doctoral students in dominant positions (1st or 2nd author) and to include technical staff in the authors. 69% of the total number of publications was published in open access.

As an example, they have recently identified a novel cardiac stromal cell sub-population (expressing PW1) which acquires a pro-fibrotic behaviour in response to injury (J Am Coll Cardiol). They also showed that cardiac stromal cells undergo a change in paracrine behaviour post-M with GDF3 to predict fibrotic cardiac remodelling (Circulation).

Contribution of research activities to society

Non-academic interactions take different forms including the financing of CIFRE grants (n=2) with a big Pharma (Servier). In addition, the team has demonstrated its ability to obtain funding from private companies in three collaborative research programs. Moreover national collaborative projects (SME Company, France) and international (Pliant therapeutics, USA) for the development of molecules linked to the team's themes (cardiac organoids; markers of fibrosis potentially involved in cardiac and vascular stiffening) have been initiated.

The team leader is a consultant for pharmaceutical companies (Astra Zeneca, Alnylam, Bayer).

In this evaluation period, the team has filed three patents and plans to create a company attesting to involvement in the economic world.

Other recurring activities (scientific popularisation, science festival, social networks) reflect a desire to communicate with the cultural and social world.

The team regularly shares its knowledge with the general public through the participation of specific events (science festival) and schoolchildren. Radio and press interviews were also carried out by the two PIs.

Weaknesses and risks linked to the context

It appears that this significant activity is mainly carried by the team leader (Mr JS Hulot) and Mr P. Boutouyrie. The fact that two DR INSERM has left the team early 2021 will increase this dependence to the two PIs activity in this evaluation area.

A large number of publications results from collaborative work. In its self-evaluation, the team highlights the importance of the delay in three publications directly related to the team's themes due to the shutdown of activity during COVID. Three publications out of the 134 original publications listed over the period might not seem important. However, this concern about these three publications illustrates that the team is concerned about maintaining a significant number of publications directly linked to the theme to continue to ensure that it corresponds to the research potential of the team.

Analysis of the team's trajectory

In this four-year period, the trajectory of this team appears very clear and seems to have been well managed. From the initial creation at the beginning of this period to the integration of another team for the next, this team has strived to develop an innovative and public interest research axis.

The team has endeavoured to respond to the comments of the previous in terms of scientific productions, scientific collaborations (within PARCC or outside) and interaction with the socio-economic environment.

RECOMMENDATIONS TO THE TEAM

The team is required to join a larger team at the end of this evaluation. Due to the origin of this team and what it has implemented regarding heart failure with preserved ejection fraction in a translational approach, it is essential to ensure that this line of research will remain important in the future. This is important, both for the research theme and for the staff who have been participating in it for five years and who perhaps hope for continuity in their activity. It would also be necessary to a lesser extent to ensure that the activity of the members of this team 07 in the future team does not take a collaborative orientation solely with an experimental platform type operation.

Team 8: Renal and vascular signalling: from development to pathology
 Name of the supervisor: Mr Pierre-Louis Tharaux (& Mr Eric Camerer)

THEMES OF THE TEAM

The team is focused on:

- 1) Studying glomerular repair with a particular focus on epithelial cells
- 2) Studying interactions among inflammation, vascular and epithelial repair in diabetes, hypertension, autoimmune vasculitides, sickle cell disease.
- 3) Studying possible therapeutic targets for kidney diseases even though extended clinical trials
- 4) Studying the role for S1P signalling in cerebrovascular function and the recovery from ischemic stroke (by a co-Team leader that will now move to Team-9)

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations were to keep going on their excellent scientific activities with a better involvement of PhD students in the production and life of the team.

The report shows the specific contribution of PhD students to scientific publications and their receipt of awards in national and international conferences.

Concerning the scientific strategy, they are working at implementing another murine model of vasculitis and expended their involvement in clinical studies.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	9
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	2
Post-doctorants	3
Doctorants	7
Sous-total personnels non permanents en activité	14
Total personnels	23

EVALUATION

Overall assessment of the team

During the past five years, the Team has given outstanding contributions in the field of kidney as well as vascular biology, as testified by their publications, grants and dissemination activity in the academic and non-academic world. In the kidney domain, the group stands as outstanding in the European domain. The team is successful in competitive calls for projects by obtaining 21 grants for which the members of the team were coordinators including four ANR grants, one team labelled by Fondation pour la Recherche médicale (FRM), one ERC (proof-of-concept grant) and one focused FRM grant for a total of 4.9 million euros. One post-doc was recruited as CRCN Inserm researcher (2017) and obtained a young researcher grant from ANR.

The scientific production is of high quality in top disciplines of the field and some multidisciplinary journals with 87 original articles (2 Nature Comm (2017, 2019), 1 Circ Res (2021), 1 Science (2020), ...).

The team has filed five patents and the team leader obtained seed support from the public agency SATT Paris-Orsay (750 K€) and received institutional support to launch a multicentre randomised clinical trial throughout France (PHRC 600 K€).

The team has established a collaboration and contract with Alentis Therapeutics.

The planned changes in the group give the chance to amplify the work on the kidney in the whole Unit, which is essential to better address the problem of cardiovascular risk and outcome.

Strengths and possibilities linked to the context

Profile, resources & team organisation

PARCC Team 8 consists of two research groups: one that studies the pathophysiology of kidneys, coordinated by Mr Pierre-Louis Tharoux and on microvascular diseases with a focus on G protein-coupled receptors (GPCRs) and receptor tyrosine kinases (RTKs) in vascular and immune cells. The other group works on GPCRs in vascular development and disease led by Mr Eric Camerer's group. The team has resources that well complement basic research with well-organised capacity to execute clinical trials on deeply characterised cohort of patients.

Rules and Directive on human resources management, safety, environment, ethical protocols are respected.

The team involves researchers and students of different nationalities underlining its international attractiveness. They have supervised thirteen PhD students (six were defended) for seven HDR and six post-doc fellows of six different nationalities (France, Algeria, Pakistan, Italy, Germany and Lebanon).

Attractiveness

The team stand in the European research area in the kidney field where they have given important contributions to the understanding of glomerular pathophysiology. In particular, the mechanisms of parietal epithelial cell response to injury can unlock potential therapeutic targets. The cohort of sickle cell disease patients is a unique asset to better study and understands kidney injury related to microvascular damage. The team had a very good success in competitive calls for projects by obtaining 21 grants for which the members of the team were coordinators including four ANR grants, one team labelled by Fondation pour la Recherche médicale (FRM), one ERC (proof-of-concept grant) and one focused FRM grant for a total of 4.9 million euros.

One post-doc was recruited as CRCN Inserm researcher (2017) and obtained a young researcher grant from ANR.

The team has a wide spectrum of advanced technologies, and 3D *in vitro* modelling strategies that are certainly attractive for kidney researchers and are pivotal for their international collaborations (numerous) and to raise a new generation of young scientists.

Recognition

The team leader is member of editorial board of the top speciality journal Kidney international and an advisory board at Nature Reviews Nephrology (2020 present).

Members of the team are invited in international conferences (Gordon research conferences, American Society of nephrology, FASEB conferences, ...) and international research institutions (Oklahoma Medical research foundation, National university of Singapore, Zürich Neuroscience center, ...).

Members of the team are also active in scientific evaluation and peer review for french (ANR, Inserm) and international (European Research Council, Kidney research UK, ...) grants.

One junior researcher was awarded the Gabriel Richet Young Investigator award of Fondation du rein (2017), the research prize from the French society of nephrology dialysis (2021) and the Albert Sezary price from the French academy of medicine (2021).

Scientific production

Scientific production is of high quality in top disciplines of the field and some multidisciplinary journals with 87 original articles in peer-reviewed journals (25 as first, last or corresponding authors), and is internationally

recognised for its contribution to kidney research, including 43 original basic science articles, 29 clinical research articles, seven invited reviews and eleven editorials. Some of the articles represent important contributions in the field as PI such as two Nature Comm (2017, 2019), one Circ Res (2021) and one Science (2020). Scientific production is proportionate to the potential of the team and quite distributed between its personnel. The team respects the principles of scientific integrity and ethics. The two groups have four joint publications, and one is under review.

As an example, they have dissected mechanisms driving the development of extracapillary lesions in atherosclerosis and glomerulonephritis (Nat Commun, Nat Rev Nephrol, Am J Kidney Dis). They described a critical role for S1P signalling in cerebrovascular function and recovery from a stroke (Circ Res, Blood Adv). They demonstrated the key roles for the myeloid ETB receptors in the control of systemic vascular resistance and blood pressure (Eur Heart J, Kidney Int).

Contribution of research activities to society

The team leader obtained seed support from the public agency SATT Paris-Orsay for the maturation and development of a therapeutic protein (750 K€) in a preclinical model of immune kidney disease. They also gained institutional support to launch a multicentre randomised clinical trial throughout France to evaluate a therapeutic approach developed in the lab for patients with vasculitis and kidney injury (PHRC 600 K€).

The team has established a collaboration and contract with Alentis Therapeutics to evaluate a potential novel therapeutic antibody for rare kidney diseases (2022-2024).

The team has filed five patents based on the therapeutic exploitation of new insight into pathological renal and cerebrovascular disease.

The involvement of the team in multiple non-academic initiatives, particularly association of patients (association des maladies du syndrome néphrotique, Fondation du rein,...), international societies and foundations is wide and there is also a clear strategy to increase awareness of kidney diseases. This is very important and needed, considering that kidney diseases affect about 10% of the population all over the world. From this perspective, it is also noteworthy that the team interacts at multiple levels with the general audience also hosting students from high school to the university level, which is also an important initiative to increase awareness of kidney disease.

Weaknesses and risks linked to the context

The growing importance of kidney biology in cardiovascular health has shifted a lot of attention on the kidney as a therapeutic target for patients with heart failure and other cardiovascular disorders. This evidence can for example be inferred from results of clinical trials with SGLT2 inhibitors. With this strong evidence coming up, the role of the kidney is currently largely underestimated in a unit that has a major focus on cardiovascular research and this is certainly a weakness that limits the possibilities of the center. Expanding the work of Team 8 and interaction with the other Teams beyond the vascular part or eventually even recruiting other scientists working in different subjects of the kidney field could strongly benefit the whole unit and its possible achievements in the research about cardiovascular disorders.

Analysis of the team's trajectory

The team is currently focused on mechanisms of epithelial repair, particularly of glomerular repair, and microvascular damage of the kidney. One of the two leaders of the team, Mr Eric Camerer, will move to another team to better focus on the role of S1P in the microvasculature of the brain. As a consequence, the Team will be more focused on the kidney and has the possibility to amplify its focus of work with also Ms Olivia Lenoir becoming co-Team leader. In the trajectory, the group states that the focus will become 'Kidney and Vessels, Inflammation and Metabolism'. Obviously, these points are important, particularly considering the work performed by the team in glomerular damage that is highly relevant for human vasculitis and for the large cohort of sickle cell diseases available for their studies. However, the reorganisation can become a great chance for the whole unit to amplify the work on the kidney and particularly on the tubule-interstitial compartment, that is already among the topics of the group but may be enlarged and supported in the future, given the evidence of the crucial role of this kidney component in the pathogenesis of CKD and cardiovascular damage coming from gliflozin and finreneone trials.

RECOMMENDATIONS TO THE TEAM

For the future of a unit focused on cardiovascular risk, work on the kidney should be extended. The kidney is, indeed, the most important risk factor for cardiovascular disease. Expanding the work on the tubulo-interstitium may be strategically relevant to remain linked to the areas where there will likely be more progress in the future. Including APOL1 among the topics may also be strategically convenient given the potential clinical impact in the CKD population in France and the large epidemiological overlap with the sickle cell disease population. I would also recommend continuing and even potentiating the constant exchange between basic research and participation or organisation of clinical trials that is one of the major strengths of Team 8. To realise all these objectives, the kidney team will obviously need more space and support, but this can ultimately benefit the entire unit.

Team 9: Development and vascular pathologies

Name of the supervisor: Ms Anne Eichman

THEMES OF THE TEAM

The themes of the team are the analysis of 1) Endothelial Barrier function manipulation – blood and lymphatic vessels; 2) Mechanisms of BBB integrity and reversibility; 3) Endothelial homeostasis and function and 4) Lymphatic tissue drainage and anti-glioma immune surveillance.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous HCERES recommendations were

1. *to maintain a high level of scientific production at PARCC,*

2. *to reinforce training and mentoring of PhD students*

3. *to develop synergistic interaction with other PARCC teams.*

1. They have obtained an ERC advanced grant in 2019 and the productivity has remained high.

2. They have trained several Master's students and one PhD student during the 2017–2022 period, a second PhD student is currently in training. They state that they have failed to obtain support from the doctoral schools over the past funding period.

3. They have reinforced collaborations within PARCC by merging with Mr Eric Camerer's group. The two groups have overlapping scientific interest in signalling pathways that regulate endothelial barrier function, and their labs are adjacent to one another on the third floor of PARCC. Moreover, they have already successfully collaborated (*Circ Res* 2021).

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	3
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	3
Doctorants	0
Sous-total personnels non permanents en activité	3
Total personnels	6

EVALUATION

Overall assessment of the team

This is an outstanding team, led by Ms Eichmann. The team has a very high scientific productivity, with papers in top journals including *Science* as dominant position. Discoveries are at the leading edge of vascular research such as the identification of targets to manipulate vessel growth and function in several pathologies. They have generated monoclonal blocking antibodies that can transiently open the blood-brain barrier, potentially allowing drug delivery into the diseased central nervous system. They have developed an MRI method to visualise the meningeal lymphatics in human patients with neurological diseases that will be tested for hospital practice (funds obtained 2023).

Ms Eichmann is a leader in the field with a strong international profile. Grant income is excellent (total of 3,900 K€), includes an ERC Advanced grant (2019–2024), two grants from Leducq network and two ANR grants as PI. One post-doc fellow obtained Fondation pour la Recherche Médicale (FRM) 'amorçage' funding (400 K€).

They have filed two patents. A very strong point is Ms Eichmann's double appointment at Yale.

Outreach, public engagement and science communication are excellent. Merger with a member of team 8 following recent feedback is likely to enrich both teams.

Strengths and possibilities linked to the context

Attractiveness

The team focuses on vascular development and vascular diseases. They have made important discoveries that have significantly advanced the field and influenced other researchers' work. The development of a patented Antibody against the blood-brain barrier (BBB) is an example of translational focus.

The team is extremely successful in raising funding. The combined affiliation with Yale provides access to US sources of funding and exchanges between the laboratories.

This is a very well-funded team for a total of 3,900 K€, with national and international funding, involved in prestigious international networks. Examples include one ERC Advanced grant Breaking Barriers (2019–2024, 2,500 K€), two grants from the Leducq Foundation, one as a member of a Transatlantic Network of Excellence (1,000 K€) and two ANR grants as coordinator.

The team is currently composed of two permanent scientists (the team leader and one CRHC CNRS), one CRCN has left the team in 2020.

The team has supervised three post-doctoral fellows and a foreign exchange MD. PhD from Brazil (Federal University of Rio de Janeiro, 2019). One post-doc fellow (who joined the team in 2022) was selected as junior group leader and obtained Fondation pour la Recherche Médicale (FRM) 'amorçage' funding (400 K€).

Examples of quality management include the recruitment of staff for the multiphoton platform. They mention the presence of five international trainees (China, India, North Africa, USA, France). All former students are still active in academia, education or industry. An extra strength is the double affiliation of Dr. Eichmann with Yale, which brings in advantages in offering trainees the opportunity to spend some time in Yale and to be exposed to the US academic and research environment.

The Team has been instrumental in the establishment of a multiphoton microscopy platform for imaging in 2019, managed by this team.

The team states that they comply with the guidelines for human resources management, safety, environment, ethical protocols and data as well as scientific heritage protection.

Recognition

The Team is extremely strong in this area. Ms Eichmann is regularly invited at the top international meetings in the area of vascular biology and is a leader in the field. The PI is frequently invited to international meetings (41 invited talks between 2017 and 2022) and to talks at institutions (28 talks since 2017), in Europe, North/South America or Asia. The PI co-organised two major international meetings (Keystone in 2018 and NAVBO (North American Vascular Biology Organization) meetings in 2020). She received the Folkman award from NAVBO for outstanding work by a mid-career investigator in 2019 (surprising that she was considered mid-career in 2019).

The team leader was the SAB chair for KAIST, Daejeon (Korea) in 2023 and she is involved in selecting the 'grand prix' Lefoulon Delalande (2021-present).

Team members are also reviewers for high standard international journals (Nature, science, Cell press journals, ...).

Production

This Team produces top quality science which opens new avenues, such as their work on lymphatic junctions. Their research is published in the highest-ranking journals. Over the period 2017–2022, the total number of

publications was 32, including 26 articles and six reviews/commentaries/chapters. They regularly publish in high-level international journals ((Nat Comm, JCI, Dev Cell, Circulation, Science, JEM) in a dominant position. The output is very strong and the report states that all team members between 2017-22 have publications. Senior postdocs or CRCN scientists sign papers as senior authors, with the PI as co-senior. Several members have presented their data at meetings. More than 90% of the papers are published in open access. Particular attention to ethics standards.

Contribution of research activities to society

The team has filled two patents.

The publications of the team are frequently picked by the public press (as ex Science 2018, 29 news stories including BBC radio).

They interact with patients as part of HHT community which assembles clinicians, patients and researchers.

The team participates in and support PARCC's policy for sharing knowledge with the general public and school populations.

Weaknesses and risks linked to the context

They stress challenges related to administrative matters. No references to EDI (equality, diversity and inclusion) policies.

There is a lack of French PhD students due to the lack of funding from the French PhD schools. Therefore, they have not been very successful in attracting French PhD students or French PhD funding.

They mention limited institutional resources as a challenge to maintain scientific excellence.

There is no industrial contract.

Analysis of the team's trajectory

The team's scientific trajectory focuses on expanding and developing the research areas currently active in Ms Eichmann's team. Moreover, the merger with the Camerer team offers the opportunity to combine interests and expertise to focus on a few specific pathways and expand the portfolio of in vivo models. The teams could provide more evidence for the integration between the Yale and Paris groups.

The research will focus around three axes, with a clear trajectory and plans for integration between the Eichmann and Camerer teams.

RECOMMENDATIONS TO THE TEAM

The Team should continue in their trajectory of valuable scientific achievements, with high-level publications and successful funding. The collaboration between the Yale and Paris teams should benefit all team members, with regular exchanges and visits of junior team members. An increase in outreach activities would be desirable. It will be interesting to see what the fusion of the two teams brings in terms of scientific output and training.

Team 10: Immunotherapy and anti-angiogenic therapy in oncology
 Name of the supervisor: Mr Eric Tartour

THEMES OF THE TEAM

The team's primary objective is to understand the connection between tumour angiogenesis and the immune responses, notably in the context of anti-angiogenic and immunotherapies. The team emphasises their research on deciphering how anti-angiogenic agents function and their potential to enhance cancer immunotherapy. The team wants to get insights on the optimisation of cancer immunotherapy strategies, particularly anti-tumour vaccination. Their research can also directly inform the discovery of biomarkers and the development of new therapeutic cancer immunotherapy strategies.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has taken into account the consideration of previous HCERES recommendations, notably in regards to interaction within the unit. In addition, the team commits to maintaining a balance between their own basic and translational research activities, while fostering collaboration and integration within the research center.

- **collaborative publications and joint grants:** The team's commitment to interaction is evident in their joint publications with other members of the research center. The team's success in obtaining joint grants with other research teams within the center demonstrates their ability to work together effectively on research projects.
- **integration of the unit research trajectory in the team's research plan:** Their research theme at the intersection of vascular and cancer aligns well with the center's research axes, ie in the area of heart and vessel immunology. This has led to productive collaborations with various research teams within the center.
- **shared technological tools:** The team's interactions extend to the sharing of common technological tools for analysing vessels and immune cells. This facilitates collaboration and ensures that resources are leveraged efficiently across different research teams.
- **active involvement in the unit development:** Members of the team are not only users of research platforms but also actively contribute to their development.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	6
Maîtres de conférences et assimilés	4
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	15
Enseignants-chercheurs et chercheurs non permanents et assimilés	3
Personnels d'appui non permanents	6
Post-doctorants	1
Doctorants	5
Sous-total personnels non permanents en activité	15
Total personnels	30

EVALUATION

Overall assessment of the team

During the last period, the team has made an excellent contribution to the field of immuno-oncology in terms of scientific production (Nat Comm 2022, Clin Cancer Res 2018) and immuno-cancerology (Nat Comm 2017, Clin Cancer Res 2022), where members are in dominant positions (first/last).

The team projects are funded through competitive national funding for a total of 3500 K€, such as two ANR grants and five INCA grants as PI. The team was also funded with Ligue Nationale contre le Cancer label (Equipe Labellisée).

Team members are also regularly invited to national/international conferences (ESMO, European Society for molecular imaging) and are involved in the organisation of meetings through local/national/international scientific societies in the field of Pathology and Immuno-Cancerology. The team successfully trained MD/PhD students and is involved in many aspects of peer evaluation and management of research. The outputs from fundamental research are less visible than the translational aspects.

The team was also involved in Clfre program for a PhD thesis, 4 patents were filled, and the team has obtained industrial contracts (Imcheck, Vaxéal, Sanofi, ...).

The team is also committed to lay-audience communication via charities (Ligue), patient association (Prostate cancer), as well as via main media in France.

Strengths and possibilities linked to the context

Attractiveness

The team demonstrates a high success rate to competitive national grants as coordinator to ANR (n=2) and INCa (n=5) for a total of 3500 K€. The team was notably recognised and funded with Ligue Nationale contre le Cancer label (Equipe Labellisée).

The PI is also co-leader of the ambitious program (Priority Research and Resources Program (PEPR)) on mRNA-based mucosal vaccination. Noteworthy is also interactions with industrials.

The team has trained thirteen MD/PhD thesis (nine defended) for thirteen HDR who were well positioned in research papers, and several pursue their career in translational research.

Recognition

The team is proactive for integration of its research/expertise within the overall themes of the Unit team, through collaborative scientific works and technological developments (imaging and flow cytometry).

Several members, including PI, demonstrate a strong involvement for the scientific community and dedicated significant efforts to the organisation of meetings through local/national/international scientific societies in the field of Pathology and Immuno-Cancerology, as well as for national evaluation and panel (HCERES, INSERM, CNU, SAB, etc.), reviewing for multiple research agencies and charities in France and Europe.

PI and team members are also regularly invited to national/international conferences in the field of Immuno-Cancerology (ex: ESMO 2017, 2019, European Society for molecular imaging 2021, ...). Team members are also part of editorial boards for specialised journals and clinical French reviews.

Several actual and former members were granted academic positions/advances.

Production

The team has made some notable contribution in the field of tumour angiogenesis (Nat Comm 2022, Clin Cancer Res 2018) and immuno-cancerology (Nat Comm 2017, Clin Cancer Res 2022), where members are in dominant positions (first/last). The total number of publications is 141 including 84 original articles, 32 reviews or editorials and twenty communications. All PhD students and post-docs have published articles as first author.

The team has also participated to collaborative works (e.g. Cell Stem Cell 2022).

Contribution of research activities to society

This team was successful in transferring knowledge and valorisation of the research, as illustrated with Clfre program for a PhD thesis, four patents were filled and consulting activities with major industrial companies (Sanofi, BMS, Astra ...). The team has obtained industrial contracts (Imcheck, Vaxéal, Sanofi, ...).

The team is also committed to lay-audience communication via charities (Ligue), patient association (Prostate cancer), as well as via main media in France (TV, newspapers on a regular basis). The team is also involved in science fair events (la fête de la science) and actions towards young students (high school, apprentis chercheurs).

Weaknesses and risks linked to the context

The team's scientific production remains mainly in specialised journals from the immuno-cancerology fields and MDPI associated journals.

The contributions to train the next generation of researchers (PhD and post-doc that are not clinicians) remain limited.

Analysis of the team's trajectory

The team's trajectory aims to balance translational research (biomarkers, vaccine) and fundamental research (interplay with diet, pro-angiogenic responses in T cells). The potential for clinical applications is high. The mechanistic insights, however, remain at their infancy in axis 2 and 4.

The first axis is embedded within the unit's research themes and wants to pursue an exploratory path.

The second axis seeks biomarkers to be useful for clinicians in decision-making. Future perspectives towards more comprehensive research are not in place yet.

The third axis will combine the team's expertise in immune responses to vascular biology, with a strong translation vision.

The fourth axis positions at the crossroad to better understand from a mechanistic standpoint the contribution of angiogenesis factors to immune functions.

RECOMMENDATIONS TO THE TEAM

The appropriate resources (notably manpower and permanent researchers) should be allocated to the fundamental aspects of the research axis (e.g. VEGF signalling and myeloid population characterisation).

The contribution and efforts of the team should be distributed between all research axis with focused attention on progress with regards to axis 3 (cancer vaccine).

The efforts towards intramural collaborations should be maintained, making sure to benefit to the overall team's strategies.

Team 11: Rejection in solid organ transplantation
 Name of the supervisor: Mr Alexandre Loupy

THEMES OF THE TEAM

The team is focused on the understanding of the trajectories of patients with solid organ transplantation. The team is mainly interested in the rejection of allograft with a description of new rejection forms, new ways to stratify the risk associated with the various forms of rejections, and new ways to cure it. The team developed tools to better integrate and automated the processing of medical information.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Please note that Team 11 was an AVENIR Team and therefore has not been evaluated by the previous HCERES committee

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	4
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	9
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	14
Post-doctorants	3
Doctorants	5
Sous-total personnels non permanents en activité	22
Total personnels	31

EVALUATION

Overall assessment of the team

The team is outstanding. It is one of the major research teams in the world focusing on transplantation with original and unique tools (iBox, Precision pathology platform, ICDOT). The scientific production is of top level regarding the quantity (125 original articles) and the quality (1 NEJM, 2 Lancet, 1 BMJ, 2 Circulation, 1 PLOS Medicine, 1 JAMA internal medicine, 1 Lancet Public Health) as dominant position. In addition, the team are able to obtain important grants from French or European agencies (5 million euros). Their research lead to the creation of a start-up. It is a real success story. The global assessment is outstanding.

Strengths and possibilities linked to the context

Attractiveness

The major strength of the team is the ability to have clinically relevant objectives and the engagement and the opportunity to build the databases and the tools to fulfil its. The various international databases and the multidisciplinary team was a way to success. During the period the team showed its ability to have resources from various origins to aim its goals in excellence.

The team was successful to obtain several large-scale grants for a total amount of 5,000 K€ for the team. The team coordinates two European programs H2020 Eu4health BRAVEST (2022–2025) and H2020 EU-TRAIN (2018–2024).

The team has supervised eleven PhD (6 PhD defences from France, Korea and USA) for four HDR and numerous masters plus postdoc (n=3) and one Italian fellow suggest an excellent hosting policy.

Seven major grants with the ability to fund 9 clinical research assistants were obtained. It is a key function to be sure of the data quality the main fuel for the research program of this team.

The combination of ICDOT (International Consortium for Diagnostics & Outcomes in Transplantation), a huge data repository focusing on rejection of kidney transplant with a platform of measuring the free cell DNA and the creation of a digital pathology platform are particularly attractive. The association of dry and wet lab in the same structure is of high interest.

The team complies with the rule's human resources management, safety, environment, ethical protocols, and data.

Recognition

There is a strong involvement of the team leaders in all the scientific societies important in the field of transplantation.

The team leader received several awards: Clinical science investigator awards: American Society of Transplantation (2017), Stronger Together Award: European Society of Organ Transplantation (ESOT) (2017, 2019, 2021), French National Academy of Medicine Award (2018).

The team leader is also KDIGO (global nonprofit organisation developing and implementing evidence-based clinical practice guidelines in kidney disease) expert in kidney transplantation (2022).

The team leader is member of the editorial board of Kidney international (2020 present), Associate Editor for American Journal of Transplantation (2016-present) and Appointed Scientific Director of the International Banff Classification (2015-present).

Production

The production is outstanding with more than 125 original articles with numerous major papers in high visibility generalist (1 NEJM 2018, 2 Lancet 2019, 2020, 1 BMJ 2019, 1 PLoS medicine 2018) and speciality (2 Circulation 2017, 2020) journals as dominant position. The scientific production is higher than we could imagine regarding the size of the team. The authorship is clearly well shared. All the works were done in the respects of the principles of scientific integrity, ethics and open science.

They have an integrated approach to respond immediately and sustainability to challenges for improving kidney transplantation and they have constructed a unique international database (ICDOT collecting tissue molecular data as well routinely transplanted patient data to understand the physiological mechanisms involved in transplant rejection, develop precision transplantation medicine for better predicting the risk of graft loss and death as an example).

Contribution of research activities to society

The team collaborate actively with industries (MSD Avenir, Nanostring) and with regulatory agencies in Europe in the field of transplantation.

The team has created new tools for the prognosis of the outcome of a kidney transplantation validated as an endpoint in clinical trials by the EMA (European Medicines Agency).

A start-up Cibiltech was created in 2019, two patents were filed and two softwares are created by the team, there are the main deliverables of the RHU KTD-innov.

Some achievements were done but not so turn to the general public but more to patients and or government through the Paris Transplant Group (PTG).

Some team members are present on the so-called social networks.

Weaknesses and risks linked to the context

The main weakness could be a modification in the policy of data sharing between the various countries involved in all the projects. The insufficient institutional funding could be a concern to maintain the databases despite the effort to align with industry and in the same line, the weakness of the number of support peoples, only three, could be a concern to maintain the databases and the software.

If the parity is close to be achieved for the students (10 out of the 24), this is not the case for the statutory employees (one woman for five men).

The transformation of the precision pathology platform for transplantation in a service platform could diminish the interaction between the dry and the wet lab reducing the interaction and the maintaining of excellence and innovating tools to fuel the algorithmic pipeline.

There is a lack of visibility in the general public to stimulate the donation of organs.

Analysis of the team's trajectory

The team's trajectory is in line with the previous project. The group will focus on the use of artificial intelligence and big data on three axis: Allograft allocation and precision diagnosis, prognosis of the transplant and the transplanted patient, patient care. The program seems rational with the past and the strength of the teams. The envisaged sources of funding are rational (ERC and ANR). One question not discussed is the strategy of IA that will be using (GPT for example) and the relation with the big companies involved in the field of IA. It could be difficult to compete with this kind of huge companies. The idea to collaborate with these companies and to discuss with them by the ethical aspect is the good way to have a part of control on the use of IA in transplantation. The trajectory will be financed by an ERC consolidator obtained by the PI in 2023.

RECOMMENDATIONS TO THE TEAM

We recommend to maintain the quality of the research, the ability for granting, the ability to produce high-impact articles in the fields of transplantation and the capacity to translate in the industrial fields (start-up, collaboration with industry) to improve the care of transplanted patients.

We recommend securing the data sharing and the maintenance of the database by recruiting more supporting staff like engineers and technicians for the maintenance of database and the software.

Team 12: Genetic mechanisms of aldosterone related pathologies – towards precision medicine in hypertension

Name of the supervisor: Ms Maria Christina Zennaro

THEMES OF THE TEAM

The Team focuses on the pathogenesis of arterial hypertension and in particular of primary aldosteronism as a major cause of secondary forms of hypertension. The Team covers the full translational spectrum from discovery of novel mechanisms, dissection of pathophysiology, biomarker development, to first steps to clinical implementation. There is strong focus on training a next generation of hypertension researchers and international collaboration often in a leading role.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

There were three major recommendations in the previous report.

The Team was asked to engage with the 'non-academic' world and in particular with the pharmaceutical industry. There are now links with biotech and patents have been filed which is a step in the right direction. There is not currently active collaboration with major pharmaceutical and major diagnostic companies and this could be further developed in the future. One would also expect for closer collaboration with public and patient representatives to guide research activities and generally more outreach and engagement activities.

The Team was also asked to train a larger number of PhD students. They are now part of EJD 'MINDSHIFT' and thereby provide training beyond students who work directly with the Team. The total number of students is capped by Graduate School rules and the maximum number of students is currently being supervised by the Team.

The focus of the Team is on primary aldosteronism and this is in line with advice given at the previous visit. The Team is locally, nationally and internationally recognised in this field.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	4
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	7
Sous-total personnels non permanents en activité	8
Total personnels	12

EVALUATION

Overall assessment of the team

Team 12 has done very well in research into primary aldosteronism as evidenced by impactful research output (including papers in Nature Communications and Nature Genetics), significant grant income (including three major European Commission Grants as PI (one EU Horizon 2020, one EU Horizon Europe) and one as partner (Horizon H2020), leadership at national and international level (as evidenced by leadership of major grants such as two ANR as PI (one as partner), labelisation of the team by FRM as PI ... and membership of guideline committees) and a strong ethos of developing a next generation of translational researchers (as evidenced by the team's trajectory in the last five years, support for ECRs and leadership in the MINDSHIFT Consortium). The mix between fundamental and clinical scientists supports the Team's ambitions.

Whilst major successes in the current evaluation period are in the areas of fundamental and discovery science, the team is now in a position to translate findings into the clinic, which provides evidence of the impact of their work.

The team has filed two patents.

The Team participated for sharing knowledge with the general public: interview in radio programmes (Radio France 2021), for FRM (YouTube 2020) for the Italian TV (RAI) and one member participated in 'Association Femmes et sciences' at university Paris-Est.

Overall the achievements over the last five years and the proposed trajectories are outstanding in all areas.

Strengths and possibilities linked to the context

Attractiveness

The Team aims to understand the pathogenesis of primary aldosteronism (PA) and based on this they aim to develop new biomarker-based diagnostic tools that will translate into risk stratification and precision treatment. The Team is well connected with other experts in hypertension and PA in Europe and worldwide and contributes to collaborative work. The idea of using PA as a model for primary hypertension and learn about mechanisms that may affect patients other than those with 'traditional' PA is excellent, has already shown relevant outputs and has indeed also worked with other forms of secondary hypertension including the 'Liftonian' rare mutations in renal transport mechanisms.

There is excellent diversity in the Team with six individuals (three Inserm researchers, two clinicians and one engineer) with productive research output and excellent contribution of team members at all stages to these outputs. The breadth of techniques and the range from fundamental to clinical research makes this Team very attractive to researchers at all stages of their careers.

The Team is very well resourced and nicely bridges the translational gap from discovery research to possible clinical implementation.

The Team benefits from strong and consistent leadership by Ms Zennaro. There is reasonable turnover in research staff with appropriate career development. Work adheres to ethical standards and IP is protected where appropriate.

The Team has recruited a permanent researcher, Inserm CRCN in 2018. One member of the team has succeeded in having a promotion as assistant engineer in 2021.

The Team has supervised ten PhD students with three who have defended their thesis and five post-docs from eight nationalities (Italy, Brazil, Greece, Denmark, Lebanon, Portugal, China and Iran).

Recognition

The reputation of Team 12 is evidenced by its involvement and leadership of major collaborative grants and educational programmes with coordination of funds of €12 M with a budget available for the team of 2,500 K€ (two EU horizon grants: ENSAT-HT and HT-ADVANCE. The focus on education and training in the H2020-MSCA-ITN-2020 program MINDSHIFT as partner but also in other activities of the Team is laudable. What is unique is the close link between discovery science and clinical translation. There are few groups that can do both, GWAS and molecular dissection of the top signals. Team 12 is doing this very well. The group is well funded and provides a secure space for ambitious research, especially of early career researchers who bring in no or limited own funding. The Team is a Fondation pour la Recherche Médicale-labelled team since 2015 and has coordinated two international ANR projects. The leader is a member of the Endocrine Society's primary aldosteronism guideline development panel (2022–2025).

Ms Zennaro has been a guest editor of a J Endocrinol special issue '30 years of the mineralocorticoid receptor' (2017). She has been awarded the prize 'Etoiles de l'Europe' of the Ministère de l'Enseignement Supérieur et de la Recherche (2022), and the 'European Medal' of the Society for Endocrinology/British Endocrine Society (UK,

2018). Team members have been invited to give symposia or plenary lectures at 37 international meetings. Ms Zennaro has been invited to give a lecture at the Académie Nationale de médecine in 2022 and is a member of the US Endocrine Society's Annual Meeting Steering Committee. Members of the team have organised 4 international meetings and eight ENSAT-HT consortium meetings.

Scientific production

Team 12 is particularly strong in fundamental science. Findings from the GWAS into PA or the discovery of a new molecular mechanism of PA are among the strongest outputs of the Team and are highly competitive at international level. The first impactful papers are now emerging from the ENSAT-HT project. In total, the team has published 52 articles including 34 original articles, fourteen reviews and 4 editorials. The most significant have been published in high visibility journals (Nat Commun 2022, Nat Genetics (2018, 2021) Trends in Mol Med (2020) as first, last, corresponding authors but also one Nat Commun 2019 in collaboration. The Team also contributes to relevant clinical outputs such as fourteen review articles (Endocrine Rev 2017, Nat Rev Endocrinol 2020) is a good example of the breadth of quality outputs.

The output is quantitatively fully appropriate for the Team's size and resources and in terms of quality there are examples of absolutely stellar papers that describe new concepts and discoveries. Postdocs and students participate in the papers, often in leading positions in the author list.

All PhD students and postdocs who have completed their training have published original articles in the first author position. Approximately 60% of the papers are published with an open access model. There are absolutely no concerns regarding integrity and ethics.

Contribution of research activities to society

The team has filed two patents.

The team has performed educational activities particularly within the MINDSHIFT programme and contributions to the Graduate School. There is strong collaboration with other hypertension networks.

The Team participated for sharing knowledge with the general public: interview in radio programmes (Radio France 2021), for FRM (YouTube 2020) for the Italian TV (RAI) and one member participated in 'Association Femmes et sciences' at university Paris-Est.

Weaknesses and risks linked to the context

Data on the reproducibility of the MOMICS approach are to be generated/provided.

There are proposed plans to explore metabolic diseases by Team 12 and this could in part link to Team 13's metabolic approaches and Team 4's epidemiological approaches. One would also think that closer collaborations with Team 8 (kidney; another common cause of secondary hypertension), Teams 3 and 9 (genetics and vascular diseases) and Team 7 (heart failure – the RAAS plays a major role here) could further enrich Team 12's work. The Team is already collaborating where appropriate and for example studies vascular phenotypes that were not on their original agenda.

Within PARCC there are many opportunities to collaborate and bring in other techniques where required so that there are no real weaknesses regarding to Team 12's current setup. Open access publication could be further increased in this Team. Where public funders such as the European Commission are involved, the funders request open access.

Which of these activities are going over and above what is expected from academics in this field? It is not entirely clear if all Team members contribute to these activities or if they are mainly linked to the Team Lead. As above, many of these activities are driven by the leader of the Team and there is an opportunity to more strongly involve other Team members. The training provided to team members is outstanding.

There are opportunities to more closely work with members of the public, e.g. through membership of patients in steering committees, as co-applicants of grants, internal assessments, etc. The Team may want to look creatively into such opportunities.

Analysis of the team's trajectory

The team will reshape as of 2025, both in size and in contribution of further clinicians, mirroring the overall research trajectory and the proposed growth in 2025 is proportionate and appropriate.

In the current period, the Team has focused on research into primary aldosteronism and training of a next generation of researchers. This path is proposed to continue into the next period.

Whilst translation into clinical practice is one of the strengths of the Team, the exact pathway to clinical implementation could be better defined. It is noted that from 2025 onwards, three clinicians will be part of the Team. It is currently not clear if they work on fundamental science projects or clinical studies or both. The Team has gained considerable experience in designing and conducting multicentre clinical studies but may benefit from further collaboration on clinical trials to support translation and implementation, also within ADVANCE-HT.

The overarching aim in this trajectory is the development of precision medicine in hypertension. This is a large topic where in reality the focus of the Team is on primary aldosteronism. The reasoning behind this is that this condition comes with disproportional organ damage and in 'milder' forms affects more than 5% of people with hypertension, with estimates reaching up to 10 or even 20%. As such the refined aim of 'Genetics of aldosterone-related disorders – towards precision medicine in hypertension' is entirely plausible.

The proposed axes of future research include:

1. Studies into the link between genetic variants and aldosterone production. This will include in vitro and in vivo work and translation to human samples. Details will have to be explored at the site visit.
2. Translation into clinical practice by conducting a biomarker-led precision medicine trial (HT-ADVANCE). This is a major strategic goal, and data supporting this goal as well as current progress will be reviewed at the site visit.
3. Studies into the pathogenetic mechanisms of primary aldosteronism, looking at miR-139-5p and calcium signalling. These are novel approaches and may to some extent link to axis 1.
4. Further studies into the role of aldosterone and the MR in the adrenal gland, cardiovascular and adipose tissues. This axis is welcome as it is a first step towards a metabolic strategy (adipose tissue) and could provide opportunities to collaborate with other Teams in PARCC e.g. studying the heart and the vasculature.

These axes are based on the Team's current strategy and take it further, supported by data generated in the previous period and particularly in ENSAT-HT. Discussing details of this trajectory and any anticipated challenges will take place at the site visit.

RECOMMENDATIONS TO THE TEAM

The overall strategy of the Team is fully appropriate and we recommend continuation with the proposed trajectory. Specific areas for consideration include translational activities (e.g. contribution to major guidelines); utilising rather than just protecting IP where possible; and closer work with members of the public. The Team is very focused on its leader and there are opportunities for Team members to develop and stand out. Steps in these directions have already been taken. Collaborations with other Teams within PARCC could be more actively explored, namely in the areas of heart failure and vascular biology.

Team 13: Genetics and Metabolism of Rare Cancers
 Name of the supervisor: Ms Judith Favier (& Ms Anne-Paule Roqueplo)

THEMES OF THE TEAM

The team performs highly translational research concerning the diagnosis and management of pheochromocytoma and paraganglioma (PPGL). They use standard pathology, genetics, epigenetics and physiology, as well as innovative clinical investigations.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Based on the self-assessment, the previous recommendations were mainly to continue to be as productive as before and to expand the team with a full-time researcher. They have addressed the first one successfully, but have been unable to recruit another researcher.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	9
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	2
Doctorants	1
Sous-total personnels non permanents en activité	5
Total personnels	14

EVALUATION

Overall assessment of the team

The team overall is excellent. Within their highly specialised field, they perform outstanding translational research with direct benefit to patient care by improving diagnosis and management of PPGL. The mechanistic insights gained by their research provide a platform for the development of novel and specific therapies. They have excellent publications mostly in the top journals of their field such as Clin Cancer Res, Cancer Res, Nat Rev Endocrinol) or in generalist journals (Cell Rep, Theranostics) as leading authors. The record on grant income is also excellent (total 3200K€), mostly from foundations and national agencies such as (Ligue Nationale contre le cancer, INCa, ANSES) and in collaborations (INRAE, INCa, ARC foundation). As collaborator, they are involved in one Horizon H2020 grants (ENSAT-HT). The track record in training and promotion of team members is outstanding given the relatively small size of the team. The team has filed one patent extended internationally in 2019. The team has an important activity of clinical valorisation and are involved as partner in two clinical trials on PPGL, a European trial testing the efficacy of sunitinib and a trial of targeted therapies 'à la carte'.

Strengths and possibilities linked to the context

Attractiveness

The team leaders are clearly internationally recognised in the field of PPGL research and have leadership positions in international consortia and societies.

They obtained grants totalling >3000K€ mainly from national funders both as PI (Ligue Nationale contre le cancer, 2017-2022 ; INCA, 2019-2023 ; ANSES, 2022-2022) and in collaborations (INRAe, 2019.2024; INCA, 2021–2024, ARC foundation, 2021–2024. As collaborator, they are involved in one Horizon H2020 grants (ENSAT-HT) which is coordinated by the leader of team 12.

All investigators have been encouraged to apply to different types of funding and have been successful with a Pfizer-research grant, 'Foncer contre le cancer 2018, SIRIC-CARPEM 2019, 2021 and « association surrénales » (2022).

The team has supervised nine PhD (with two PhDs defended) for eight HDR and four post-doc fellows. All PhD students and post-docs have gone on to further employment, several with competitive fellowships and 1st author publications. All MDs doing a master 2 and PhD students have obtained highly selective fellowships for their salaries, for a total amount of around 850K€. Four members of the team obtained their 'habilitation' to direct research (HDR) and four were promoted.

Two of the PhD students have been recruited as MCU-PH and perform their research in the team. Five out of nine PhD and post-docs and six out of seven statutory employees were women.

They describe themselves in compliance with all relevant regulation and that they are actively promoting diversity and well-being, but apart from gender, no other data to support this have been provided.

Due to the highly translational nature of their research, the team uses an exciting mix of technologies and skills that combines conventional pathology with state-of-the-art clinical (spectroscopic magnetic resonance imaging sequence (1H-MRS) and laboratory imaging (live cell video), physiology (seahorse) and state-of-the-art genetics and epigenetics.

Recognition

Senior researchers are regularly invited to give symposia or plenary lectures in the field of onco-metabolism (ECE, EACR, EMBO,...). During the last mandate, 9 PhD students and postdocs have attended 33 meetings, presenting oral and twenty poster communications.

One member of the team was invited to be editor of a Special Issue of Molecular and cellular Endocrinology 'Hormone Resistance' (2020–2022) and the team leader is associate editor at Endocrine-related cancer.

The team leader is member of the scientific board of 'Groupe des Tumeurs Endocrines' (2017-present), vice-president of the research innovation commission at University Paris Cité (2019-present) and member of the management committee of the COST Action (HARMONISATION, 2021–2025).

Both leaders have been elected to the board of the European network for the study of adrenal tumours (ENS@T-Cancer) since 2017.

Production

The team has been very productive with 128 papers including 62 original research articles (29 as first, last or corresponding), 32 reviews or editorials and 34 clinical research articles several highly cited, providing important clinical and mechanistic insights into PPGL. The most significant articles as leading authors have been published in high-level journals of the oncology or endocrine disciplines (Clin Cancer Res 2019, Cancer Res 2018, 2021, Nat Rev Endocrinol 2017, 2021); or in generalist journals (Cell Rep 2020, Theranostics 2021). According to external analysis (Front Oncol. 2022), the team was the second most cited in the world in the field of PPGL.

Members of the team were involved in the consensus statement on next-generation-sequencing-based-diagnostic testing of hereditary PPGL (publication in Nat Rev Endocrinol 2017).

All junior team members appear to be productive, with only the most recent team members not having publications yet. Those working there for more than one year all have multiple publications.

They use practices, such as electronic lab book to ensure reproducibility of experiments.

Contribution of research activities to society

The team has filed one patent extended internationally in 2019.

The team has an important activity of clinical valorisation and are involved as partner in two clinical trials on PPGL, a European trial testing the efficacy of sunitinib and a trial of targeted therapies 'à la carte'.

The team participates in and supports PARCC's policy for sharing knowledge with the general public and school populations.

Weaknesses and risks linked to the context

Very few potential weaknesses. Most publications are in speciality and subspeciality journals with few in top journals. International grants organised by the team are mainly from a charitable foundation, rather than institutional (e.g. EU) funds.

Analysis of the team's trajectory

The team is clearly an international leader in the field of PPGL. There is no doubt that they will continue to be productive and relevant. Yet, due to the specialised nature of their topic, it is unlikely that they will gain higher visibility outside this specific field.

RECOMMENDATIONS TO THE TEAM

The team is leaving the unit to join a cancer-specific research group. It is possible that in collaboration with other cancer researchers the team may rise above the subspecialist nature of their current research so that they can gain even broader recognition, by providing mechanistic insights that go beyond PPGL.

CONDUCT OF THE INTERVIEWS

Dates

Start: 22 novembre 2023 à 8 h 30

End : 24 novembre 2023 à 16 h

Interview conducted : on-site

INTERVIEW SCHEDULE

Agenda of the visit

Unit : « **UMR_S 970: Paris Cardiovascular Research Center** »
22–24 November 2023

Address: UMR 970/salle de conférence rez de chaussée
 56 rue Leblanc, 75015 PARIS

Present director: Ms Chantal BOULANGER

Proposed Director: Mr Jean-Sébastien SILVESTRE

HCERES scientific advisor: Ms Florence PINET (Lille, FR)

Visiting committee: Mr Thierry PEDRAZZINI (Lausanne, Switzerland) President
 Mr Olivier MEILHAC (La réunion, FR), Vice-president (CSS3)
 Mr Stéphane TANGUY (Grenoble, FR) (CNU 66)
 Ms Patricia MUNROE (London, UK)
 Mr Guy FAGHERAZZI (Luxemburg)
 Ms Nathalie JOUY (PAR) (Lille, FR)
 Mr Christian DELLES (Glasgow, UK)
 Mr Deflef BOCKENHAUER (Leuven, Belgium)
 Ms Anna RANDI (London, UK)
 Ms Paola ROMAGNANI (Florence, Italy)
 Ms Julie GAVARD (Nantes, FR)
 Ms Serena ZACCHIGNA (Trieste, Italy)
 Mr Lucio BARILE (Bellinzona, Switzerland)
 Mr Stéphane BURTEY (Marseille, FR)
 Mr Matthias STUBER (Lausanne, Switzerland)

Observer member of CSS3 inserm: Ms Amélie BONNEFOND (Lille)

Observer member of CSS6 inserm: Ms Aline MEIRAEGHE (Lille)

Day 1: Wednesday 22 November 2023

10:45-11:00

Welcome

11:00-11:30

Welcome (closed-door): Visiting committee with the HCERES Scientific advisor (the role and procedures of HCERES)

CSS6: <https://hceres-fr.zoom.us/j/95038902279?pwd=RHNra1F3b012Q0JtbGpWR0hGTFd4QT09>

11:30 – 11:35

Presentation of the evaluation process to the unit by the scientific advisor

Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members

11:35-12:35

Highlights of the Unit

'**Ms Chantal BOULANGER – Mr Jean-Sébastien SILVESTRE**', past and present director of the unit 30 min + 30 min discussions

Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members

12:35-1:05 p.m.

Meeting with the representative of the managing bodies

Attending: committee members, HCERES scientific advisor, representative of institutions

1:05 p.m.-2 p.m.

Lunch break

CSS6: <https://hceres-fr.zoom.us/j/93001460014?pwd=a3FVck5wTmdKUElzUm5ZdW1MNvZBdz09>

2 p.m.-2:40 p.m.

Team 4: Integrative Epidemiology of Cardiovascular Diseases. Xavier Jouven (& Jean-Philippe Empana)

(20 min +20 min discussion)

Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members

- 2:40 p.m.-3 p.m.** **Team 1:** Endothelial pathophysiology and extracellular vesicles. **Chantal Boulanger**
(10 min +10 min discussion) only past
Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members
- 3 p.m.-3:20 p.m.** **Team 7:** Biology and pharmacology of heart failure. **Jean-Sébastien Hulot**
(10 min +10 min discussion) only past
Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members
- 3:20 p.m.-4:25 p.m.** **Team 6:** Regenerative therapies for cardiac and vascular diseases. **Jean-Sébastien Silvestre**
(35min +30 min discussion) past and trajectory (Teams 1, 6 and 7)
Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members
- 4:25 p.m.-6:40 p.m.** **Committee debriefing (closed doors)**
- 8 p.m.** Diner of the member of committee together
Attending: committee members, HCERES scientific advisor, without any unit members
- Day 2: Thursday 23 November 2023**
- 8:30 a.m.-9 a.m.** **Welcome coffee**
- CSS6:** <https://hceres-fr.zoom.us/j/97987867665?pwd=VFhQc1RkV1Z5OHphZ1JDU1o1Nk44UT09>
- 9 a.m.-9:40 a.m.** **Team 3:** Genetics to Understand Arterial Disease. **Nabila Bouatia-Naji (& Xavier Jeunemaitre)**
(20 min +20 min discussion)
Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members
- 9:40 a.m.-10:20** **Team 5:** Immuno-metabolic mechanisms of cardiovascular diseases **Hafid Ait-Oufella (& Ziad Mallat)**
(20 min +20 min discussion)
Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members
- 10:20-11:00** **Team 8:** Renal and vascular signalling: from development to pathology. **Pierre-Louis Tharaux (& Eric Camerer)**
(20 min +20 min discussion)
Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members
- 11:00-11:15** **Coffee break**
- 11:15-11:55** **Team 9:** Development and vascular pathologies. **Anne Eichman**
(20 min +20 min discussion)
Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members
- 11:55-12:35** **Team 10:** Immunotherapy and anti-angiogenic therapy in oncology. **Eric Tartour**
(20 min +20 min discussion)
Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members
- 12:35-1:35 p.m.** **Lunch break**
- 1:35 p.m.-2:05 p.m.** **Committee debriefing (closed doors)**
- 2:05 p.m.-3:05 p.m.** **Meetings in parallel** 'committee members, HCERES scientific advisor will split in the different meetings' **(closed doors)**
- Meeting with researchers.**
Attending: all researchers except team PIs and director, committee members, HCERES scientific advisor
- Meeting with students and post-docs.**
Attending: all PhD students and post-doctoral fellows, committee members, HCERES scientific advisor
- Meeting with technicians, engineers and administrative staff (in French).**

Attending: All technical staff, PAR committee member

3:05 p.m.-3:20 p.m.

Coffee break

3:20 p.m.-4 p.m.

Team 2: Life imaging. **Bertrand Tavilian**

(20 min +20 min discussion)

Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members

4 p.m.-7 p.m.

Closed-door meeting of the visiting committee (in presence of the HCERES scientific advisor)

8 p.m.

Diner of the member of committee together

Attending: committee members, HCERES scientific advisor, **without any unit members**

Day 3: Friday 24 November 2023

8:30 a.m.-9 a.m.

Welcome coffee

CSS6: <https://hceres-fr.zoom.us/j/99197670306?pwd=TWNOUm5wSmhzLzVDUjRzK0tQNHFrzd09>

9 h-9 : 40 a.m.

Team 11: Rejection in solid organ transplantation. **Alexandre Loupy**

(20 min +20 min discussion)

Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members

9:40 a.m.-10:20

Team 12: Genetic mechanisms of aldosterone related pathologies – towards precision medicine in hypertension. **Maria Christina Zennaro**

(20 min +20 min discussion)

Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members

10:20-10:35

Coffee break

10:35-10:55

Team 13: Genetics and Metabolism of Rare Cancers. **Judith Favier (& Anne-Paule Roqueplo)**

(10 min +10 min discussion) only past

Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members

10:55-11:15

Future Team: Endotheliopathy and hemostasis disorders. **David Smadja**

(10 min + 10 min discussion) only trajectory

Attending: committee members, HCERES scientific advisor, representative of institutions and all unit members

11:15-11:45

Meeting with the head of the unit. **Chantal Boulanger & Jean-Sébastien Silvestre**

11:45-12 : 30

Lunch

12:30-3:30 p.m.

Closed-door meeting of the visiting committee for deliberation (in presence of the HCERES scientific advisor)

3:30 p.m.

End of the visit

PARTICULAR POINT TO BE MENTIONED

N/A

GENERAL OBSERVATIONS OF THE SUPERVISORS

Le Président

Paris, le 22 janvier 2024

HCERES
2 rue Albert Einstein
75013 Paris

Objet : Rapport d'évaluation de l'unité DER-PUR250024192 - PARCC - Paris centre de recherche cardiovasculaire

L'Université Paris Cité (UPCité) a pris connaissance du rapport d'évaluation de l'Unité de Recherche **PARCC - Paris centre de recherche cardiovasculaire** et remercie le comité pour la qualité de son évaluation.

Ce rapport a été lu avec attention par la direction de l'unité, le vice-doyen recherche et le doyen de la Faculté de Santé d'UPCité, par la vice-présidente recherche d'UPCité et par moi-même.

La direction de l'unité n'a pas signalé d'erreurs factuelles (cf courrier de Jean-Sébastien Silvestre joint)

Le Doyen de la Faculté de Santé souhaite confirmer que le PARCC fait partie des centres de recherche qui sont très importants pour la Faculté de Santé ; que le changement de direction (Jean Sébastien Silvestre a pris la direction du PARCC en cours de quinquennat suite à la nomination de Chantal Boulanger à la direction de l'ITMO Physiopathologie, Métabolisme, Nutrition) s'est fait dans une totale continuité ; que la restructuration de certains équipes du PARCC a été réalisée en concertation avec la Faculté, l'Université et l'INSERM qui ont accompagné ces changements.

Pour ma part, je n'ai pas pas d'observations d'ordre général supplémentaires à apporter.

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



Édouard Kaminski

Dr Jean-Sébastien Silvestre

Paris, 15 december 2024

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HCERES EVALUATION CAMPAIGN 2023-2024 - GROUP D

General observation on the evaluation report of the Unit Paris centre de recherche cardiovasculaire under the supervision of Université Paris Cité & Institut national de la santé et de la recherche médicale – Inserm

To whom it may concern,

We acknowledge receipt of the HCERES report regarding the evaluation of the Paris Cardiovascular Research Center Inserm UMR 970, University Paris Cité. We have no specific comments to assert.



Dr Jean-Sébastien Silvestre
Director – PARCC

The Hcéres' evaluation reports are available online:
www.hceres.fr

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