

Research evaluation

EVALUATION REPORT OF THE UNIT CAP Paris-Tech – CArcinose péritoine paris technologie

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

Rapport publié le 10/01/2024

High Council for evaluation of research and highter education



In the name of the expert committee¹:

Come Lepage, Chairman of the committee

For the Hcéres²:

Stéphane Le Bouler, acting president

Under the decree n° 2021-1536 of 29th November 2021:

¹ The evaluation reports "are signed by the chairperson of the expert committee". (Article 11, paragraph 2); ² The president of the Hcéres "countersigns the evaluation reports established by the expert committee and signed by their chairperson." (Article 8, paragraph 5).



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

Chairperson:	Mr Come Lepage, Université de Bourgogne, Dijon		
Experts:	Mr Franck Carreiras, Cergy Paris Université Mr Pierre Martineau, Inserm Montpellier (representative of the CSS Inserm) Mr François Pattou, Université Lille 2 (representative of the CNU) Ms Stéphanie Venteo, Inserm Montpellier (supporting personnel)		

HCÉRES REPRESENTATIVE

Mr Kamel Benlagha

REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Ms Claire de Marguerye, Inserm Ms Christine Guillard, Université Paris Cité Ms Marie-Josèphe Leroy-Zamia, Inserm Mr Michel Vidal, Université Paris Cité



CHARACTERISATION OF THE UNIT

- Name: CArcinose péritoine paris technologie
- Acronym: CAP Paris-Tech
- Label and number: UMR U1275
- Composition of the executive team: composition of the executive team

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement SVE6 Physiologie et physiopathologie humaine, vieillissement

THEMES OF THE UNIT

The unit is centered on the study of peritoneal carcinomatosis both in basic science and in translational research. The first axis concerns the tumor implantation, promotion and progression of peritoneal carcinomatosis using *in* vitro and preclinical models. The second axis is translational and focuses on the development of new approaches to treat peritoneal carcinomatosis using original approaches to deliver drugs.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The unit has been created in 2019 following another unit established in 2009 (ART: Angiogenesis and translational Research) with the same head (Dr Marc Pocard). The unit is located at the Lariboisière Hospital, a university hospital in Paris (France).

RESEARCH ENVIRONMENT OF THE UNIT

The research unit is associated with the surgical units located at Lariboisière hospital, Pitié Salpêtrière and Begin Hospital. The unit is affiliated to Inserm and Université Paris Cité. The unit is part of the RENAPE (INCa) and BIGRENAPE (French society devoted to peritoneal diseases) networks.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	12
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	5
Total personnels	17



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

Nom de l'employeur	EC	С	PAR
UNIVERSITÉ PARIS-CITÉ	3	0	2
AUTRES	1	2	2
INSERM	0	1	1
Total personnels	4	3	5

GLOBAL ASSESSMENT (the unit is closing)

The unit (monoéquipe) is centered on the study of peritoneal carcinomatosis both in basic science and in translational research. The first axis is around tumor implantation, promotion and progression of peritoneal carcinomatosis using *in vitro* and preclinical models. The second axis is translational and focus on the development of new approaches to treat peritoneal carcinomatosis using original approaches to deliver drugs like the pressurized intraperitoneal aerosol chemotherapy (PIPAC) technology. PIPAC consists of spraying chemotherapy, directly into the patient's abdomen during a laparoscopy of the abdomen, in aerosol form to treat peritoneal carcinomatosis.

The scientific production is very good. The unit has published 109 papers with more than 50 in leading position, published in good specialty journals (*Pleura Peritoneum*, *Ann Surg Oncol*, *Br J Surg*), and for some frequently cited (>30), in *British Journal of Surgery*, *European Journal of Cancer*, *Critical Care*. Several of them have a clear clinical potential, in particular for PiPAC (14 publications between 2017 and 2022 and five in 2022). Some other papers provided convincing arguments to further explore specific targets / pathways, such as AHR receptor or Kallikrein. In addition, the unit has contributed to several collaborative clinical studies, published in high profile journals, including three highly cited articles in *Lancet*, *Lancet Oncology*, and *J Clin Oncol*. However, the overall scientific production of the unit could be higher in term of visibility and impact. There is no article in high profile journals which was produced or coordinated by members and collaborative publications across the various themes and senior scientists of the unit are missing, suggesting the development of parallel projects, in silos with little interactions among them.

The unit attractiveness is good, as demonstrated by the fact that the lab has successfully established an International Society for the Study of Pleura and Peritoneum (ISSPP) and is committed to promoting and fostering all aspects of it through an inclusive approach. However, the unit was not successful in its efforts to obtain fundings, in particular in basic and clinical researches. This context created some difficulties to recruit post-doctoral fellows and new full-time researcher. With its multidisciplinary approach (radiologists, surgeons), the unit has also contributed to a European research network on the peritoneum and contributed to the implementation of "PIPAC training course" in organizing international meetings in 2018 and 2023. Nevertheless, the visibility of the head of the lab is excellent in this field of research.

The valorization is good: the unit has interactions with 2 private companies (Stago, Gamida), collaborates with one patient association AMARAPE, and has developed a website for professionals, patients, and general public audience.

Altogether, the unit should invest in grant applications in order to finance their projects, hire permanent scientists and focus on large audience publications. The unit will closed and members will join a unit of physicists in the Faculty des St Pères. The overall assessment of the unit is very good.



DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Previous committee recommended to target generalist journals with better impact factor and to get more funding through national and international calls.

Some efforts have been devoted to publishing in high impact and generalist journal in particular with the publication of the PRODIGE7 clinical trial in the *Lancet Oncol*. There is however no indication in the report that other publications from the group, in leader position, have been submitted to more generalist journals as requested in the previous report. The policy is to publish as open access but this is not incompatible with high impact. Concerning national and international funding, none is reported and there is no information in the report showing that the group has indeed applied to such funding.

The recommendation of the committee to recruit high-level researchers to stabilize bench activity and help in recruiting postdocs has been taken in consideration but has been unsuccessful. For the future, Dr Pocard proposes to merge with a larger unit to solve this problem. We do not have information in the text that researchers of this larger unit may indeed interact with Dr Pocard project to solve the need in laboratory researchers in the group.

Future research program flow, WP, deliverable, RH and budget should be defined.

As requested by the previous committee, a definition of the objectives of the team, with work packages, budgets, planning, is still missing in the report, including the trajectory. How the research of the unit will be incorporated in and profit from the new team is not explained, but will be in the new unit.

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 assessment on scientific objectives is very good regarding, notably, the new PIPAC technology.

The objectives are cohesive and relevant around questions about peritoneum carcinomatosis.

Assessment on the unit's resources

The assessment on the unit's resources is good however, projects are not funded at a level allowing the recruitment of postdocs and engineers to be competitive at an international level.

Assessment on the functioning of the unit

The functioning of the unit is good regarding the respects of regulatory and ethical aspects, and management. Several aspects are however not been taken into consideration (gender parity, non-discrimination, resource savings, waste processing)



1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The unit focuses on peritoneal diseases. The skills and specialties of the members of the unit allow to address different aspects of these pathologies. The presence of researchers (one DR2 and two CR1) specialized in gastric, ovarian, and colon pathologies is a real asset and allows to address the global theme of the unit according to different approaches, methodologies, questions and models of carcinomatosis. The link with the clinical activity of Dr. Pocard is a strong asset. Each research axis can potentially go towards a therapeutic or clinical solution. Moreover, research focuses on peritoneum and carcinosis, so the unit developed a common culture, and surgical and chemotherapeutic strategies.

The formation of MD to research (masters and PhD) is a relevant objective of the unit, and a strong asset.

The participation to national networks on carcinomatosis, RENAPE and BIGRENAPE are relevant and a strong asset.

Weaknesses and risks linked to the context

The scientific objectives and the link between each research groups is not clearly apparent. Each group has a good independent activity but common collaborative research is lacking with no publication in common between the 3 scientific researchers.

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

From 2017 to 2022, the unit received 519 k€ in funding from Inserm and Université Paris cité (no funding in 2017 and 2018, then 156, 120, 135 and 108 k€ annually). The resources were distributed by researcher and according to the number of students supervised. The unit is structured in four groups (colon, gastric, ovarian and pseudomyxoma), each group leaded by a scientist.

The unit benefits from an "angio-in vivo" platform that is common to three research units. Technologies such as Micro CT Scan, Echodoppler or bioluminescence can be used to evaluate the angiogenic process.

Weaknesses and risks linked to the context

The unit failed to obtain specific funding for their projects. Most of the resources are from the Inserm and the university. The unit did not get enough funding from independent competitive sources (associations, INCa, ANR, Europe, private companies). In particular, national and international funding are sparse and did not allow to recruit engineers and postdocs.

The ability (or time) of unit members to seek funding appears insufficient.

Scientific resources are limited in each group with one clinical scientist, but no postdoc and a single phD in the unit since 2020.

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

Student supervision is very good and all PhD students published their work. The unit management of student resource is also to be noted during the containment and the Covid period, with virtual meetings to ensure proper follow up of the students.

There is a good balance between man and female in the team, both for researchers and PhD.



Weaknesses and risks linked to the context

No policy for gender parity and discrimination is presented. No policy for resource savings, waste, carbon footprint is presented.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The unit attractiveness is good, as demonstrated by the fact that the head of the lab has successfully established an International Society for the Study of Pleura and Peritoneum (ISSP) and is committed to promoting and fostering all aspects of it through an inclusive approach. However, the unit was not successful in its efforts to obtain fundings, in particular in clinical research. There is no strategy to recruit post-doctoral fellows and new full-time researcher.

- 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

The head of the unit is internationally recognized for his expertise in peritoneal carcinomatosis and was founding president and is involved in the International Society for the Study of Pleura and Peritoneum (ISSPP) created in 2018. With its multidisciplinary approach (radiologists, surgeons), the unit has also contributed to an European research network on the peritoneum and contributed to the implementation of "PIPAC training course" in 2018 and 2023 (international meetings).

The head of the lab was member of the scientific boards of the Francophone Federation of digestive oncology the most important French intergroup in digestive oncology. As such he was involved in the development of randomized trials and educational programs. Two members of the unit are editor in chief of the only specialized French journal in radiology and digestive surgery. The unit also contribute to the creation of a new journal (peerreviewed open-access journal) with Elsevier group named SODA (Surgery Digestive Open advance): first publication February 2021. The goal is to provide useful knowledge focused on technical aspects and basement for major strategical evolution.

Regarding the unit's scientific reputation: the leader has multiple national and international teaching activities.

The number of students recruited was satisfactory over the period: the lab has supervised 11 PhD (a single drop out) and 6 defended within 3 years. The majority of PhD students in the unit have valued their work through publications. From 2 to 12 publications per PhD student very often with first author workers. The supervision of PhD students is appropriately shared between the 9 HDR members of the team. They managed to raise at least two of them to the level of "Habilitation à Diriger des Recherches". The formation of MD to research (masters and PhD) is a relevant objective of the unit, and a strong asset.

Several master students were supervised.

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

With regard to the unit's attractiveness, the committee notes that there are difficulties to recruit new full-time researcher. Only 2 HDRs are held by full-time researchers. A unique post-doc was financed and recruited over a 5-year period (2013-18). This is problematic because with a limited number of permanent scientists and post-docs the management should be based on other qualified team members who are clinicians and have limited



time for supervising students. At the valuation date, only 2 PhD students still registered which reflects the team's loss of steam and may slow down the valuation of the studies of the unit.

The unit's strategy of open science was to publish most of the paper in open journals, even if the cost is higher and the exposure is often less obvious. Moreover, some of the unit participate to create a peer-reviewed openaccess journal not yet meddling referenced.

With regard to the unit's success in competitive calls for projects: the unit was not extremely successful in its efforts to obtain funding, in particular in clinical research. The recurring allocation has existed since 2019. With the exception of 2019, the vast majority of the budget has since come from the recurring allocation.

Attempts to develop clinical research with trials have been unsuccessful due to lack of funding. But this axis is essential to validate the effectiveness and tolerance of PIPAC and in case of success the clinical development.

The research work of the unit is essentially based on the use of animal models. In this context the unit has requested to be merged to gain access to other animal models and to more efficient means of research evaluation (Bioluminescence machine vs animal CT or MRI).

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The overall quality of scientific production during the period has been good to very good, with several articles published by the team members in very good specialty journals as well as contributions to multicenter clinical studies published in high profile journals. The number of published articles has been important (109 articles) in regard to the size of the unit, and appears well distributed across the period and among the senior members. However, regarding its clear potential for clinical translation, one may have expected some higher visibility and impact publications.

- 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

Between 2017 and 2022, the unit had published 109 papers. Half (more than 50) of these publications were produced and/or supervised (first/last/corresponding author) by a member of the team, including several articles published in good specialty journals (*Pleura Peritoneum, Ann Surg Oncol, Br J Surg*), and were for some of them frequently cited (>30). These publications have also been regularly distributed, both across the period (between 14 and 26 per yer) and among the various research themes of the unit. Most papers concerned physiopathology, tumor implantation or cancer progression. Several of them have clear potential for clinical translation, in particular for PiPAC (14 publications between 2017 and 2022 and 5 in 2022). Some other papers provided convincing arguments to further explore specific targets / pathways, such as AHR receptor or Kallikrein. In addition, the unit has contributed to several collaborative clinical studies, published in high profile journals, including 3 highly cited articles in *Lancet, Lancet Oncology*, and *J Clin Oncol*.

The overall scientific production is proportionate to the research potential of the unit and well shared between senior members. All six PhD students in the unit have valorized their work through publications (2 to 12 publications per PhD student, most often as first author). The supervision of PhD students is appropriately distributed between the HDR members of the team.

The scientific production of the unit clearly complies with the principles of research integrity, ethics and open science. Laboratory notebooks as well as computer resources that stay in the unit, are used by all students and



researchers. The exclusive use of human samples with anonymisation process and signature of patient consent even in case of surgical samples, is enforced. All animal research were approved by the ethic committee. Finally, the unit has well defined its open science policy, sharing animal model and ressources as required, and promoting the use of journal in open access.

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

Regarding the potential for translation and clinical impact of its research, the overall scientific production of the unit could be higher in term of visibility and impact. There is no article in general audience / high profile journals which was produced or coordinated by the team members (first last or corresponding author).

Lack of collaborative publications across the various themes / senior scientists of the unit, suggesting the development of parallel projects, in silos with little interactions among them. The number of PhD students has decreased in recent years, with a risk for a reduction in scientific production in future years.

The policy for selecting journals for the submission of articles from students and/or senior authors from the team is not clear, with a significant number of articles published in journal from publishers with recently questioned editorial policies, such as *MDPI*, *Frontiers*.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The valorization is good: the unit has interactions with 2 private companies (Stago, Gamida), collaborated with one patient association AMARAPE, and has developed a website for professionals, patients, and general public audience.

- 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

Because of its position as surgeon and its national and international recognition in the field, the unit have good opportunities to collaborate with private companies. The unit has strong interactions with private company. In particular, this resulted in the creation of a common research team within the unit with Stago company (one scientist, one MD and one Cifre PhD) to study the role of circulating DNA and Neutrophil extracellular traps on fibrin structure and metastasis implantation process in patient affected by carcinomatosis.

In a second collaboration, the unit has participated to the development and the validation of a new nebulizer for PIPAC treatment (GAMIDA company), demonstrating that the unit is seen as a reference in the field. There is also a strong interaction with Lariboisière, Pitié Salpêtrière and Begin Hospitals.

The unit collaborates with AMARAPE, an association of patients that help patients with rare peritoneal carcinomatosis diseases. The association has funded the development of an Echodoppler to help predict recurrence of the disease.

The unit has developed a website that contains information for patients and general public. This represents a very important contribution to help patients suffering from this relatively rare disease.

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



The mentioned Industrial collaborations only resulted in limited funding for the research unit (20 k€ in 2022 and one Cifre) and no patent has been deposited. The contract with Stago results in IP for the company, not shared with Inserm.

The national and international recognition of the director did not result in a more active interaction with patients and the general public. No patent has been deposited by the unit, which may limit transfer to the clinic.



ANALYSIS OF THE UNIT'S TRAJECTORY

For the next mandate the proposal is to merge with a research unit to build a new research unit named "Nanomédecine, Biologie extracellulaire, Intégratome et Innovations en santé" (NABI) based in the Saint Père (university Paris Cité). The new unit will be a joint management CNRS & Inserm. The local authorities are in favor of this combination.

An extensive research program is planned and include:

- Develop a rescue kit to offer to the digestive surgeon a solution in case of identified per-operative situation associated with an increased risk of peritoneal metastatic process;
- Develop a solution to increase the drug delivery chemotherapy using PIPAC procedure with EVs;
- Understand carcinomatosis process to help patient regarding thrombotic risk by interaction between cDNA, Nets and coagulation / depressive risk by cytokine interaction and / prognosis factor using cDNA and exposome evaluation.

Some aspect of this program should probably delegated/ treated in collaboration with other research units specialized in SHS (depressive risk by cytokine interaction).



RECOMMENDATIONS TO THE UNIT

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

The unit is closing.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit is closing.

Recommendations regarding Evaluation Area 3: Scientific Production

The unit is closing.

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

The unit is closing.



CONDUCT OF THE INTERVIEWS

Dates

Start: November 10th of 2023 at 12.45 pm

End: November 10th of 2023 at 7 pm

Interview conducted online

INTERVIEW SCHEDULE

- 12h45-13h45: Connexion du comité seulement
- 13h45-14h00: Présentation du comité à l'unité

14h00-15h00 : Présentation scientifique : Marc Pocard (DU) : Bilan U1275 (2017-2022). 20 min (14h00-14h20) Massoud Mirshahi : 10 min (14h20-14h30) Projet Nabi : Marc Pocard : 10 min (14h30-14h40) Questions du comité (20min)

Rencontres du comité avec les groupes :

- 15h00-15h20: Entretiens étudiants
- 15h20-15h40 : Entretiens chercheurs
- 15h40-16h00: Entretiens avec les ITA AI
- 16h00-16h30 : Rencontre avec les tutelles (université et Inserm) Inserm : Mme Claire de Marguerye IT Techno: MJ Leroy Zamia Université Paris Cité Vice-Doyen Recherche : Michel Vidal Directrice du pôle Recherche et Innovation de la faculté de santé : Christine Guillard
- 16h30-17h00 : Entretien du comité avec le DU
- 17h00-19h00 : Finalisation du rapport par les experts



GENERAL OBSERVATIONS OF THE SUPERVISORS



Le Président

Paris, le 14 décembre 2023

HCERES 2 rue Albert Einstein 75013 Paris

Objet : Rapport d'évaluation de l'unité **DER-PUR250024162 - CAP Paris-Tech - Carcinose Péritoine Paris Technologies**

Madame, Monsieur

L'Université Paris Cité (UPCité) a pris connaissance du rapport d'évaluation de l'Unité de Recherche **CAP Paris-Tech - Carcinose Péritoine Paris Technologies**

Présidence

Référence Pr/DGDRIVE/2023 Ce rapport a été lu avec attention par la direction de l'unité, qui nous a signalé ne pas avoir de correction à apporter (cf courrier du Pr Marc Pocard), le vice-doyen recherche de la Faculté de Santé d'UPCité, par la vice-présidente recherche d'UPCité et par moi-même.

Affaire suivie par Christine Debydeal -DGDRIVE

Je vous adresse nos remerciements pour la qualité de ce rapport d'évaluation et vous informe ne pas avoir d'observations de portée générale à apporter.

Adresse

85 boulevard St-Germain 75006 - Paris

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

www.u-paris.fr

Édouard Kaminski

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2 rue Albert Einstein 75013 Paris, France T.33 (0)1 55 55 60 10

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