Research evaluation

EVALUATION REPORT OF THE UNIT
Immunité et Cancer

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Institut Curie

Institut national de la santé et de la recherche médicale - Inserm

Université Paris Sciences et Lettres

EVALUATION CAMPAIGN 2023-2024
GROUP D

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High Council for evaluation of research and highter education

In the name of the expert committee :

Matteo Iannacone, chairman of the committee

For the Hcéres :

Stéphane Le Bouler, acting president

In accordance with articles R. 114-15 and R. 114-10 of the Research Code, the evaluation reports drawn up by the 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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Experts:	Mr Michael Dustin, University of Oxford, United Kingdom Mr Wolfgang Kastenmüller, University of Würzburg, Germany Mr Enrico Lugli, Humanitas University, Italy Ms Nuria Izquierdo Useros, IrsiCaixa AIDS Research Institute, Spain Mr Jacques Nunes, CRCM, Marseille (representative of CSS Inserm) Mr Ho Ping-Chih, University of Lausanne, Switzerland Mr Christophe Vanbelle, Inserm, Lyon (supporting personnel)

HCÉRES REPRESENTATIVE

Ms Birke Bartosch

REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Ms Tatiana Malherbe, Institut Curie
Ms Patricia Renesto, Inserm

CHARACTERISATION OF THE UNIT

- Name: Immunité et Cancer
- Acronym: Immunité et Cancer
- Label and number: U932
- Composition of the executive team: Ms Ana-Maria Lennon-Duménil (director), Mr Olivier Lantz (deputy director)

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement
SVE4 Immunité, infection et immunothérapie

THEMES OF THE UNIT

The main scientific goal of the Inserm unit 932 is to understand the molecular and cellular bases of immune responses at steady state, upon viral infection or cancer. This fundamental research is linked to the development of translational immuno-oncology projects for increasing opportunities to generate innovative immunotherapies

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

Upon a remodeling in 2017, U932 comprises currently 10 research teams located in two different buildings at the Paris site of Institut Curie. In 2018, the Institut Curie created the Center for Cancer Immnunotherapy, aiming at combining in one structure all the U932 activities applied to drug development and clinical applications. There are also plans to develop some new activities of the unit at the Saint-Cloud site.

RESEARCH ENVIRONMENT OF THE UNIT

Institut Curie (IC) employs 3,700 researchers, physicians, and health professionals across three sites (Paris, Orsay and Saint-Cloud), focusing on three missions: research, care, preservation & transfer of knowledge. In February 2018, IC has been awarded the "HR Excellence in Research" label by the European Commission for its European human resources strategy for researchers. Within its organization, IC is largely concerned by several crucial values such as “scientific integrity”, “gender equality, diversity, and inclusion”, “health and safety regulations”. Its 86 research teams cover a broad scope of research that encompasses cell biology, genetics, epigenetics, immunology, soft matter physics, organic and medicinal chemistry with 19 state-of-the-art technological platforms organized as the CurieCoreTech. IC is a member of the PSL (Paris Sciences & Lettres) university. Institut Curie has a Carnot Institut named Curie-Cancer and IC is recognized as an integrated cancer research site (SiRIC) by the French National Cancer Institute (INCa) a label that has since been renewed twice. U932 has been part of the three successive SIRICs.

U932 benefits from all these IC supports and participates to add value to these supports (especially in Immunology) by structuring ambitious programs (i.e. CIC Biotherapies IGR-Curie, IMOCA industrial chair with Sanofi, LabEx DCBIOL in IdEx/PSL University, RHU EpCART, France 2030 Biocluster PSCC).

UNIT WORKFORCE: 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	8
Chargés de recherche et assimilés	13
Personnels d'appui à la recherche	47
Sous-total personnels permanents en activité	**68**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	27
Doctorants	29

Sous-total personnels non permanents en activité	**56**
Total personnels	**124**

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	C	PAR
Inst Curie	0	1	41
Inserm	0	12	4
Autres	0	4	1
Total personnels	**0**	**17**	**46**

GLOBAL ASSESSMENT

The unit is recognized as a paragon of excellence, with a distinct focus on the nexus between immunology and cancer. Its evident drive for translational impacts, especially in the realm of cancer immunotherapy, positions it uniquely in the research llandscape.

Occupying two distinct geographical locations, the unit boasts a formidable collective of 178 personnel. What's striking is the cohesive research environment that emerges, despite potential spatial challenges.

Resource-wise, the unit has demonstrated prowess in mobilizing funds and infrastructure, as reflected in the establishment of several biobanks and a promising pipeline of advanced medicinal products.

There's a pervasive sense of a constructive work environment, supported by a systematic management approach and unwavering commitment to safety.

On the international stage, the unit commands considerable attention, majorly due to its leadership in both fundamental as well as clinical research endeavors. It's noteworthy to mention that four members from the unit are among the top 2% of globally cited scientists.

An academic inclination is apparent in the unit's robust mentorship of a significant number of PhD students and international postdocs.

In terms of funding, the unit's achievements are commendable, securing approximately 138 grants during the review period. This success translates to both leadership and collaboration, amounting to funds nearing 2M euros/year.

Publication-wise, the unit's portfolio is substantial, with over 1 000 scholarly articles, 20% of which are among the top 10% most cited works.

Commercially, the unit showcases a robust clinical pipeline, an impressive intellectual property suite (with 8 patents and 3 licensed), and lucrative industrial partnerships exceeding 3M euros. The launch of two spinoffs further accentuates their translational drive.

Among the diverse teams, specific units have made standout contributions.

- Team 1 is lauded for seamlessly integrating foundational observations into high-impact translational studies.
- Team 3 has showcased exemplary dedication and outputs in understanding MAIT cells and their broader health implications.
- Team 4 stands out with pivotal insights into the adaptive immune system, enriching our understanding of immune responses.
- Team 6 consistently delivers top-tier research in innate immunity, indicating a promising trajectory.
- Team 8, although nascent, has carved a robust niche in stem cell immunity research, with their innovative approach hinting at a bright future ahead.
- Team 7 has embarked on an upward trajectory, especially within the domain of translational immunotherapy, laying the foundation for significant future breakthroughs.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The conclusion of the previous global assessment of U932 was: "*Overall the unit was assessed as outstanding with strengths in productivity, international reputation, collegial atmosphere, student training and world-leading science, as well as recognition of clinical applications of their work. No weaknesses were noted in the review*".

The unit is still running with several major contributions to fundamental research in Immunology developing in some cases, new real opportunities in immunotherapies. To encourage internal communication, a written report of each group leader meeting is sent to all unit members and all unit members can ask to join the group leader meetings that take place 1-2 times a month. To be independent of the DCBiol SAB, a new U932 SAB has been created including the followings: Daniel Louvard (Institut Curie, Paris, France), Alain Fisher (APHP, Paris, France), Miriam Merad (Mount Sinai, New York, USA), Arnaud Echard (Institut Pasteur, Paris, France), Eric Vivier (CIML, Marseille, France), and Caetano Reis e Sousa (The Francis Crick Institute, London, UK), (1st meeting on December 2022).

All U932 team leaders have implemented their specific recommendations.

B - EVALUATION AREAS

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 to understand the molecular and cellular bases of immune responses at steady state, upon viral infection or cancer. Overall, the scientific objectives of the unit are outstanding.

Assessment on the unit's resources

The unit resources and the unit's vision of resource management are outstanding.

Assessment on the functioning of the unit

The way the unit is functioning, is reaching an outstanding level and comprises meetings between management staff and the various categories of employees, a Gender Equality, Diversity and Inclusion Plan, involvement of the Health and Safety department of the IC Research Center, a Data Management Department, as well as an IC Tech Transfer Office and a legal department. The latter are helping the unit members to negotiate public-private partnerships.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The unit is located at the heart of the Institut Curie campus, which provides a number of facilities for developing its projects. The presence of world-leading science in this unit (see publications 2017-2022) has opened up the possibility of applying and being successful in numerous national and international calls for their research projects. Major scientific collaborations have been established in major research centers around the world (for instance, in New York: Mount Sinai School of Medicine & Memorial Sloan Kettering Cancer Center). The high quality of the fundamental research in immuno-oncology and also in the immune responses against viral infections gave several opportunities to communicate with the medical (participation to clinical trials) and biotechnology fields (3 spin-offs of U932 (2016 Stimunity, 2019 Mnemo-Tx and 2020 Egle-Tx)).

From the translational and basic research emerged outstanding opportunities to develop innovative immunotherapies (such as peptide vaccination, mono-specific antibodies, bi-specific antibodies, activators of innate immunity, and quite recently on regulators of immune cell migration, inhibitors of tumor regulatory T cells (Tregs), and cell therapies (CART-T). This continuum is in line with the objectives of the institutions as "Strengthening the continuum of health research, while encouraging breakthrough research".

Weaknesses and risks linked to the context

None.

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

The resources of the unit include funding (almost 64 M€ for 2017-22 period with a recurrent budget by Inserm, 360 k€/y and IC, 314 k€/y), personnel (with some stable positions *via* Inserm and/or IC, in house start-ups…), access to technology platforms (see CurieCoreTech), research support by the Proof of Concept (PoC) lab and a scientific project management team.
This PoC team (created by the unit) is key for nascent public-private collaborations with U932 PIs or for maturating spin-off projects. It is also involved in the filling of numerous patents and the establishment of several collaborations with the private sector as described in Domain 4.
The members of the unit got access to training opportunities (PSL University and also by the LabEx DCBIOL and the RHU EpCART grants).

With its high capacity to raise funds, the unit was able to recruit approximately 80 post-doctoral researchers, technicians and engineers, project managers, to participate and develop several state-of-art technological platforms (cytometry, EVs platform), educational programs (via DCBiol labex). This involvement gives also an access to all the platforms on the IC site (CurieCoreTech).

All the unit staff is involved in the scientific strategy via different discussion forums.

Weaknesses and risks linked to the context

In developing this huge program around immunity and cancer, the lack of space and the limited possibility of securing permanent staff may become a problem in terms of maintaining the standard of world-leading science. There are no permanent positions from the university associated to the unit, however almost all the researchers from the unit are involved in the educational programs at the university.

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 benefits from several support structures set up at the Institut Curie (H2020 project LIBRA member, Health and Safety department of the Institut Curie Research Center, IT department).
The unit organizes scientific integrity courses and workshops at Institut Curie. A "manifesto" as the result of reflection and synthesis by numerous U932's members has been established to really take in account many points linked to the functioning of the unit such as the implementation of hygiene safety, psychosocial risks or green lab.
A *Gender Equality, Diversity and Inclusion Plan* with a dedicated budget has been created to respect parity and are non-discriminatory in terms of training, career development. Involvement of the Health and Safety department of the IC Research Center, four safety assistants in the unit and a Unit referent group to deal with psycho-social risks). A Data Management Department has been created at IC to deal with all data aspects (both scientific and medical). An IC Tech Transfer Office and a legal department are helping the unit members to negotiate the public-private partnerships.

Weaknesses and risks linked to the context

No weakness.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the unit in respect to its international scientific reputation, its staff hosting policies, grant leverage and technological equipment is outstanding.

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

Strengths and possibilities linked to the context

The unit has high international visibility with an important number of invitations as speakers to key congresses in its fields of activity (Keystone Meetings, Gordon conferences, International Immunology congresses...) or by renown laboratories (Mount Sinai USA, Karolinska Institute Sweden, Osaka University Japan...). Members have participated to organization of 10 international congresses (Keystone Meetings, Immunology Congress of Argentina, Annual AACR meeting USA) or workshops (EMBO, summer school south America). Unit members are editors or board members of journals of high reputation (Journal of Immunology, European Journal of Immunology, Journal of Extracellular Vesicles…). Members sit on the scientific evaluation committees of French or international charitable research funding associations (FRM, Ligue, Welcome Trust Foundation), of the Young Investigator EMBO and of foreigner national organization (MRC, DFG) and European (ERC) funding evaluation committees. The unit is well involved in research networks on the French, European and international levels (NIH, Horizon 2020, HFSPO, Cancer Research UK, DFG, EMBO). The unit is also a major player in the structuration of French research (French Dendritic cell society, French Society of Extracellular Vesicles, Club Francais de Therapie Cellulaire, etc.).

Weaknesses and risks linked to the context

None

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

Strengths and possibilities linked to the context

The unit is in symbiosis with Institut Curie and newcomers benefit from the actions set up by the two structures. The unit has put in place a very structured procedure to present the operational, organizational functioning, health and safety of the unit within the site. It is highly implicated in the integration of any newcomer, whatever her/his status. For example, specific actions are carried out for doctoral students and postdoctoral researchers in order to facilitate exchange between them and their rapid integration into the unit. The unit also benefits from the actions organized by Institut Curie to allow its doctoral students and postdoctoral researchers present on the site to interact either as part of scientific or social activities. Foreigners also benefit from the "Science Accueil" organization to help them with the steps necessary to settle in France. Doctoral students and postdoctoral fellows have access to all training activities organized by the unit and Institut Curie. An ethical unit charter guarantees the scientific integrity of all research stakeholders and scientific transparency helps to reassure by providing a framework for all new entrants. All these procedures have been summarized by the unit in a MANIFESTO. The whole of this environment and these actions allowed the unit to attract over the evaluation period two new young team leaders, 79 PhD students and postdocs, of whom 29 were French and 46 foreign. From 2017 to 2022 37 PhD theses (average of 6 per year) were defended, with 17 personnel with HDR being present in 2022 and an HDR/PhD ratio of 1.6.

Weaknesses and risks linked to the context

In view of the upcoming retirement of several senior researchers, there is a risk of not having enough young researchers with HDRs.

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

Strengths and possibilities linked to the context

Although benefiting from the support services of the Institute Curie for preparation of applications for the various calls to which it is eligible, the unit has invested heavily in a support service for the drafting of tender documents to assist project leaders. Thus, a researcher has in house and/or in Institut Curie all the skills required to prepare an application for complex tenders. Coupling this administrative support to the national and international unit recognition, the unit succeeded on very competitive national and international calls for tenders (2017-2022: six ERC, six NIH, 15 PIA, 41 ANR, 27 INCA, 5 ANRS, 1oneATIP-Avenir, four ITMO Cancer, eight Regional, 25 caritative association;) and was very well-funded (64 M€ with 75% international funding). This reinforces the unit's international visibility and supports its world leading role in its scientific domain. The recent success in a RHU EpCART is strategically important for the translational and clinical projects. The 2022 operating budget, excluding governmental and Institut Curie salaries, was €16.3 million, 95% of which came from financing by tender. With 134 staffs in 2022, all categories combined, the budget per staff ratio was €120k/staff. The unit therefore has the means to support its research ambitions, making it very attractive for external collaborators and to attract staff or new team leaders.

Weaknesses and risks linked to the context

None

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

Strengths and possibilities linked to the context

The unit has full access to all CoreTechCurie platforms. Given the activities of the unit, all instrumental resources and human skills are available either in the CoreTechCurie platforms, or internally within the unit, via its equipment acquisition strategy or the pooling of human resources of teams like for bioinformatics. The unit is also involved in the management of the flow cytometry CurieCoreTech and is the main contributor to the creation of the extracellular vesicle platform. The massive investment of Institut Curie on single-cell and spatial transcriptomic will support state of the art technologies required by the future projects of the unit. This proves that the unit has been and remains committed to having the technologies needed for its projects. The unit also broadly shares its expertise. All the technologies required to support the unit projects are easily accessible. This provides security of the means usable by all its members. It reassures and attracts any new person or external academic or private collaborators.

Weaknesses and risks linked to the context

None

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The output reputation and appeal were assessed as outstanding based on the high quality of the science emerging from the unit. The total number of publications in 2022 was 76, with an average citation per publication of ~60.

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

Strengths and possibilities linked to the context

The unit has maintained a steady level of publications in international peer reviewed journals, with an increasing trend. The total number of publications in 2022 was 76, with average citations per publication of ~60. The unit consistently publishes in the top scientific journals, including Nature, Cell and Science and in the top Immunology journals, including Immunity, Nature Immunology and Science Immunology. This is an outstanding output by international standards. The unit's teams consistently produce a significant volume of scientific publications.

Weaknesses and risks linked to the context

None.

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

Strengths and possibilities linked to the context

The unit's scientific accomplishments, in terms of both publication numbers and funding acquisition, align with team sizes. Larger teams tend to contribute to a higher volume of publications. While the team leaders have a commendable success rate, early career researchers within the unit also showcase an impressive publishing record. 84% of the unit's PhD students and 74% of its postdoctoral researchers have contributed to published articles. Among those PhD students, 69% achieved first-author recognition. Meanwhile, 58% of the postdoctoral researchers have been credited as the first author. Notably, the unit's permanent researchers are actively engaged in publishing: 92% have contributed to publications, with 58% securing the coveted first author position and 42% being recognized as the last author. This underscores the pivotal role of permanent researchers in the unit and demonstrates their active encouragement to spearhead research endeavors.

Weaknesses and risks linked to the context

None.

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

The research at U932 adheres strictly to the "Charte nationale de déontologie des métiers de la recherche", complemented by several other international and national codes and charters ensuring scientific integrity and research ethics. This commitment extends to the comprehensive care and ethical treatment of animals, as mandated by European and French regulations. In terms of documentation, data quality, and data management, Institut Curie has garnered various certifications, including ISO 9001:2015 and other relevant accreditations, showcasing the high standards maintained.

The unit actively fosters a culture of scientific integrity and ethical research practices. Numerous initiatives, including scientific integrity training sessions, internal surveys, and weekly journal clubs, ensure continuous dialogue on the importance of honesty and ethics in science. This integrity extends to data management, where the unit employed rigorous standards for products, protocols, and data storage, with tools like the "ElabFTW" electronic lab book. The unit also upholds transparent authorship criteria, advocates for open science policies, and is cautious of avoiding predatory journals, emphasizing the necessity of publishing in reputable and recognized journals.

Weaknesses and risks linked to the context

None

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The contribution of research activities to society was assessed as outstanding based on patent filings, start-up creations, industrial collaborations, public engagement and knowledge dissemination.

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

Strengths and possibilities linked to the context

U932 has established a strong reputation in non-academic interactions, as evidenced by significant collaborations with private sector entities, patent filings, and start-up creations.
U932 engages profoundly with educational institutions, with several researchers actively involved in training activities at PSL University. The unit stands firm on scientific integrity and innovation, evident from its proactive approach to protecting intellectual property, establishing effective tech transfer processes, and building bridges between academia and industry.

Weaknesses and risks linked to the context

None

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

Strengths and possibilities linked to the context

Between 2017 and 2022, U932 has launched two start-ups (Egle Therapeutics and Mnemo Therapeutics - Stimunity was previously created in 2016), linked 39 contracts with notable industrial partners (Stimunity, Servier, Institut Roche, Sanofi, Mnemo Therapeutics, among others), and amassed about 12.8 M€ in research funds. This robust industrial partnership ecosystem not only facilitates project development in health applications but also shapes career perspectives for early career researchers.

Weaknesses and risks linked to the context

None.

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

Strengths and possibilities linked to the context

U932 is deeply committed to public engagement and knowledge dissemination. Members have secured a notable media presence across various platforms, discussing their research and advocating for evidence-based solutions. Outreach extends to school students through programs designed to foster curiosity and critical thinking. Creative collaborations with artists and involvement in exhibitions further amplify U932's commitment to make science accessible to the public. Additionally, diverse initiatives, ranging from book consultations to engagements with patient associations and multimedia content development, reinforce the unit's aim to merge science with society at large.

Weaknesses and risks linked to the context

None.

ANALYSIS OF THE UNIT'S TRAJECTORY

The primary aim of the "Immunity & Cancer" unit is to bolster both its foundational research program and expand into translational and clinical research domains. Key actions include:

1. Fundamental Inter-Disciplinary Research: The unit strives to safeguard its global standing in fundamental immunology by recruiting young scientists. This effort is to ensure the evolution of science based on emerging challenges from the global immunology community and interdisciplinary interactions.
2. Translational Efforts: The unit supports its Principal Investigators (PIs) in moving their findings from the lab to the clinic. The emphasis is on autonomy, with PIs free to pursue translational paths if they choose.
3. Clinical Trials in Immunotherapy: A short-term goal is to introduce first-in-human clinical trials to test immunotherapies resulting from U932 discoveries.
4. Translational Research on Human Samples: The unit aims to extensively describe and categorize immune cells in human cancers using multi-dimensional methods. The objective is to refine immunotherapy selections for patients based on their tumor type and development stage.

Core Scientific Focuses: In basic cancer immunity research, U932 will target seven domains, including Myeloid cell biology, T cell biology, Innate sensing, and Cancer immunity, among others. For translational onco-immunology research, the focus will be on five immunotherapy programs. These encompass areas such as immune prognostic markers, vaccination, CAR-T cell engineering, and tumor stroma & stem cell targeting.

RECOMMENDATIONS TO THE UNIT

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

The PSCC Biocluster will give excellent opportunities to develop associated PSCC platforms actually linked to the unit such as immunomonitoringand cell therapy. This project will generate new space for the U932 teams/platforms.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit should ensure that sufficient new young permanent researchers obtain their HDR diploma.

The unit is encouraged to maintain its efficient administrative task force to support any researcher for their grant applications.

Recommendations regarding Evaluation Area 3: Scientific Production

Recognize Outstanding Achievements: The unit has demonstrated an impressive level of scientific production, with many teams contributing to high-quality research outcomes. This commitment to excellence should be regularly recognized and celebrated.

Continue Targeting High-Impact Publications: Teams have shown prowess in publishing their research in notable journals. This trajectory should be maintained and even enhanced, as the depth and relevance of the research warrant submissions to journals with high visibility.

Encourage Interdisciplinary Collaborations: The existing collaborations among teams have resulted in groundbreaking interdisciplinary studies. Continuing to foster such collaborations will only enrich the unit's scientific findings and broaden publication opportunities.

Maintain Engagement in Scientific Workshops and Seminars: The unit's active participation in academic events has been commendable. By consistently hosting and attending more of these events, teams can further their scientific visibility and keep abreast of global advancements.

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

Acknowledge Existing Societal Contributions: The unit's research has already made significant societal impacts, especially in healthcare. These contributions, whether through practical applications or industry partnerships, deserve acknowledgment and celebration.

Increase Public Engagement: The efforts in hosting public seminars and outreach programs have been noteworthy. Expanding these initiatives can further disseminate findings and foster a deeper connection with the wider community, encouraging scientific curiosity and appreciation.

Build Upon Established Industry Collaborations: The unit's existing ties with industry partners have facilitated the real-world application of its research. There's potential to further deepen these partnerships, ensuring the research's benefits reach an even broader segment of society.

Uphold Ethical Standards: The unit's commitment to ethics in its research activities has been commendable. It remains essential to consistently uphold these high ethical standards, ensuring societal benefits are always at the forefront of research endeavors.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Immune responses to cancer

Name of the supervisor: Mr Sebastian Amigorena

THEMES OF THE TEAM

The group focuses on the analysis of immune responses to tumors, with a special focus on T cell differentiation, identification of new antigenic peptides in both human and mouse models. More recently, the group established the Center for Cancer Immunotherapy, conducting clinical trials and patient-oriented research.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous recommendation was to continue the trajectory and do a major effort in focusing on translational projects. This has been done as the team has created the center for cancer immunotherapy and, lately, has published interesting papers on clinical trials conducted at the Curie site.

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	6
Personnels d'appui à la recherche	10
Sous-total personnels permanents en activité	**17**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	5
Doctorants	7
Sous-total personnels non permanents en activité	**12**
Total personnels	**29**

EVALUATION

Overall assessment of the team

Overall evaluation of the team is considered outstanding. The scientific production of the team has been impressive over the years. The establishment of the Center for Cancer Immunotherapy and the creation of companies aiming to translate basic science to the clinic are particularly appreciated.

Strengths and possibilities linked to the context

The team is ranked among the top in the world in the field of T cell differentiation and immune responses to cancer. The scientific contribution in the past 5 years has been impressive, with a large number of publications (>30; Sci Immunol. 2023; Sci Immunol. 2023; Nat Commun. 2022; Proc Natl Acad Sci U S A. 2019 with the PI as last or co-last author, just to mention a few) on different aspects of cancer immunology/immunotherapy. The team has expanded its focus to new avenues of research, for instance with two recent publications in Science Immunology, reporting the identification of novel splice variants in transposable elements of the genome, which

generate possible novel peptides that are targeted by cancer immunotherapy. Moreover, the Center for Cancer Immunotherapy, established in 2018 and directed by team members, is now starting to be productive, with publications both in basic science (Cancer Res, 2022) and clinical science (JITC, 2022; Nat Comm, 2023). This is appreciated because it is particularly difficult to conduct investigator-initiated clinical trials and at the same time have funding to conduct translational research on patients' specimens.

International visibility is certainly high in terms of collaborations with different institutions (MSKCC is one of them). The Amigorena team has also been working in close contact with spin-offs the PI created in the past (totaling ~8.8M EUR since 2017). This is certainly appreciated in terms of translational development. Moreover, the Center for Cancer Immunotherapy has been interacting with big pharmaceutical companies to conduct clinical trials at Curie.

Academic funding during the evaluation period has been impressive, and included national and international projects (ERC AdG, MSCA, several ANR and INCA projects, others: for a total amount of ~18.5M EUR since 2017). The team Amigorena has been supervising a large number (n=15) PhD students during the evaluation period, 10 of whom have successfully defended, or are about to defend their thesis.

Weaknesses and risks linked to the context

None to be reported

Analysis of the team's trajectory

The team has expanded to new areas of research based on their solid prior trajectory. The study of transposable elements leading to the generation of novel immunogenic peptides is of particular interest and could translate in novel therapeutic approaches. Overall, the team's trajectory perfectly aligns with the main objectives of the unit.

RECOMMENDATIONS TO THE TEAM

The recommendation would be to expand the effort of the clinical trial unit, recruiting new (junior) principal investigators with a major focus on the study of patients' specimens collected from experimental clinical trials. Despite recent published papers clearly demonstrating the potential of the unit, focusing on mechanisms at the basis of successful antitumor responses in humans would elevate the quality of science even more. During the evaluation, Dr. Amigorena stated that this is also a transitory period, as he will retire in the next few years. The team will be in part supervised by a senior scientist. The recommendation is to make sure that this information is clearly transmitted to the members of the research team, and that it is clearly stated that whoever in charge will indeed supervise PhD students and postdocs. Leadership has to be acknowledged by the members of the team to avoid a drop in productivity or possible conflicts.

Team 2: Myeloid cells and immunity

Name of the supervisor: Mr Philippe Benaroch

THEMES OF THE TEAM

This team focuses on innate immune sensing in macrophages and dendritic cells. They now further aim at genetically modifying monocytes/macrophages for immunotherapy against cancer.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations were to prioritize objectives, take risks, pay attention to team size to perform the projects. These recommendations were only partially implemented. The problem areas are still present and should be addressed as retirement approaches

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	0
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	3
Doctorants	2
Sous-total personnels non permanents en activité	**5**
Total personnels	**10**

EVALUATION

Overall assessment of the team

The overall assessment is very good to excellent.

Strengths and possibilities linked to the context

The team is well known for its cell biological expertise on myeloid cell biology and specifically with the focus on innate signaling and antiviral immunity. The team has continued on this research topic over the last evaluation period with a focus on the interaction of HIV and human dendritic cells (PNAS 2019) as well as the cell biological processes following HIV infection of human macrophages (J cell Science 2022, Front Microbiol 2020 and J Virol 2017). It seems that the lab is now focusing more on the role of macrophages in tumor immunity, as well as their application to immunotherapy against cancer. Overall, the scientific output both in terms of quality and quantity of publications is very good (6 last- author papers and 3 co-authorships).

The visibility of the PI in the field of cellular biology of macrophages and in particular anti-viral immunity is excellent as reflected by many invitations as a speaker at internationally renowned conferences. Overall, the team has managed to secure several funds (4 ANR, Sidaction; total funding 2.55 M€).

The team has filed three patents (not published) and plans to create a new start-up company.

The team leader provides teaching for students in M2 of immunology and cell biology. He has trained 3 PhD students and participated in the defense of several PhDs.

The team is composed of two technicians, one engineer, three postdocs and two PhD Students. Two more post-docs are planned to be recruited. Team has weekly meetings and research assistants drive the various research directions with strong support from the PI.

Weaknesses and risks linked to the context

Unfortunately, the weakness (lack of focus and little risk taken) already identified in the last evaluation period could not be fully remedied. The lab appears to be in a transition from antiviral immunity of Mø towards the role of Mø for anti-cancer immunity including genetic manipulation and therapy. But this refocus however also diverges forces which could affect the overall progress in the various projects. On the other hand, the project on tumor immunology lacks innovation and risk. Specifically, the planned project on the role of TAMs is generic and lacks hypotheses ("Integration of the results will drive hypotheses"). The selected omics-approach is used by many teams around the world. This is problematic, however, because this field is extremely competitive. Therefore, it is unclear whether this transition will be successful and the team will be able to make a significant contribution to the field of tumor immunology. The current publication output is very good, however, high profile publications seem to be only achieved as supporting PI (co-authorship).

The involvement in the start-up company may further dilute the focus of this team.

There is a need to pay attention to team size and recruitments, as this can be a threat to the success of the scientific project. A higher turn-over with new people might be better to bring in new ideas and creativity to the lab in order to embark on more innovative and risky projects.

It is unclear whether the PI will be able to make a significant contribution in a highly competitive field of tumor immunity before retirement. The project B2, the analysis of human samples is not very innovative, lacks a specific hypothesis and is probably already carried out in the same way at many locations around the world. Accordingly, it remains unclear how a competitive advantage is to be achieved here.

Analysis of the team's trajectory

The proposed 5-year research program has two main angles: A) Role of Gas7 in sensing HIV and B) the role of macrophages/monocytes in tumor immunity. The former project will be done in collaboration with Team Manel. It is planned to fuse both labs following the retirement of the PI in 2026/27. The second project has two subparts: 1) expressing CARs in monocytes as a basis for a future company and 2) analysing TAM in human tumor samples.

While the team is competitive in its core program (antiviral immunity in macrophages/DC), the planned project on TAMs lacks innovation. Promising preliminary data on CAR-Monocytes are also lacking therefore, this part is currently difficult to assess, but heavy competition may be expected as well.

RECOMMENDATIONS TO THE TEAM

With its expertise and rigor, the team could be at a higher level by focusing on key issues and by taking risks.

The team should pay attention to team size and recruitments as this can be a threat for the completion of the scientific projects. The future prospects of post-docs and permanent employees should be clarified before retirement.

Achieving strongly in highly competitive and diverse areas of research will be extremely difficult given the size of the team and the funding. Close collaboration in particular for the tumor immunological projects are recommended. We suggest that the PI establishes a priority among the objectives (tumor immunology projects) described in particular in view of the approaching retirement.

Team 3: Integrative analysis of T cell activation

Name of the supervisor: Ms Claire Hivroz

THEMES OF THE TEAM

This team is focusing on the regulation of T cell receptor in response to conventional stimulation and mechanical force, which tailor T cell behaviour and activation. By combining cutting-edge imaging platform and biochemical analyses, this team provided impactful findings in this research area. In the past five years, they published several exciting studies on delineating TCR signaling.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

This team followed the recommendations of the previous report. In the previous report, no major weakness had been raised. Of note, the group started to examine how PD-1 signal axis is engaged to hamper T cell reactivity against target cells, which is one of the major efforts on pushing translational angle. In this regard, the group did an excellent job on delineating a new dimension of PD-1 biology.

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	1
Doctorants	3
Sous-total personnels non permanents en activité	**3**
Total personnels	**7**

EVALUATION

Overall assessment of the team

The team is considered to be excellent.

Strengths and possibilities linked to the context

The team is well known for its cell biological expertise on T cell biology and specifically with the focus on T cell signaling and membrane dynamics in T cells. In the past five years, this team continued on their research theme and produced three major research articles in Nature Communications 2019, J. Exp. Med. 2018 and eLife 2017, which revealed interesting findings. Research funding, including one FRM and two ANR grants, and international visibility (invited to EMBO workshop in 2021 and ECI in 2019) were also excellent. This team is now focusing more on the role of PD-1 signaling, as well as their application to immunotherapy against cancer. Overall, the PI did quite well in the past evaluation period. Moreover, since 2019, there were three studies produced by this team the PI as corresponding author. Overall, it remains difficult to judge the reasons behind this decline, but this is in

part due to the effort of moving into the PD-1 signaling axis and establishing new tools for translational studies. Despite that, this team remains a top-tier research team exploring the frontier in this research domain.

The team leader has trained 3 PhD students and participated in the defense of several PhDs. The team is composed of a good number of trainees, including three PhD students and four postdoctoral researchers.

Weaknesses and risks linked to the context

Unfortunately, the weakness (lack of risk taken) already identified in the last evaluation period could not be fully remedied. The lab appears to be in a transition by combining their expertise in TCR signal and biology with the role of immune checkpoints for anti-cancer immunity. But this process however also takes more time and collaborations. Overall, the scientific production in terms of publications in the past three years was low. This is problematic, because this field is extremely competitive. However, the most recent Science Signal study suggests that the team has entered a potential production phase.

Analysis of the team's trajectory

The proposed 5-year research program has two main angles: A) TCR signaling regulation and B) PD-1 signaling. The coordination of these two angles may provide immediate impacts on our understanding in CAR T cell biology as shown in one of the collaborative publications in the past five years.

This is an exciting research domain, especially in the tumor microenvironment. The team should be able to further develop it in an impactful way based on the expertise and tools they established.

RECOMMENDATIONS TO THE TEAM

The team should consider to combine its findings with in vivo animal models. This can largely improve their impacts in this domain. The team also may consider how to transit the expertise to the institute.

The team should pay attention to recruitments as this will impact the productivity on scientific projects. The future prospects of recruitment should be clarified before retirement. The transition strategy and how the retain the expertise in the institute should be planned.

The regulation of TCR and the controls provided by mechanosensing may be applied to CAR T cells. Moreover, the understanding in TCR and PD-1 signal axis may be considered to be applied for developing new cell therapy, such as CAR T-cell. The team has established strong and unique tools to understand TCR regulations. Moreover, the research direction linked with mechanosensing is an exciting and important area. The team may consider to develop or collaborate with experts who can explore the contribution of those findings, especially mechanosensing, in disease animal models, such as tumors and fibrotic tissues. However, we are also aware of the retirement timeline of the responsible PI. In this case, we highly suggest the staff scientist in the team should align with the team head and the administrative committee in the institute to ensure the smooth transition and the completion of the ongoing exciting project. Most importantly, the institute should also consider strategies on retaining the tools and expertise established by this group.

Team 4: Innate like and CD4+ T cells in cancer

Name of the supervisor: Mr Olivier Lantz

THEMES OF THE TEAM

The team focuses on MAIT cell biology, CD4 T cell biology and anti-tumoral responses with a focus on neo-antigen discovery.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendation was to increase the translational studies, increase the number of PhD, and clarify the scientific and translation strategies (mice & human studies). The team has responded through progress on the human neoantigen project with a patent files and trials in planning. The number of students has been increased with 4 students currently in the lab. MAIT cell studies in human are being pursued. The response to the recommendations is strong.

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	8
Sous-total personnels permanents en activité	**11**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	4
Doctorants	4
Sous-total personnels non permanents en activité	**8**
Total personnels	**19**

EVALUATION

Overall assessment of the team

Outstanding productivity in the past five years in the area of MAIT T cells and neoantigen identification in uveal melanoma. Excellent productivity on the CD4 T cell diversity project. The PI of the team is an internationally well-respected authority in molecular immunology of innate like T cells and is establishing himself in the cancer immunology area more generally. Thus, the overall assessment is outstanding.

Strengths and possibilities linked to the context

The team is leading the field in the innate T cell field with a focus on MAIT cells and NKT cells. The team applies state of the art molecular immunology approaches to the problem and has made seminal basic and translational discoveries in the past 5 years. The team is well funded (8.6 M€ reported) with an ERC Advanced grant as a PI and INCA and ANR grants as PI and as co-I. They also have a contract from the US DOD, which is an indication that they can do things that cannot be done in the US in the area of uveal melanoma. The key papers in the previous five years include outstanding papers on the role of microbial metabolites in thymic

development of MAIT cells (Science, 2019) and MR1 mediated positive selection of naïve precursors vs innate like T cells programmed into tissue resident type 1 and type 17 profiles depending upon the type of presenting cells in the thymus (JEM, 2018; Nat Immunol, 2019). An exciting paper on MAIT cells in tissue healing has recently been published (Immunity, 2023). Thus, 5 of the outputs lead by the team's PI are in top general science and immunology journals. Another productive direction is to understand the origin of neoantigens in uveal melanoma, leading to the description of splicing factor SF3B1 as a mutated protein in uveal melanoma leading to characteristic neoantigens that may be targeted by immunotherapy. The productivity of the group has been outstanding and is clearly using state of the art genetic and multiomic approaches to address important topics the biology of metabolite sensing and neo-epitope identification in uveal melanoma sensing by conventional CD8 T cells (Cancer Discovery). The training of doctoral students has increased since the prior period with 1 PhD completed in 2021 and 2 PhD completed in 2022, with 4 students in training. The team's PI has presented 5 International seminars including one in Japan and presented at 2 international and 2 national conferences. The team management appears sound with 2 research officers and 8 research support staff working with the 4 PhD students and 4 post-docs. The management structure is clearly outlined. The Clinical Immunology lab operations are supported by a deputy director who is a clinician scientist with 20% clinical and 80% research responsibilities, similar to the PI. The research components will merge with the Immune Response to Cancer team as the PI reaches retirement age. However, it was explained that the PI can continue with the leadership of the Clinical Immunology lab to the end of the next review period. The strong connection between the Inserm research unit and the Clinical Immunology lab is clearly beneficial and efforts will be made to sustain this.

Weaknesses and risks linked to the context

The genetic approaches to MAIT cells sound like high risk-high gain efforts and should be encouraged despite the risks.

Analysis of the team's trajectory

This is a highly productive team involved in three core projects and many collaborations. The three areas are all generating exciting outputs with greatest momentum in the MAIT and neoantigen areas. The CD4 project that was less discussed above is generating leads towards a very plausible sounding model that Treg favour CD4 T cells responses with “high affinity” whereas T-T quorum sensing maintains diversity- perhaps through a SOCS dependent mechanism. The forward analysis of MAIT cells and neoantigens is highly innovative and outstanding.

RECOMMENDATIONS TO THE TEAM

This is a highly productive team that has made outstanding and sustained progress on MAIT cells and CD4 T cell diversity and recently made progress on CD8 T cell neoantigens. The process of team 4 joining with team 1 will need to be carefully managed. The PI will continue to head the clinical immunology lab through this process and that interaction should continue to be valued and supported by the unit. But otherwise, we look forward to more exciting science from this outstanding team.

Team 5: Spatio-temporal dynamics of immune cells

Name of the supervisor: Ms Ana-Maria Lennon-Duménil

THEMES OF THE TEAM

Molecular processes regulating sentinel functions of Dendritic cells and macrophages. Team focuses on cell biology and interactions with the ECM as well as physical parameters.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations were to continue the projects, further integrate knowledge within the multiple fields of biophysics and immunology and to further increase interaction with Pharma and/or Biotech industries, and to obtain an additional HDR (Habilitation to Supervise Research) to allow recruitment of more PhD Students.

This team has fully addressed these recommendations!

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	7
Sous-total personnels permanents en activité	**9**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	4
Doctorants	4
Sous-total personnels non permanents en activité	**8**
Total personnels	**17**

EVALUATION

Overall assessment of the team

This team is outstanding.

Strengths and possibilities linked to the context

The scientific output of this team is outstanding and consists of original and highly innovative work.
The finding that colonic macrophages regulate epithelial integrity by scavenging microbial products within the epithelial layer is seminal (Cell 2020). This opens up new projects that the PI will follow up. A further landmark paper by this team was published in Immunity 2022 identifying distinct subtissular niches of mature and immature dendritic cells in the gut. Accordingly, the PI has been invited to numerous meetings (Gordon, Keystone, EMBO…etc.) and institutional visits for external seminars both nationally and internationally. The PI enjoys a high scientific reputation and was awarded both with an ERC advanced and ERC synergy grant during this evaluation period (total funds= 3.44 M€).

There is evidence of considerable public engagement activities (Various science-art projects, books, movies, etc.) and a long record of training PhD students. The PI teach at the Master "Approches Interdisciplinaires du Vivant" (2017-2020)

The team currently comprises four PhD students, four post-docs, one engineer, one CNRS and one Inserm permanent researcher. In total, six former lab members were able to start their own independent careers in academia. The lab has weekly team meetings.

The scientific approach and endeavors are exceptionally ambitious and innovative, building upon the team's past accomplishments. The project encompasses profoundly demanding and forward-thinking concepts. Specifically, the projects benefit from the interdisciplinary approach and combine physical aspects of the tissue with cell biological factors. Basic concepts and newly identified molecular players are investigated in the context of relevant human diseases like cancer or inflammatory bowel disease.

Weaknesses and risks linked to the context

There are no significant weaknesses. The team has further improved and addressed previous recommendations.

Analysis of the team's trajectory

The team has had a fantastic track record in the last evaluation period, and all the conditions are in place for this to continue with the same momentum in the coming years. The projects of the next period are built around two main directions, four specific questions based on interesting hypotheses. Building on its recent discoveries the team focuses on projects such as the ballon-like protrusions of macrophages in the colon and now asks how they form the protrusions from a cell biological perspective. Additionally, the team wants to dive further into the exact function of these protrusions. The second main direction deals with how physical properties of tissues (including cancer) impact on myeloid cell function. This research direction will likely provide new insights that can be used for translation projects. Overall, several projects, including ERC funded proposals, are highly ambitious and groundbreaking. These projects, if successful, will most likely yield breakthrough results. The comprehensive evaluation indicates that this team is exceptional, possessing an outstanding strategy and a promising future research plan.

RECOMMENDATIONS TO THE TEAM

We are excited to see more of the teams work in the future.

Team 6: Innate immunity

Name of the supervisor: Mr Nicolas Manel

THEMES OF THE TEAM

The team aims to investigate the mechanisms of self/non-self-detection in innate and aging immunity, and has four dedicated themes to pursue this goal: 1) Intracellular detection of viruses; 2) Regulation of cGAS-STING signaling;3) Erosion of intracellular identity in aging; and 4) Applications for cancer immunotherapy.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous recommendation was to continue the trajectory and do a major effort in securing important and long-term funding. This has been done as the team has attracted competitive funds along with industrial partners that have contributed to secure long-term funding.

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	6
Doctorants	2
Sous-total personnels non permanents en activité	**8**
Total personnels	**11**

EVALUATION

Overall assessment of the team

The trajectory of the group is outstanding, with an impressive track record of sustained high-quality scientific achievements overtime, even during the pandemic.

Strengths and possibilities linked to the context

The scientific output of the team is impressive mostly by the number of high-quality papers led during this period, not only related to innate viral sensing, but also to new research areas such as vaccines and cancer. In total they have published 19 papers, being corresponding authors in seven of them, along three manuscripts not reviewed by peers but deposited in repositories (preprints). The team has continued with their initial research line dedicated to innate viral sensing and produced ground-breaking studies that have identified NONO as the sensor of HIV capsid proteins in the nucleus that activates cGAS (Cell. 2018), also describing how different DC subsets are affected by viral infection (Science Immunology. 2017) and identified possible new targets for antiviral treatments (Cell Reports. 2021), among other viral-related publications. In addition, the team has expanded the initial scope of their research, producing high quality research that has attained the same

outstanding level of excellence. These studies are related to DC response to vaccines (Science Signaling. 2021) or pro-tumoral mechanisms related to aging (Cell. 2021). Is important to highlight that this impressive track record of scientific achievements was obtained during the pandemic period. The team collaborated in publications with 7 out of the 10 teams of the unit, clearly showing the highly dynamic atmosphere built among them and the perfect alignment with the rest of their colleagues.

The group has produced several patents and has already licensed one of them to Stimunity Biotech, which is providing 1.8 M € of R&D contracts to Institut Curie. This interaction with the industry will help to bring marketable innovations based on their fundamental oriented research.

They have demonstrated a strong capacity to train researchers including postdocs (5), PhD students (5) and master students (10), with one HDR in the team, and are linked to EU actions such as the Innovative Training Network INITIATE.

The capacity to attract funds as a PI is also excellent and the association with industry partners will contribute to secure long-term resources, one of the recommendations done by prior evaluators. The team obtained several important grants (24 in total, with 15 as a coordinator). Funding from four ANR, one ARC, one BFM Foundation, 1 FRM, 1 H2020 ITN, one INCA, four Sidaction, etc., has allowed the team to secure a total of about 4 M€. In addition, the collaboration with Stimunity Biotech leads to 1.8 M€ of R&D contracts for Institut Curie.

Finally, the international recognition attained by the group in the past years is demonstrated by the high number of invited conferences and seminars (53) achieved and the organization of high prestige meetings such as EMBO.

Weaknesses and risks linked to the context

None detected.

Analysis of the team's trajectory

The team has expanded to new areas of research based on their solid prior trajectory. They master the capacity to decipher unknown innate molecular pathways, supporting ground-breaking fundamental interdisciplinary research. They also foster an active translation of their findings to develop new therapies and already foresee launching a phase 1 clinical trial with Stimunity Biotec. Overall, the team's trajectory perfectly aligns with the main objectives of the unit.

RECOMMENDATIONS TO THE TEAM

Continue with this excellent performance. Looking forward to see the future studies of the group and learn how the knowledge already built studying innate viral sensing throughout the years continues expanding to other research areas while producing innovative solutions to treat diseases.

Team 7: Translational immunotherapy

Name of the supervisor: Ms Eliane Piaggio

THEMES OF THE TEAM

The group focuses on the analysis of immune responses to tumors, with a special focus on T cell immune responses in human cancer and Treg-mediated immunosuppression. More recently, the Piaggio group also contributed to identify novel populations of macrophages in breast cancer.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations were to concentrate on specific lines of research, especially translational, and avoid dispersion of effort. Moreover, at the time, production was considered a bit limited, possibly because of the young nature of the team. In the past five years, the team did an outstanding job to bring ongoing projects to completion (publications in prestigious journals), to expand analyses to samples from patients in different conditions and treatments and to conduct clinical trials in collaboration with other members of the Unit. Therefore, we consider previous concerns completely solved.

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	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	**6**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	3
Doctorants	3
Sous-total personnels non permanents en activité	**6**
Total personnels	**12**

EVALUATION

Overall assessment of the team

Overall evaluation of the team is considered outstanding. The scientific production of the team has been excellent over the years. The creation of Egle-Tx to translate basic science to the clinic was particularly appreciated by the committee.

Strengths and possibilities linked to the context

The team has been exceptionally productive in the last few years in the field of T cell immune responses in cancer, immunotherapy and identification of novel populations of immunosuppressive cells. In collaboration with the Helft team, the team has recently reported the identification of FOLR2+ macrophages in cancer (Cell, 2022). Moreover, they also reported on the analysis of Tregs from tumor draining lymph nodes (Nat Comm, 2020),

an important site that tended to be ignored in the last decade, and on the characterization of rhaboid tumors (Cancer Cell, 2019).

Academic funding during the evaluation period has been excellent, and included national and international projects (several ANR and INCA projects, others: totaling ~2.8 M EUR since 2017) or funding from pharmas (see below).

The team has been supervising six PhD students during the evaluation period, three of whom have successfully defended, or are about to defend their thesis.

Team management has been excellent, with former trainees who are now PIs in different institutions and the team published very competitive papers (total number of papers: >40, some of which of particular interest and have the PI as last or co-last author: Nat Comm. 2022; Nat Comm. 2020; Cell. 2022; Cancer Cell).

The creation of the start-up Egle-Tx, which secured 45 M EUR in funding, is expected to translate the basic scientific knowledge gained on Treg biology. Collaborations with industrial partners are in place and are considered extremely important to boost the patients' based scientific activity of the lab (including Bristol Myers Squibb, Novartis, Egle Tx or others; totaling 2.6 M EUR since 2017). Considering the strong translational nature of the team, collaborations with clinicians are stated and scientific production is ensured. Collaborations with international partners (CIS, NIAID, USA; National University of Cordoba Argentina) resulted in nice publications with Dr. Piaggio as co-author (Nat Biotechnol. 2020; Front Immunol. 2021).

Weaknesses and risks linked to the context

None.

Analysis of the team's trajectory

The team has expanded to new areas of research based on their solid prior trajectory. The creation of Egle-Tx is of particular value to translate basic results to the clinic. Overall, the team's trajectory perfectly aligns with the main objectives of the unit. Nevertheless, the projects that are proposed (identify biomarkers of Treg activity in the blood, profiling patients with single cell technologies) are very competitive and are carried out by a number of groups in the world. The team will now focus on novel possible targets of immunotherapy they discovered by comparing tumors and the draining lymph nodes. This is promising to open novel areas of research.

RECOMMENDATIONS TO THE TEAM

To continue on this line of research to identify novel targets of cancer immunotherapy in the tumor microenvironment or related sites with a focus on novel, less explored topics, to avoid competition at least in part, and maximize productivity. The team conducts a number of translational studies on patients' specimens, either investigator-initiated or sponsored. A suggestion would be to expand contacts with pharmaceutical companies willing to collaborate with the team in order to secure additional funding.

Team 8: Stem cell immunity

Name of the supervisor: Mr Enzo Poirier

THEMES OF THE TEAM

The team focuses on discovering and understanding mechanisms of defence implemented specifically in stem cells, both in a steady or cancer context. They study three different axes: 1) AviD-driven antiviral immunity via the study of the new isoform of Dicer that they had previously identified; 2) Novel mechanism of defence by comparison with bacterial antiphage pathways; 3) Mechanisms of defence in cancer, to understand if certain stem cell-specific mechanisms can be expressed in cancer cells and subjected to new therapies.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was created in 2021 so there are no prior reports.

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	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**4**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	0
Sous-total personnels non permanents en activité	**0**
Total personnels	**4**

EVALUATION

Overall assessment of the team

Impressive launch of a group funded in 2021 within the pandemic context. The team and PI have shown an outstanding capacity to obtain highly competitive and prestigious grants, such as ERC Starting Grant. They have also delineated several research axes that have already produced high-quality results pending to be published along a patent application. All these quality indicators combined to the great potential and novelty of the research proposed by the team warrants an excellent near future and ground-braking science yet to come.

Strengths and possibilities linked to the context

The team explores a novel approach to identify unknown antiviral defence mechanisms in humans and other eukaryotes by comparing it with the well-known and numerous antiphage mechanisms described for bacteria. This unique hypothesis has allowed the group to identify new antiviral human strategies and develop a methodology to identify novel immune responses. This work is led in collaboration with another team and is already shared via BioRxiv, holding the potential to be published in a top-quality journal. The group has also

contributed with a review in the field of antiviral immunity in mammals (Biochemical Society Transactions, 2023). The new transversal methodology developed along the strong expertise in stem cell biology brought by the team is well aligned with the research interest of the unit, as already demonstrated by the active interaction and collaboration with at least four teams of the unit. They have also published two other reviews in Biochemical Society Transactions.

The group has a patent application based on their novel work. The possible applications of this particular methodology to identify new therapeutic targets holds great promise and will probably lead to more patents.

The team is actively engaged in training courses at the Institute Curie and has recruited postdocs even under the current situation where attracting postdoctoral talent is difficult. At the end of 2023, the team will be composed of two engineers with 2-3 years of experience, two postdocs and two PhD students, some of them co-supervised with other PIs from the unit.

The group is starting to have international visibility and has already presented work at international meetings (ie. Annual Meeting of the RNA Society of Japan)

Among all the impressive achievements of the team, it is worth highlighting the funding attraction capacity of this group, not only for the quality and prestige of the grants obtained, but also for the large number of them. Furthermore, the team has already important funds for several years. The group has obtained 8 funded projects from national competitive grant agencies (Inserm CRCN (2022), ANR JCJC (2022), Émergences Ville de Paris (2022), ATIP Avenir (2022), Fondation Chercher Trouver (2022), FRM Amorçage Jeune Équipe (2022), Paris Sciences et Lettres Amorçage Jeunes Équipes (2021)) and most remarkably an ERC Starting Grant in 2022. This latest achievement clearly highlights the great potential of the research line of this new team.

Weaknesses and risks linked to the context

None detected. The highest risk of a novel group is to secure enough funding sources.

Analysis of the team's trajectory

The trajectory is outstanding and quite unique as it is based in comparative studies with prokaryotes, and this is especially true if we frame the commencement of the group in the pandemic context. This has not been a limitation, and is really impressive to see what the PI along his group has achieved in so little time.

RECOMMENDATIONS TO THE TEAM

Continue as planned and now that funding is secured for several years, concentrate in publishing ground-breaking research associated to the axis pursued. We look forward to see how these research lines evolve to unlock all their potential. Contacts with industry should be pursued.

Team 9: Stroma and immunity

Name of the supervisor: Ms Hélène Salmon

THEMES OF THE TEAM

This team is working on the interactions between stromal cells, especially cancer-associated fibroblasts, and T lymphocytes and delineate how these interactions can instruct and impair T cell-mediated immunity. In addition, this team also collaborates with clinicians to understand how a bi-specific antibody against TGFb and PDL1 can reprogram the stroll compartment in HNSC patients. By applying these technologies and samples from a clinical side, this group is developing a solid research theme on broadening our understanding of firbroblasts in tumors.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

This is a new group who join in 2019. There is no recommendation of the previous report.

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	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	2
Sous-total personnels non permanents en activité	**3**
Total personnels	**8**

EVALUATION

Overall assessment of the team

Overall evaluation of the team is considered excellent.

Strengths and possibilities linked to the context

This team was initiated in 2019, one year before COVID pandemic. In fact, most of junior faculty starting independent research groups during this period largely suffered. However, this team efficiently established critical mass and foundation on approaching this research field. They even published an outstanding study in Cancer Discovery in 2022 to demonstrate how CAF modulate tumor infiltrating leukocytes migratory pattern in tumors (total number of publications two as senior authors, one biorxiv, one review). Moreover, the group obtained 5 grants from ARC, INCa, ITMO-Cancer, Unicancer and Fondation Chercher et Trouver, of those 3 as leader (ARC, INCa, Unicancer). Based on the presentation, we further see other ongoing studies conducted by the group, including analysis of samples from a clinical trial with Bintrafusp-alpha, a fusion protein targeting PD-L1 aand TGFband collaborations with 2 industrial partners. The combination of these research directions further warrant the foundation of this team on delineating the stromal biology in tumors. Overall, this team did

tremendously well and laid a critical foundation for the next five years. Overall, a fruitful research output can be easily anticipated.

The team has a well-designed plan on combining their expertise on analysing clinical samples and drug candidates developed in other pharmaceutical companies. Overall, this is a balanced and well-defined strategy that can lead to exciting findings in basic biology on stromal compartment.

The team provides a unique expertise and exciting research direction to this unit. Based on the complementary research theme of this team, the integration with other groups in this unit is excellent. Moreover, this team established strong tools and recruited members on exploring this critical topic. The junior group leader is also considered as a rising star in her research field and got several invitations for prestigious symposiums (AACR, SITC) and invitations for lectures (3) and is involved in teaching ("International Course of Immunotherapy organized in collaboration with Icahn School of Medicine at Mount Sinai (USA), Institut Curie and Sorbonne Université (France) and University of Sao Paulo (Brazil)). Overall, this team shows everything we would like to see in a junior group which is going to become leader in the research field.

Weaknesses and risks linked to the context

There are two major concerns on this team. First, this team mainly relies on collaborations for clinical samples and other available tools. On the long run, this team should consider the core of their value and strength to approach fundamental tumor immunology questions. These should be better defined and position the team as a potential leader worldwide on addressing those questions they raised. Second, the spatial analyses and multiplex imaging need huge amount of support on bioinformatic analysis. It is not clear whether the team can sustain it in the current design.

Analysis of the team's trajectory

This team is developing in an excellent direction. The collaboration with other teams (Manel, Benaroch) in this unit is highly encouraging since these collaborations may result in exciting findings. Furthermore, how to reprogram CAF for launching stronger anti-tumor immunity can also be considered. In addition, the PI may consider the major research questions this team would like to address in the next five years. The tools and findings generated so far will be critical foundations for this team. We also anticipate the group leader should compete for international grant and collaboration grants in addition to industrial collaboration.

RECOMMENDATIONS TO THE TEAM

This team should continue on developing this direction they pursued in the past years. The outstanding research output and impact can be anticipated. However, sustaining the international visibility and becoming competitive for international grants should be prioritised by the PI in the next 5 years. Furthermore, this team can identify key questions they would like to address in addition to taking the advantage of samples they can obtain. Overall, we believe the PI can further establish her group as a leading team worldwide by taking the advantages on addressing these points we raised here.

The team is collaborating with clinical and industrial collaborators. Overall, the interactions may have some impacts. However, the impact on economy is too early to be determined, but it is highly encouraged.

The team leader provides teaching for students. She has trained two PhD students. During the development of this group, the principal investigator is highly encouraged to take more responsibility on training and guiding students.

The team is composed of a good number of trainees, especially considering the career stage. However, this should be further expanded to fulfil the demand on bioinformatic analysis and in vivo works.

Team 10: Extracellular vesicles, immune responses and cancer

Name of the supervisor: Ms Clotilde Théry

THEMES OF THE TEAM

The PI of the team is an international leader in the study of extracellular vesicles in the immune system with seminal contributions to the basic research in the area and a strong leadership role in developing the broader field of extracellular vesicles, which cuts across all areas of biology.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendation was to continue to lead the field of ECVs, to build on the recruitment of the new statutory researchers and new staff, to further initiate studies of the relevance of subsets in translational situations. The team has responded to the recommendations with new recruitment, but also there was turnover as a past CR has left to start their own group, and increased translational activity including filing a patent on a novel mechanism for EV mediated modification of the tumour microenvironment to improve outcomes. Therefore, the team has responded well to the previous recommendations.

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	2
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	2
Sous-total personnels non permanents en activité	**3**
Total personnels	**8**

EVALUATION

Overall assessment of the team

This is an excellent to outstanding team led by an international leader in the field of extracellular vesicles who has also had a strong leadership role in positively shaping the field as president of the international society and a champion of setting technical standards for the field. The work on the team has evolved from descriptive studies and technical development to uncovering novel mechanisms for action of extracellular vesicles. This work as also led to progress on translational efforts through basic understanding of extracellular vesicle biology in triple negative breast cancer.

Strengths and possibilities linked to the context

The PI of the team is a leader in the field of extracellular vesicles (EV) and has had a significant role in establishing a thriving field. One of the key contributions to the field has been to both innovate in the methods for isolation and characterization of EV, publishing primary papers from her lab, and has been involved in a series of guideline papers with the Journal of Extracellular Vesicles, which has continued during the review period. The team published nine original articles, including Nature Communications, and the Journal of Extracellular Vesicles, and nine review articles as leader, plus five original articles and nine reviews as co- author, between 2017 and 2022. A recent breakthrough is published in Proceedings of the National Academy of Sciences in 2022 and is also the subject of a patent application. Pro and anti-cancer activities of EV from different sources have been reported previously, but the mechanisms have been difficult to pin down. The team now shows that colony stimulating factor 1 on the surface of EV from a subset of triple negative breast cancer clinical isolates synergizes with cGAS/STING mediated innate sensing to guide differentiation of pro-inflammatory macrophages. Patients with this EV profile had better outcomes and, the team shows in a patent application that EV bearing CSF-1 induce anti-cancer effects in a pre-clinical mouse model. The team has also published on the potential of ACE2 positive EVs to neutralize SARS-Cov2 viruses. EV biology has also been a focus of collaboration in the larger team at IC over many years generating a number of highly cited and seminal papers. Members of the team established an EV core facility in the IC in 2020 and are establishing this with part time contributions with a proposal to have a full-time staff member to run it in 2024, which should be supported. The team has grown during the period from 2017 to what will be considered the ideal size going forward, with 12 team members including 2 director level scientists, 3 support staff, 1 post-doctoral researcher and 2 PhD students. The team has had three PhD students complete training between 2020-2022. The groups funding is strong with 3 INCA, 2ANR and 2 ARC grants as PI and co-PI and an international collaboration with another leader in the EV field at Johns Hopkins. The PI is leading on 1.46 M€ in funding during the evaluation period. The PI of the team has been extensively involved in international organization of meetings including major society meetings as president and chairing a Keystone meeting, which is the best specialised meeting with very strong central funding and organization. A clinical trial is mentioned, and an industry contract had been obtained (BMS - Bristol-Myers Squibb).

Weaknesses and risks linked to the context

It is hard to find weaknesses in the combination of strong basic science, translational activity and service to the research community. The main risk is the small size of the group and the discussion that a senior post-doctoral scientist may not be able to achieve a permanent position, which could result in loss of key expertise.

Analysis of the team's trajectory

The groups trajectory is outstanding. They are developing flow cytometry methods to in the core facility to support single EV profiling and are using other state of the art methods to track EV in vivo and follow their activities. They will continue to work on the biologically active components such as CSF1, improve ACE2 positive EV for SARS-Cov2, and to expand work on EV in cancer. The focus of the group remains on basic understanding with an eye to translate when possible.

RECOMMENDATIONS TO THE TEAM

The team is highly successful so these suggestions are made with this in mind. The authors have made progress on technologies to deconvolve information about EV heterogeneity from cell biology and bulk biochemical and genetic approaches. Flow cytometry offers a good method, but initial instruments focused on sub 100 nm particles have limited multiplexing. Spectral flow cytometers with modifications to detect sub 100 nm particles may offer the greatest potential to identify sub-populations as has become routine with cells. It is possible that some imaging approaches using nucleic acid probes, like MER-FISH and its commercial version, could offer multiplexing opportunities and such efforts might be considered in the core facility in partnership with single cell analysis facilities that may have this technology established for single cell analysis.

CONDUCT OF THE INTERVIEWS

Dates

Start: 02 octobre 2023 à 09h00

End: 03 octobre 2023 à 17h30

Interview conducted: online

INTERVIEW SCHEDULE

Agenda October 2nd

9:00-9:10 **Hcéres Rules and procedures by *B. Bartosch***
Public Session (all unit members)

9:10-10:00 ***Administrative and Scientific presentation of the Unit***
Including Question Answer Session
Public Session (all unit members)

10:00-10:20 **Debriefing committee and break** *(closed door meeting)*

10:20-11:00 ***Team "Spatio-temporal dynamics of immune cells"***
Mrs Lenon-Dumenil
Including Question Answer Session
Public Session (all unit members)

11:00-11:40 ***Team "Innate Immunity"***
Mr Nicolas Manel
Including Question Answer Session
Public Session (all unit members)

11:40-12:20 ***Team "Integrative analysis of T cell activation"***
Mrs Claire Hivroz
Including Question Answer Session
Public Session (all unit members)

12:20-12:40 **Debriefing committee and break** *(closed door meeting)*

12:40-13:40 **Lunch Break**

13:40-14:20 ***Team "Stem cell immunity"***
Mr Enzo Poirier
Including Question Answer Session
Public Session (all unit members)

14:20-15:00 ***Team "Extracellular vesicles, immune responses and cancer"*** **Mrs Clotilde Thery**
Including Question Answer Session
Public Session (all unit members)

15:00-15:40 ***Team "Stroma & Immunity"*** **Mrs Hélène Salmon**
Including Question Answer Session
Public Session (all unit members)

15:40-16:00 **Debriefing committee and break** *(closed door meeting)*

16:00-16:40 ***Team "Immune responses to cancer"*** **Mr Sebastien Amigorena**

Including Question Answer Session
Public Session (all unit members)

16:40-17:20 ***Team "Translational immunotherpay"*** **Mrs Eliane Piaggio**

Including Question Answer Session
Public Session (all unit members)

17:20-18:00 ***Team "Myeloid cells and immunity"*** **Mr Philippe Benaroch**

Including Question Answer Session
Public Session (all unit members)

Agenda October 3rd

9:30-10:10 ***Team "Innate like and CD4+ T cells in cancer"*** **Mr Olivier Lantz**

Including Question Answer Session
Public Session (all unit members)

10:10-10:30 **Debriefing committee and break** *(closed door meeting)*

10:30-11:10 **Meeting with ITAs (in French)**
In the absence of any managing staff

11:10-11:50 **Meeting with researchers**
In the absence of any managing staff

11:50-12:30 **Meeting with post-docs and students**
In the absence of any managing staff

12:30-12:45 **Debriefing committee** *(closed door meeting)*

12:45-13:45 **Lunch Break**

13:45-14:30 **Meeting with institution representatives** *(closed door meeting)*

14:30-15:00 **Meeting with the Management Team of the Unit** *(closed door meeting)*

15:00-18:00 **Redaction of the final report** *(closed door meeting)*

18:00 **End of the visit**

GENERAL OBSERVATIONS OF THE SUPERVISORS

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Objet

Comments to HCERES Evaluation report of the Unit
Immunité et Cancer
DER-PUR250024481 - EV 0753172R
Evaluation campaign 2023-2024 / Group D

HCERES
For the attention of HCERES President,
Mr Stéphane Le Bouler
and the HCERES Expert Committee

Paris, 22nd December 2023

Dear All,

We would like to thank the HCERES for the evaluation of the U932, comprising the reading of the HCERES manuscript and the auditions that took place in October 2023.

We deeply appreciate the interactions we had during the audition, the evaluation, the feedback on the past and future trajectory of the Unit, and the concerns that were raised as they will lead to improvement.

However, we would like to take this opportunity to clarify and/or rectify some points of the present evaluation report, that you will find in the dedicated document that is attached.

In addition, our feeling is that these mistakes or misunderstanding could have been easily avoided if the Committee could have visited us physically rather than virtually.

Yours sincerely,

Pr Alain PUISIEUX
Directeur du Centre de Recherche de l'Institut Curie

Dr Ana-Maria LENNON
Directrice de l'Unité U932

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