Research evaluation

EVALUATION REPORT OF THE UNIT

Institut Cochin

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université Paris Cité

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

Centre national de la recherche scientifique - CNRS

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 :

Stefano Casola, 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.

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CHARACTERISATION OF THE UNIT

- Name: Institut Cochin
- Acronym: /
- Label and number: INSERM U1016, CNRS UMR8104
- Composition of the executive team: Ms Florence Niedergang (director since January 1st, 2022), Ms Sophie Vaulont (deputy director) & Mr Yannick Allanore (deputy director).

SCIENTIFIC PANELS OF THE UNIT

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

THEMES OF THE UNIT

The Institute Cochin (IC) is a pluri-thematic unit which has hosted in 2022 around 640 members dedicated to research, teaching and clinical activities. In the past term (2017-2022), IC has witnessed a progressive evolution of the unit structure. Between 2017 and 2021, research teams were compartmentalized into three major departments, each represented by one Director and two co-directors. In 2018, technological platforms converged to form a fourth department. Since January 2022, the appointment of a new Scientific Director was accompanied by restructuring of the research axes to better integrate intramural activities and improve cross-fertilization of knowledge between laboratories. Currently, IC is structured into 5 scientific axes and one technological axis. Each IC team can be affiliated to one or more axes, each of which is represented by one director and one deputy director. The latter meet with those of other axes once a month to discuss common research strategies. Topics covered by the 5 research axes include: 1) Cancer (16 teams affiliated of which 5 as primary axis), 2) Immunology (16 affiliated teams with 8 as primary axis), 3) Microbiology (16 teams affiliated with 12 as primary axis), 4) Metabolism and Endocrinology (12 affiliated teams of which 9 as primary axis), and 5) Cellular Plasticity and Reproduction (19 teams affiliated of which 7 as primary axis).

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

Institute Cochin benefits from the joint supervision of Inserm, CNRS and Université Paris Cité. The Institute is located within a campus hosting the Cochin-Port Royal Hospital. Funded in 2002 through the merging of twelve independent laboratories affiliated to Inserm and CNRS, IC was directed between 2002 and 2008 by A. Kahn, from 2008 to 2021 by PO Couraud and since January 2022 by Florence Niedergang. IC research activities are distributed within 4 buildings (Faculty, Cassini, Gustave-Roussy and Méchain) based in the Cochin-Port Royal hospital campus. A technological facility was hosted until 2021 in a fifth building in the Campus until it had to be relocated to the Faculty building.

RESEARCH ENVIRONMENT OF THE UNIT

IC activities are supervised by Inserm and CNRS. It takes advantage of programs from the CNRS national strategic plan and is affiliated to 'Université Paris Cité through which it benefits from Idex funds. Based within the campus hosting the Hospital Cochin (HC), it has built over the years a strong connection with multidisciplinary clinical departments based in HC as well as other hospitals belonging to the Groupment Hopitalo-Universitaire Paris Centre. IC teams include a group of nine headed by academic physicians, whose activities are well integrated within the GHU Paris Centre strategic plan for the coming years. IC has participated from 2011 to several Laboratories of Excellence initiatives. Until 2020, 18 teams were involved in six Labex initiatives, of which one (Who am I? Exploring Identity from molecules to individuals) has grouped all teams of the Institute since its renewal in 2020. IC teams have also participated to the "Institut Hors Murs" initiative, creating two networks (MICROB'UP and Institute of Immunology and Immunopathology) and participating to others (Institut du Diabète, Institut des Maladies Ostéoarticulaires and Institute de la Santé des femmes). Finally, IC technological facilities are integrated within the local network of facilities of Université Paris Cité and belong to five national and international infrastructure consortia, including France Bioimaging/Euroimaging (IMAG'IC facility), France Live Imaging (PIV Facility), or ProFI (PROTEOM'IC facility).

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

Catégories de personnel	Effectifs
Professeurs et assimilés	51
Maîtres de conférences et assimilés	33
Directeurs de recherche et assimilés	59
Chargés de recherche et assimilés	60
Personnels d'appui à la recherche	195
Sous-total personnels permanents en activité	**398**
Enseignants-chercheurs et chercheurs non permanents et assimilés	64
Personnels d'appui non permanents	41
Post-doctorants	12
Doctorants	132
Sous-total personnels non permanents en activité	**249**
Total personnels	**647**

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
INSERM	0	63	88
UNIVERSITÉ PARIS CITÉ	80	1	44
CNRS	0	54	32
Autres	3	1	30
Total personnels	**83**	**119**	**194**

GLOBAL ASSESSMENT

The global performance of the Institut Cochin Unit is excellent to outstanding.

In the past mandate, Institut Cochin has set itself ambitious scientific objectives, most of which were successfully achieved. Experimental activities using both pre-clinical models and human biological specimen have focused around five major research axes, leading to major discoveries in the fields of immunology, infectious diseases, cancer, development & cell plasticity, reproductive biology and endocrinology. Unit functioning has been excellent to outstanding, benefiting in particular from the recent change of the scientific direction, which has reinvigorated the daily management of the Institute through the implementation of several working committees. The latter operate at multiple levels to implement the scientific vision of the institute, attract high-level scientists, stimulate cooperation between laboratories, attract and collaborate with clinical colleagues, offer high-level undergraduate, graduate and post-graduate training, as well as supporting the functioning of core technological platforms. Attention is given to research integrity, gender balance, quality of life, and fair representation of the different types of scientific personnel in the governing bodies of the institute.

Unit activities have been conducted at the best of their capacity, considering ongoing contraction of technical/engineer staff personnel due to retirement, and infrastructural limitations. The Units' resources have been excellent, with participation to several PIA programs, including labex, idex, equipex, i-site, and IBiSA infrastructure programs. The Unit coordinates two Institutes Hors Murs (MICROB'UP and Institute of Immunology and Immunopathology) and is member of three other ones (Institut du Diabète, Institut des maladies OstéoArticulaires and Institut de la Santé des Femmes). Unit funding via competitive calls is excellent to outstanding, having secured a conspicuous number of generous grants from regional (i.e., Ile-de France), national (i.e., Cancéropole, ANR), and international (i.e., European Union) funding agencies. Unit attractiveness has been excellent-to-outstanding, culminating in the past mandate in the hiring of 5 new team leaders, who have started to confirm their strength publishing in high-ranking journals (i.e., Cell, Nature, Science) and securing

generous grants from highly competitive national and international funding bodies, including four (three starting and one consolidator) European Research Council grants, and one ATIP avenir award. The hiring of new team leaders was achieved through open international calls, satisfying criteria of transparency, gender balance and excellence for the selection of candidates. Unit international visibility has improved through initiatives including organization of international conferences (i.e., 2019 EMBO meeting, Institut Cochin Miltenyi and JC Dreyfus annual symposia), participation to international collaborative networks, redesign of the Institute website in English and establishment of a joint research laboratory with the Indiana Biosciences Research Institute. The scientific production of the Unit is excellent to outstanding, with over 1 800 articles published in the past mandate. In response to previous recommendations, teams have improved quality of the research output, reaching publication of original manuscripts in generalist journals (i.e., Nature, Cell, Science), while securing a steady publication of original articles in top-ranking specialist journals (Nature Immunol., Nature Cell Biol., Journal of Experimental Medicine, EMBO Journal, etc.). The contribution of the Unit to society is excellent, as witnessed by strengthening of the relationship with clinical Departments of Hospital Cochin and beyond, active participation to educational programs for high-school students, and attention to science communication to the lay public using social media. Very good technology transfer activities have led to the creation in the past mandate of two spin-off companies (Frema and Skin-dermic). Yet the Units' potential to transfer knowledge in the industrial sector and to establish industrial partnerships appears under-exploited, given the strong potential for clinical cooperation, several ongoing translational research projects, local presence of the incubator Paris Biotech Santé and several intra-mural initiatives promoted by the technology transfer office including the proof-of-concept program.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Comments

C1. Article: none as principal authors in the highest impact generalist journals of basic science (Science, Nature, Cell).
In the past mandate IC has heightened its quality level of publications, contributing research articles to both generalist journals (Nature, Cell and Science), as well as top-ranking specialty journals.
C2. The number of international PhD students, postdocs or group leaders remains limited, and no advanced or consolidation ERC grants.
IC has given strong emphasis in the past mandate to hire new team leaders, who have already secured competitive fundings from national (ATIP Avenir) and international (ERC Starting and Consolidator grant) funding agencies. Representation of foreign students and postdoctoral fellow has improved.

C3. The support provided by the Proof of Concept (POC) program is relatively limited in term of numbers of grants awarded (2 per year) and of the amount of support (15 k€/grant).
IC continues with the same POC intramural funding scheme. Additional projects positively evaluated by the POC committee succeeded to secure funding through Erganeo, Inserm-Transfer, the Prematuration Programmes of CNRS, Université' Paris Cite', or Elsevier.

C4 and C5. There is room to even further develop technological transfer, given the amount of work performed in the Institute and its privileged access to primary patient samples. The funding coming from industry (0.5M€) and the number of Cifre PhD grants obtained (6) appear low.
Technology transfer office currently coordinated by former IC Director has implemented initiatives to attract the pharma/biotech world and improve industrial valorization of the research. The POC Program, the annual technology transfer meeting, the creation of two spin-off companies (Frema and SkinDermic) as well as the creation of industrial partnerships enabling sharing of core technology facilities, represent the efforts to improve IC valorization of its science.

C6. The Institut Cochin does not seem to have a policy at the level of the Institute to track the career development of former trainees (PhD students, postdocs).
An IC alumni organization was established.

Recommendations

R1 The uptake of new talented team leaders has been limited for the 3I department and might need to be addressed in the next international recruitment calls. IC has been active over the past mandate in repeated international calls to hire team leaders.

R2. The committee advises to promote the recruitment of even more foreign students and postdocs (exchange program with foreign universities) and organise courses and summer schools (EMBO courses...), in order to increase the international visibility of the Institute.

R3. The engagement in international training activities is limited.
An EMBO meeting was organized in 2019 at IC. IC team leaders have been engaged in educational courses at the international level including EMBO workshops (ImmunoBiophysics) EMBO-Global Exchange Lecture Course in Madurai, India, the training course on Elimination of Malaria and Artemisinin Resistance for ASEAN+ Countries, WHO, China. A joint international laboratory was established with the Indiana Biosciences Research Institute by IC team leaders.

R4. Unit organization: i) internal grant committee to review and advise on grant applications; ii) paying a specific attention to non team' leaders; iii) mentor young promising PIs (with the help of the SAB).
It is noteworthy that a career management and support ("Comité de Suivi de Carrière et d'Accompagnement") committee was established at IC in 2022 to provide mentorship and counselling to junior team leaders, postdoctoral fellows and engineers.

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 Institut Cochin are outstanding.

Assessment on the unit's resources

The unit's resources are excellent to outstanding based on external resources and PIA support (idex, i-site, labex, equipex, etc.), with outstanding IbiSa platforms.

Assessment on the functioning of the unit

The functioning of the unit is excellent to outstanding with regular meetings at multiple level, attention to the career of unit members and implementation of new management rules.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The objectives of the departments of Institut Cochin are clear and well defined, and ensure a continuum of research from bench to bedside and vice versa. The teams have complementary expertise and assets to perform high impact biomedical research. The scientific objectives of Institut Cochin were defined within three departments, including the development, reproduction and cancer department, the endocrinology, metabolism and diabetes (EMD) department, and infection, immunology and inflammation department. The research teams of the first department are involved in the regulation of gene networks and its disruption in pathology, the biology of stem cells and cell proliferation and differentiation. The EMD department proposes a continuum of research aiming at better understanding mechanisms of chronic diseases such as diabetes and obesity, endocrine tumorigenesis, and developing novel therapeutic approaches. The research teams of the third department investigate the cellular and molecular mechanisms of host-pathogens interactions. To meet its objectives and to reinforce the topics of its departments, Institut Cochin launches regularly international calls, which allowed to attract two researchers in 2018 who were recruited by Inserm and received ERC and ATIP-AVENIR grants. In 2020, another call led to the recruitment of two researchers, one of whom received an ERC grant in 2023. Finally, the 2021 call allowed the joining of another researcher. These calls had beneficial effects in all 3 departments. The integration of the teams within the hospital warrants an adequate environment for a clinical and technological transfer of the basic and translational research findings obtained by the different teams. Good dynamics has followed the recruitment of new scientists and group leaders with new ideas and projects. These additional staff seem to integrate efficiently in the existing research framework as attested by the success in obtaining European and national grants. In addition, the teams of Institut Cochin have a high rate of success in recruiting researchers, as 18 young investigators got permanent positions during the last term in competitive calls of Inserm, CNRS and University. Thus, the scientific objectives of the previous term were largely achieved.

Weaknesses and risks linked to the context

New axes were organized recently to accommodate the scientific affinities of the teams and to foster synergy. However, this orientation was not accompanied by a clear definition of the scientific objectives of the new axes. The titles of the axes cover a rather broad spectrum of topics (Cancer, Immunology, Microbiology, etc.) and do vaguely reflect strategic scientific objectives linking different teams within each axis, either primary or secondary. The Institute governing bodies should place more efforts to identify topics with high scientific potential and stimulate adequate taskforces to ensure more top-level publications.

Two major concerns regard the human resources of the institute. The first one is the unfavorable aging tendency of staff members with a high number of retirements planned for the next years to be partially compensated by new recruitments which remain unpredictable. The second one is related to the number of engineers/technicians whose affectation depends on the supervision bodies. Not much advantage is taken of the close proximity of the hospitals.

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

A recurrent budget of Institut Cochin comes from its supervising institutions, *i.e*. Inserm, CNRS and Université Paris Cité. Each year, the Institute receives around 2.4 M€ from these institutions. In addition to this amount, the institute raises more than 12 M€ each year from external sources. This represents more than 600 projects supported by grants from national agencies (225), charities and foundations (214), PIA (66; idex, i-site, labex, equipex, etc.), international grants (39, non-European), European grants (31), and grants from non-academic partners (59). The core budget is used as follows: 1 M€ is redistributed among the teams based on the number of staff and the rest is used for common expenses of the Institute including maintenance, lab renovation and scientific animation. A small part of the budget is dedicated to support internal collaborative projects between teams of different departments as well as technology transfer. It should be noted that the personnel of the technical facilities in collaboration with scientists of the institute raised about 4.7 M€ to acquire new equipment. The funds received by the institute either from the supervision bodies or from various external sources are adequate for the number of teams within the institute and the high-level biomedical research performed to reach the objectives of the different research axes. The external resources are multiple and various, including national, European and non-European fundings. In addition to functioning, the income from external sources allowed to recruit more than 140 non-permanent staff excluding PhD students. The Institute benefits from PIA (government investments for the future) funds which is a non-negligible complement for some universities and centers.

Weaknesses and risks linked to the context

The funds received by the institute from its supervising institutions are largely dedicated to cover the common expenses and therefore cannot allow a significant support for the functioning of teams. It is surprising that there is no contribution from the contracts to the general expenses, which would leave some more funds to redistribute on the recurrent institutional budget. The part of the core budget dedicated to internal collaborative projects and to valorization is limited. Most of the fundings of the teams come from national agencies and charities (64%) and less from European (8%), international (3%) and non-academic partners (10%). The low rate of the latter resources and the absence of ERC senior grants limit somewhat the international recognition of the Institute.

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

Institut Cochin research personnel currently includes 111 full-time, permanent research scientists, 77 professors/assistant-professors and 143 permanent engineers/technicians. In addition, the institute has hosted 54 non-permanent engineers/technicians, 60 postdocs, 108 PhD students and about 117 interns. The women to men ratio is satisfactory in most categories of personnel. The institute was successful in hiring 18 new permanent staff members at the level of researchers (16, mainly at Inserm) and assistant professors (2). This effort has been, and will continue to be vital for the Institute given the high number of retirements registered during the last contract (17), and the additional ones planned in the next mandate. An internal human resource office ensures paperwork preparation and interaction with local and national institutions to implement recruitments, and complies with the Human Resource Excellence in Research label for good practices. For engineers and technicians, a follow-up committee centralizes the procedures for applications to get promotions.

Untill 2022, the institute was governed by a Scientific director supported by a Deputy Director. They were assisted by an executive board including a head of core facilities, a head of clinical affairs and a head of international affairs, in addition to a general secretary. The board of directors was made of elected directors of the departments and their deputy directors. This board met every month to discuss scientific policies, financial issues,

and the organization of the Unit. A laboratory council was composed of the board of directors and representative staff members. This council used to meet 2 to 3 times a year.

In January 2022, a new Scientific Director was appointed. The activity of the Director is supported by two Deputy Directors respectively for Scientific affairs and Medical affairs. Currently, the board of directors includes the heads and deputies of the 6 axes who meet every month to discuss scientific and organizational matters. A laboratory council was also constituted, in continuity with the past directorship. A general assembly is organized each year to report on activities of the institute. *Ad-hoc* meetings to discuss internal organization of laboratories located in the different buildings of the institute, and meetings with the hospital officers are regularly organized.

Institut Cochin's scientific activity is supervised by an international Scientific Advisory Board (SAB) consisting of 15 members with expertise in the fields of studies of the Unit. The SAB provides advice on topics investigated in the Institute, team performance and team leader selection.

The governing body of the Institut Cochin is well structured with an executive board, a board of directors and a laboratory council which meet monthly or several times a year. Particular attention is given by the Scientific Direction to the management of human resources and to the respect of rules and regulations implemented through the action of several committees and services, which support the administration's daily work. The current and previous director are supported by 4 committees to inform, advise, and support researchers and engineers/technicians during their daily activities and career. The Health and Security office is run by 2 full-time officers. Two further committees are active to implement an environmentally friendly laboratory life, and for PhD/postdoc life animation. The latter accompanies new trainees and organizes each year a highly attended scientific symposium.

A general secretary manages the administrative services of the institute, which is composed of 10 services, including a financial department, a human resource office, a risk prevention service and technology transfer unit among others. Several working groups are active in the institute such a board of Technicians which addresses issues related to the living of engineers/technicians, and a PhD student committee which supervises PhD affairs. Young scientists of the institute are organized into an association named jeCCo which participates to the scientific and social animation. The young scientists organize a two-day symposium each year with about 100 attendees and 15-18 invited speakers.

The potential risks at work are addressed by a quality of life at work committee (QVT group) which proposes actions to raise awareness in this field. Another 2 committees created by the new direction are dedicated to the follow up and management of researchers and engineer/technician careers. These committees are set as a complement to the hierarchical path for accompanying and informing these categories of personnel.

The prevention at Institut Cochin is managed by 2 full-time officers. Together with the director and the general secretary, they define the objectives to comply with regulations and their application. These officers coordinate a local network of prevention, set working procedures in at-risk laboratories, and establish each year a risk assessment document transmitted to the supervising bodies.

Institut Cochin has also a committee to raise awareness about sustainable development and to propose actions to decrease the impact of laboratory activities on the environment. Among the actions, IC has already implemented recycling procedures, reduction of electrical consumption or purchase of recycled paper, etc. Finally, a Business Continuity Plan for work management in the institute during the COVID-12 pandemic is provided as an annex.

Weaknesses and risks linked to the context

The low number of technical personnel (retirement age pyramid) endangers the functioning of the Unit.

The building infrastructure is a big concern for the staff and the needs for renovation are obvious and urgent.

Some researchers feel some lack or not sufficient transparency for the intra-mural assignment of ITA.

There is an accumulation of administrative tasks for researchers.

There is disparity in the promotion potential depending on the employer (University, Inserm or CNRS).

There is need for support of foreign personnel.

A directory of Alumni could be helpful for networking and information of future trainees.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractivity is excellent to outstanding by succeeding in developing strong connections between fundamental and medical research. Institut Cochin has implemented 9 state-of-the-art high technological platforms run by high-profile engineers, and disposes of a large, which contribute to enhance its attractiveness. IC recruited during this period a high number of PhD, postdoctoral fellows and engineers. IC is highly visible thanks to the success in securing highly prestigious grants including European Research Council grants, participation to national and international research and funding committees.

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

Strengths and possibilities linked to the context

IC staff members are dynamic in organizing internal, national and international meetings, as well as weekly internal and external seminars. Departmental seminars have been also regularly organized during the past mandate. IC has organized two yearly international IC symposia until 2022, and a large scientific event to celebrate the 20 years of the Unit. A communication office is active to inform on the activity of the teams as well as to maintain the web site for internal and external users. All these actions contribute to improve the visibility of the IC as well as to ensure constant intramural information.

The attractiveness of the institute is also contributed by the recognition of its staff members. Several are members of national committees (CSS Inserm, CoNRS, ANRS, InCA) and charities (including FRM, ARC, LNCC). Several prizes were awarded as well as 3 ERC grants. IC members have also important positions within funding bodies of scientific or evaluation committees (including Pasteur COMESP, Scientific committee of Inserm, VP research Paris-Descartes, Head of ITMOs, Scientific Director of INSB).

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

Strengths and possibilities linked to the context

The institute is organized around 5 scientific axes (Cancer, Immunology, Metabolism and Endocrinology, Microbiology, Cellular Plasticity and Reproduction). An important strength of the institute are the interactions between fundamental and medical research. This allows to promote translational research with high clinical impact. The website of IC, including an English version, clearly illustrates the intramural structure and allows to position each team in the Institute organization. The quality of the publications reported each year by IC confer a high visibility and attractiveness is illustrated by a high number of PhD students and postdoctoral researchers recruited during the last term (292 PhD students and 258 postdoctoral researchers). IC also hosts a solid number of engineers and technicians on contracts (238). Several visiting scientists have visited IC during the last mandate. These figures illustrate a dynamic and attractive institute for investigators active in the Institute's fields of interest.

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

The mean amount of external resources collected every year is 10,3 M€ (salaries included). In 2022 for example, the total budget was 11,6 M€, from which the institutional participation is of 2.5 M€, representing 21,5 %.

Over the 2017-2022 term, the contracts correspond to 648 funded or on-going projects, representing a mean of 130 projects/year. ANR grants represents between 15 and 20 % of the teams funding, corresponding over the period to 97 contracts, among which 48 were coordinated by the unit. Fundings from foundations and charities (ARC, FRM, Sidaction, Ligue contre le cancer) represent between 20 and 27% of the team budgets. Members of the unit have been also successful in International and European calls, 39 and 31 contracts were obtained, respectively. Of note, four ERC contracts were received and coordinated by the recipient team leaders.
The percentages of grants based on "grand emprunt" is around 10%, based on international organisms between 3 and 5% and those obtained within industrial partnership of 8%. Translation research is also well funded through RHU (Recherche Hospitalo-Universitaire) and FHU (Fédérations Hospitalo-Universitaires) bodies.

Part of these grants are used for hiring staff, core funding and, to a lesser extent, to buy equipment.

The salaries of the 292 PhD students trained originate from government agencies (168), international funding or foreign universities (18), charities (47), European union (7). In total during the last term, Institut Cochin hosted 258 postdoctoral researchers. Their salaries are from various sources: government agencies (103), international funding or foreign universities (16), charities (55), European union (17), Hospital (APHP, 31), PIA programs (21) and industrial partnerships (15). Few of them were recipient of prestigious international fellowships such as the Marie Sklodowska-Curie actions. The short-term contracts of engineers and technicians are also financed by external resources.

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

Strengths and possibilities linked to the context

A 6th axis includes the technological facilities and services. IC has implemented 9 core facilities plus an animal facility. All facilities are equipped with cutting-edge instruments thanks to the securing of substantial funding (4.7 M€ over 2017-2022 period). Five facilities are formally recognized by IBISA and 3 belong to national infrastructure. All have high standards in the management process recognized by the ISO9001 and NFX50-900 labels. The platforms are headed by high-profile engineers and scientific advisors. The IC facilities constitute an important attractiveness of the institute to attract new teams and to enhance national visibility.

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

No major weaknesses are reported. Teams are recommended to improve frequency of retreats to further nurture scientific exchanges between the various research groups and technological support units. Four core facilities are recommended to acquire the IBiSa label as they have already gained the quality label. The IC's facility should implement actions to empower partnerships with industry and increase the proportion of services performed for the private sector.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of the unit is excellent with over 1800 original publications produced in the past mandate by the 38 teams. Publications in generalist journals have been achieved while securing a steady strong publication record in top-ranking specialist journals. The IC continues to produce a robust number of clinical articles.

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

Strengths and possibilities linked to the context

The scientific production with more than 1800 original publications is excellent. Selected publications are in generalist journals such as Nature, Cell and Science. At the same time IC has maintained a strong publication record in top-ranking specialist journals including EMBO Journal, EMBO Reports, Cell Reports, The Journal of Experimental Medicine. A good proportion of articles were signed by IC team members, as first or/and last authors. Publications are recurrently the result of internal and external national and international collaborations, (18% USA, 12% UK; and 11% Germany). The citation rate of the articles with an average of 18.8 is excellent.

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

All PhD students have at least one publication, with average more than 2 articles per student. All publications are in HAL to comply with IC effort to support open access publication. The responsibility for authorships is at the level of the teams, but the rules on authorships are discussed at a "conseil de laboratoire".

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

A special attention is given to recording research data, which will be strengthened by the end of 2023 with the use of the electronic laboratory notebook. IC has a Data Management Plan (DMP).

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

No major weaknesses are reported. For a few teams, too many review articles are published in respect to the original research publications. Although this gives visibility, these teams should increase the number of original articles.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The contribution of the unit to society is excellent through close interaction with Hospital Cochin, very good technology transfer activities, and excellent interactions with the general public.

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

The Cochin Institut interacts actively with the Hospital Cochin with 71 medical doctors that have an academic position. Nine teams are headed by medical doctors. It participates to the "Groupement Hospitalo-Universtaire Paris Centre) that includes 16 multidisciplinary departments. Seven of these departments have members within IC. Three members are department directors. Six of the 16 department deputies that participate at the GHU research committee are from IC. A dedicated grant system (PIC-H) aims at developing projects with hospital members. Six teams of IC and the genomics, proteomics, life imaging and cytometry facilities are involved in the "Integrated Research Center in Oncology" (CARPEM). Since 2022, IC organizes meetings to foster interactions between physicians and scientists.

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

Strengths and possibilities linked to the context

Interactions with industrial partners are very good securing approximately 4M Euros during the past mandate. Five PhD students are on Cifre grants. Interactions with political representatives were organized twice. Attention to valorization of science is acknowledged with the establishment of a technology transfer (TT) office that organizes 2 annual events. The "Proof Of Concept" program awards 2 internal grants per year to researchers that have promising TT projects. Some of the supported projects have been further supported by Inserm-Transfertt, CNRS Prematuration program and Université Paris-Cité. IC team members can also apply to the Elsevier Innovation Award. On average, 6-8 patent applications per year result from TT activities. An annual TT meeting is organized together with the Incubator Paris Biotech Santé. Two start-ups were created during the past mandate (Frema and SkinDermic).

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

Strengths and possibilities linked to the context

IC participates at the "Fête de la Science" and organizes open day visits for the general public. In 2022, IC collaborated with "Akenium" a scientific illustration office to present the activities of the teams and core facilities. Meetings with different patient associations have been organized 8 times during the past mandate. High-School students are hosted for short-term research projects that are presented at the meeting "Apprentis Chercheurs" at the end of their stage. Members of IC have gained visibility to the lay public via participation to broadcasting events and articles published in newspapers.

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

No major weaknesses are reported. The number of Cifre PhD students should be increased.

ANALYSIS OF THE UNIT'S TRAJECTORY

For the next mandate, IC will be structured similarly to the present evaluation period with services, core facilities and research teams. Research teams will diminish from 41 to 32 teams, due to departure, fusion, and fission of teams. Fifteen teams will remain, with team leaders who may change because of fusion, fission or substitution with a new leader. IC research activities will continue to focus on functional assessment of cancer immunity, mechanisms of immunity and autoimmunity, cell plasticity, epigenetics, endocrine tumor development and host-pathogen interactions. IC will potentiate in the next mandate research programs centered on normal and pathological reproductive biology, given the close interaction with Port-Royal-Maternity and the advanced expertise of teams in the unit. IC will continue to encourage and further potentiate collaborative projects through intramural funding and organizing common retreats, to optimize common human and technological resources. Several activities will be devoted to foster "open science" activities, train good laboratory practices, reinforce equal opportunity and gender balance policies, mentor students and postdocs in preparation for job opportunities and competitive presentations, sustain ecological transition. The institute will continue to seek stronger international visibility supporting activities such as the consolidation of joined research laboratories with other institutions worldwide. Some of the buildings where research is carried out need renovation or reconstruction, which will cause rotation of research teams. The institute has allocated a special budget to support renovation expenses. A major concern of IC comes from the substantial number of engineers/ and technicians who will be retiring in the next mandate. Internal mobility and short-term contracts will attempt to limit the problems, but a major re-organization of the Units' engineer/technician staff is foreseen if replacements will not be granted.

RECOMMENDATIONS TO THE UNIT

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

The scientific objectives of the new axes should be defined more precisely, considering the primary and secondary affiliation of the teams to each axis.

The ITA staff members retirement in the next mandate due to the unfavorable aging pyramide in the institute is an issue and replacement should be considered with great attention.

Hiring of talented young team leaders should continue to sustain and enforce the national and international stature of the Institute.

Teams should profit more from the proximity with hospital departments to establish strong long-term translational programs.

The institute should consider the use of overheads from research grants to support high-risk projects and to further nurture scientific programs with strong potential for industrial valorization.

Application to European funding schemes should be fostered, as most of the contracts are awarded from national funding agencies and charities. Similarly, the number of contracts with non-academic partners should be increased.

A stronger participation of the personnel to the decisions regarding staff assignment to the Institute's teams is recommended.

IC could play an active, coordinating role in getting together the different governing bodies to ensure a faster implementation of decisions vital for the future of the Unit including ITA replacement and building renovation plans.

Recommendations regarding the Evaluation Area 2: Attractiveness

The Unit should continue to strengthen its already good connection between fundamental and medical research that makes IC a rather unique unit at the national level. IC should pursue its efforts to further strengthen its cutting-edge platforms, placing a particular attention to develop a strong bioinformatics core. The institute should continue its plan to attract highly-talented young team leaders. The Institute may reinforce the visibility of some of its platforms by applying for IBISA labels.

Recommendations regarding Evaluation Area 3: Scientific Production

The unit should keep maintaining the excellent level of publication, in particular in terms of its quality. A large proportion of the publications remains indeed in the clinical area. A better equilibrium between original research papers and review articles, favoring the formers is recommended.

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

IC should maintain its excellent contribution to society taking advantage of the close interaction with Hospital Cochin and the excellent interactions with the public. IC is expected to reinforce its technology transfer activities to better valorize the high number of yearly patents issued by the teams, foster the creation of new start-ups and reinforce thew interaction with the local incubators to establish long-term partnerships with the pharma industry.

TEAM-BY-TEAM ASSESSMENT

Team 1: Pathogenesis and innovative therapies in fibro-inflammatory disorders

Name of the supervisors: Mr Yannick Allanore & Mr Frédéric Batteux

THEMES OF THE TEAM

This team works on the fibro-inflammatory disorders including systemic sclerosis, rheumatoid arthritis and endometriosis. The team studies genetic susceptibility, polarization of innate and adaptative immune responses, the role of reactive oxygen species, microbiota and epigenetic marks in the fibroblast dysfunctions and chronic inflammation. They exploit primary samples from a databank as well as a preclinical models platform in order to investigate, in an in vivo context, the relevance of some identified biomarkers or potential treatments.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The last review recommended that the team would consider to stay focused on projects that offer the opportunity to publish in generalist/basic immunology journals whilst keeping their lead in translational medicine. There is very good evidence that this recommendation has been implemented since 55 manuscripts have been published over the period related to fundamental research.

According to the previous recommendations, the interactions with the non-academic world has also been reinforced.

The team followed the suggestion of the committee to recruit a full-time junior scientist.

In term of strategy, the committee recommended also to secure major international funding and more important funding with pharmaceutical companies. The recommendation was implemented with an ERC starting grant secured in 2022 as well as many contracts with industrials (see below).

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

Catégories de personnel	Effectifs
Professeurs et assimilés	8
Maîtres de conférences et assimilés	5
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	**19**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**6**
Total personnels	**25**

EVALUATION

Overall assessment of the team

The overall assessment of the team is excellent to outstanding.

The scientific outputs, reputation and appeal are excellent.

The synergy with the hospital and the participation in clinical trials is outstanding.

The contribution of research activities to society is excellent including partnership with patient associations, private companies and communication dedicated to the general population.

Strengths and possibilities linked to the context

The scientific reputation and attractiveness of the team, as reported in the self-assessment document, relies mainly on its commitment in national and European associations and networks promoting research on diseases studied by the team. The research of the team in Rheumatoid arthritis is recognized through its labelling at the European Alliance of Associations for Rheumatology network, its participation to the scientific committee of the French Society of Rheumatology as well as to a national multicenter registry collecting data for patients treated with JAK inhibitors. The active representation of the team to the Society of Endometriosis and Uterine Disorders acknowledges the endometriosis research led by the team and offers a panel of trainings and meetings to which the members of the team might attend. Of note, the team leader headed the scientific program of the last World Scleroderma Congress in Prague in 2022. The innovative research in Systemic sclerosis using CAR T cells in a mouse model has been rewarded by a prize from Elsevier. The team actively participated to National and European networks of referral centers: chairman position of the European Systemic sclerosis research network, engagement in the board of the World Scleroderma Foundation.

The team has continued to be active in training students, 9 PhD students have been hosted during the period and all of them have published at least three articles during their science thesis. Undergraduate students have been involved in laboratory research, among them 29 Master 2 students. The team members are largely engaged in teaching activities since 13 members are teachers (Pr and MCU) for a total of 14 researchers. Among the 9 PhD students trained in the team, 3 have got a permanent position in university hospitals, one occupies a postdoctoral position in Harvard medical school, the others are working in regional healthcare organizations. The training investment of the team is excellent, demonstrating the mentoring capacity and dedication of the PIs and other permanent university members of the team.

Recognition gained by the team through success in competitive calls for projects is significative. The team participated to 2 ANR grants as partners for a total amount of 110 k€ and coordinates a 22 k€ contract financed in the PIA context (Emergence Idex Université de Paris). Funds from charities and foundations have been gained: 3 grants from the French Society of Rheumatology are coordinated (total 60 k€) as well as one grant from the Fondation pour la Recherche sur l'Endométriose (10 k€). A major achievement is the ERC starting grant reached in 2022 by a young women MCU recruited in 2017 for a project related to endometriosis.

The scientific publication activity of the team has continued to be very productive. During the past period, the team has published 221 publications with 50 signed as first, last or corresponding authors, among which 55 are fundamental research manuscripts, 166 are clinical publications and 45 are reviews. The scientific productivity includes top peer review journals (Nature Comm, Annals of Rheumatic Diseases, PNAS, Arthritis and Rheumatology). The publications are well balanced between the three research axes developed by the team related to fibro-inflammatory diseases and including Systemic sclerosis, Rheumatoid arthritis, and Endometriosis.

The team is deeply engaged in translational research highlighted by the participation in several international clinical trials, among which one investigating the effect of the drug lanifibranor in systemic sclerosis and in liver fibrosis. The team leader also led a phase 2 trial for romilkimab targeting rheumatoid diseases. A team member acts as the national coordinator of several phase 3-4 international clinical trials in rheumatoid arthritis. A very close interaction is operational with the Cochin Port Royal University Hospital for expertise and patient recruitment and bio-samples supply. The team coordinates 2 grants offered by APHP and GHU center about the development of biomarkers in rheumatoid arthritis (total 41 k€). Financial and communication partnerships have been established with patient associations, like the Association des Sclérodermies de France and Association Française des Polyarthritiques.

The interaction of the team with the socio-economic world is particularly extensive. During the period, partnerships with several pharmaceutical companies, MEDSENIC, GYNOV, NOVARTIS, ALPINE IMMUNOSCIENCE, CORVUS, have been set up leading to the consolidation of 8 contracts for a total amount of 528 k€ dedicated to research activities, among which 2 doctoral Cifre programs have been signed. In addition to financed contracts, the team reached success in the valorization process of its research since 2 patents have been filled, including one licensed to MedSenic.

The team mentioned participation in communication activities towards the general public although not detailed in the DAE. Of note, members of the team have developed a mobile application (MyEndo App) to help patients to identify, evaluate and monitor their endometriosis. In the same line of research, the "Luna Platform" has been created to propose guidelines in terms of diagnostic assistance and treatment.

Weaknesses and risks linked to the context

The team reports the lack of permanent researcher as a weakness. Attention is needed to attract a full-time researcher according to the attractivity associated with the productivity of the group and the translational position.

Analysis of the team's trajectory

The proposal builds on large collection of patients' samples and important discoveries of the last review period. Regarding the research proposal dedicated to systemic sclerosis, the team will capitalize on previous GWAS (Genome-Wide Association Studies) project and built a follow-up study that already collected 1145 patients to increase the statistical power and conduct deeper molecular analyses. These data will be compared to 9000 control samples from the UK Biobank allowing high-powered meta-analysis with European data. These large cohorts will be exploited to gain a competitive advantage and identify new pathways involved in the disease. Since Lung fibrosis has becoming the leading cause of death in systemic sclerosis, the team built a multicentre cohort together with Zurich and Oslo hospitals to identify biomarkers related to lung disease in systemic sclerosis using a selection of molecules and unbiased proteomic approach. They have planned to conduct preclinical investigations in collaboration with pharmaceutical companies to test new molecules or immune-based therapies acting on immune response in systemic sclerosis. The team will also pursue their work on innate trained immunity investigating the role of environmental factors on macrophage memory and disease evolution.

In the field of rheumatoid arthritis, the team will develop a precise characterization of the synovial tissues using single cell transcriptomic of the mononuclear cells and spatial transcriptomic analysis. They plan also to develop functional studies to decipher the role of mucosal-associated invariant T cells and the deletion of Salt Inducible Kinase in myeloid cells in the development of experimental arthritis. The team will expand their research to study the synovial tissue in pigmented villonodular synovitis, a benign neoplastic condition and establish a biobank for juvenile arthritis in collaboration with other national groups.

In the field of endometriosis, the team will analyze recently generated single cell sequencing data including the developing placentas and immune cell compartments with or without endometriosis. Furthermore, these experiments include the test of different agents modulating innate immune memory.

Building on a recently obtained ERC grant, the proposal will explore the menstrual fluid as a non-invasive way to define new diagnostic or prognostic biomarkers and test new immunomodulatory treatment strategies using single cell transcriptomics, soluble protein multiplex assays and 3D organoid cultures.

These are both hot topics and while highly competitive, the team has developed several large cohorts/model systems/assays that could be exploited to give them a competitive edge.

Ideally, the projects related to systemic sclerosis and rheumatoid arthritis should present the grants secured by the team for their realization.

RECOMMENDATIONS TO THE TEAM

This is an excellent to outstanding team with excellent productivity who has strong relationships with hospital and pharmaceutical companies.

We recommend that the PIs continue to focus on producing the highest quality papers, a policy that might help to attract a full-time researcher.

Since the scientific strategy relies on development of single cell and spatial transcriptomic approaches, we could recommend reinforcing the bioinformatic capabilities of the team.

Team 2: Cutaneous Biology

Name of the supervisor: Mr Selim Aractingi

THEMES OF THE TEAM

The team's fields of research focus on skin-related pathologies. In particular, the team combines fundamental and translational research programs to explore the role of foetal stem cells in wound healing, the impact of alternative treatments in acne and the dysregulated molecular pathways involved in certain skin cancers.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations suggested improving funding for the projects developed, increasing collaborations with other Cochin teams, and improving staffing by recruiting an EPST scientist and talented postdocs.

During the period of evaluation, the team have obtained substantial funds to pursue their projects and has published several studies in collaboration with other members of Institut Cochin (33). Two postdocs were hired during the period of evaluation. The team is still running without a permanent scientist.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**8**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	4
Sous-total personnels non permanents en activité	**8**
Total personnels	**16**

EVALUATION

Overall assessment of the team

The overall assessment is excellent.

This team has a central expertise in skin diseases with several national and international collaborations. Over the evaluated period, the team had excellent tracking records for the size of the team in well-known specialist journals. The team have been granted by several national agencies and develop relationships with industrial partners.

Strengths and possibilities linked to the context

The team displays excellent scientific reputation in the dermatology and skin biology community highlighted by 54 lectures invitations in 37 national and 17 international meetings. In addition, a total of 12 oral presentations were selected in 8 national and 4 international congresses and 9 posters were displayed during the period.

The team members have also been implicated in the organization of international conferences, like the World Rendez-vous en Dermatologie (Brasil), 1st World Congress on Rare Skin Diseases (Paris), as well as national meetings like the Journées Dermatologiques de Paris.

Team members are strongly implicated in research and clinical administration with several members having key roles (president, secretary, etc.) in scientific boards of learned societies (Société Française de Dermatologie, Fondation Bioderma, CNU) and thematic groups research; a total 36 items have been reported. They also participate in scientific committees of funding and regulatory agencies: ANR, Société Française de Dermatologie, AP-HP, PHRC, Haute autorité de santé.

The team researchers are highly engaged with editorial responsibilities as reviewers and members of journals boards, in general (The Lancet, Blood, Sci Report, Journal of Clinical Investigation) and specialized publications in dermatology.

PhD students as well as young and senior researchers have been distinguished by European and national scientific prizes and awards, among which the Médaille d'Argent de l'AP-HP, section Médecine attributed to the team leader, several "encadrement doctoral et de recherche" awards, European Society for Dermatological Research Future Leaders Academy 2018, Médaille d'Argent de thèse en Médecine and 4 oral presentations and poster prizes.

The team has hosted 8 PhD students among them 3 were foreigners. A mean of 3 papers has been signed as first/co-first author for each PhD student after their defense. A total of 2 postdoctoral fellows have integrated the team during the period and were still present at the term.

One of the strengths of the team is related to its dual expertise in clinical and experimental dermatology to develop translational research which allows to raise significant fundings. Members of the team succeeded in obtaining European funding (European Academy of Dermatology, amount not available). The team coordinates an ANR grant (462 k€), a RHU grant (478 k€), 3 national PHRC (Programme hospitalier de recherche clinique) grants and 3 regional projects for translational research (total amount of 773 k€). Other national grants from FIMARAD, Ministère de la Santé, Inserm-Bettencourt and from PIA programs were also raised for a total amount of 340 k€. Lastly, 10 grants were obtained from fundations and charities, among which Fondation Léo, Société Francaise de Dermatologie, EADV (total about 400 k€).

The scientific production of the team, 186 total original articles, again is representative of the translational research activity. Among the 61 fundamental research articles, 32 were signed by team members as first, last or corresponding authors in high-ranked general journals: Nat Comm, eLife, Science Reports, EMBO J., Cell Reports. Five articles are led by another team of Institut Cochin and 24 by external collaborators (Blood, PNAS, Plos One, Front Microbiol, Science Reports, Science Advances). A total of 125 original clinical articles were published during the period: 38 signed as first, last or corresponding authors, 12 led by another team of Institut Cochin, and 75 by external collaborators. The team members were also active in reviews publications: 10 in fundamental research, 20 in clinical research, 1 book and 17 book chapters were published.

The interaction of the team with the socio-economic world relies on the filling of 4 patents on skin inflammatory disorders and wound healing and on the creation of a start-up (SkinDermic). Contracts with private companies were signed for conducting research activities (Novartis, 80 k€) and PhD student Cifre grant (IEEP 60 k€).

The team has been active by sharing its knowledge with the general public through the set-up of a MOOC in medical mycology in collaboration with the Pasteur Institute in 2021 and by about 20 communications in different media: press (Ca m'intéresse, Le Monde, Femme Actuelle, Le journal de la Santé), radio (Europe I, France Inter, RFI, France Bleu), social networks (Doctissimo.fr, Slate.fr).

Weaknesses and risks linked to the context

Although scientific output is excellent, the number of published studies in the basic sciences might be further increased through the recruitment of a permanent researcher who could promote more fundamental researches on pre-existing project's team. Furthermore, only 2 people devote 100% of their working time to research (one engineer and one ARC/technician).

It is worth noting that oral presentations are given more by statutory staff than by thesis or postdoctorate students

Analysis of the team's trajectory

The team's trajectory is clear and secure, as it has the necessary funding and personnel to pursue clinical and experimental research in its field of expertise.

RECOMMENDATIONS TO THE TEAM

The team needs to continue their excellent scientific output and attract talented postdocs with a background in the basic sciences, so that they can compete for EPST researcher positions.

Team 3: Comparative Biology of Apicomplexa

Name of the supervisor: Mr Frédéric Ariey

THEMES OF THE TEAM

The team studies Apicomplexa, which are eukaryotic intracellular parasites of great medical importance, in particular *Plasmodium falciparum* responsible for severe malaria, *Toxoplasma gondii*, whose primary infection in pregnant women can have serious consequences for the foetus and *Theileria*, which is responsible for a major plague affecting livestock in tropical areas. Among the topics studied, the team is interested in the mechanisms regulating the multiplication dynamics of these parasites, which appear to be common and sensitive to the redox balance in the various infected host cells.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations of the previous committee were the following:

- to increase visibility in *T. gondii* research: the core of the publications are still associated with *Plasmodium*; however, a few studies on Toxoplasma were published in high-value journals (Nature Comm. and PLoS Pathogens);

- to increase interactions with the non-academic world: some contracts were obtained with industrial partners (a Sanofi 18-month contract of 100 k€ was obtained in 2022);

-to increase the number of trained PhD regarding the 2 HDR holders in the team: no new HDR has been obtained; 3 students defended their PhD thesis during the reporting period;

- to avoid spreading too thinly over too many projects on Apicomplexa and regarding the integration of physicists: biologists and physicists have not yet published together; regarding Apicomplexa the team focused mainly on *Plasmodium* (20 publications), then on *Theileria* (7 publications) and *Toxoplasma* (3 publications).

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

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**7**
Enseignants-chercheurs et chercheurs non permanents et assimilés	3
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**5**
Total personnels	**12**

EVALUATION

Overall assessment of the team

The overall assessment is very good.

The team has advanced expertise in parasitic diseases mainly in Plasmodium research with several national and international collaborations. It has had very good tracking records (35 articles with 11 as first or last author, plus 8 only published by the physicists). The team has been funded by several national and European grants and has recently developed relationships with industrial partners. It had trained 3 PhD students; all are co-authors in published studies. However, the integration of physicists in 2019 in working on Apicomplexa is not visible.

Strengths and possibilities linked to the context

The team continues to have a very good publication record in *Plasmodium* (20 publications) with some published collaborative work in well-known journals (e.g., Nature Med., eLife). This success is due to the recognized expertise of the team members in this topic. In addition, 10 reviews (Trends in parasitology, Frontiers in Microbiology) have been published.

Their notoriety at the national and international levels is attested by involvement in various national and international committees and boards (Member of ERC Panel "Infection & Immunity" Starting Grants, Panel member of ANR "Infection & Immunity", Vice-President of the CSS2 of IRD).

The training through research is very good (4 postdocs, 3 PhD students and 2 Master students).

The funding ability from national and European organizations and industries is excellent (Human Frontier Science Programme: 450 k€; KAUST: 300 k€; 4 national grants including ANR as funding source for a total of 310 k€; Labex PARAFRAP: 100 k€, CNRS prematuration contract: 162 k€; SANOFI: 100 k€).

Team members are also involved in the scientific board of the platform GENOM'IC.

Weaknesses and risks linked to the context

For the next period, it is unclear how the physicists will interface with the biology of Apicomplexa. No common project is presented and the risk is to have two teams. In addition, the number of team members will decrease: two senior researchers in parasitology will retire. With only one MCU-PH and one PU-PH remaining in the team, the clinical parasitology and the research programmes on different Apicomplexa will be undermined.

The PI of the team has relatively few publications and does not sign as senior author. This is a fair policy if this favours the career of junior members, but should not be always the case.

Analysis of the team's trajectory

The team's trajectory is not convincing; there is private funding (SANOFI) to promote the interface between the two leaders but the trajectory does not clearly expose the expected benefits of such a partnership for parasitology projects, as the team will remain named "Biology of Apicomplexa". In addition, the workforce may be a limiting factor.

RECOMMENDATIONS TO THE TEAM

The team needs to better explain the benefit of the interface between the parasitologists and physicists. The team should put efforts in attracting talented postdocs so that they can compete for researcher positions in order to compensate the expected diminution of the team workforce within the next period.

The number of HDR holders as well as the PhD student/HDR ratio should be increased.

The team needs to further recruit young researchers in parasitology to boost and maintain the attractiveness associated with the group thematic on Apicomplexa.

Team 4: Cell signaling in bacterial infections

Name of the supervisor: Ms Cécile Arrieumerlou

THEMES OF THE TEAM

The team works on the host-pathogen interactions with the aim to provide novel knowledge regarding the host and microbial molecular determinants that drive either host protection or host susceptibility to infections. To do so, they are combining bacterial genetic to *in vitro* and *in vivo* approaches using human epithelial cells, mice and microscopy approaches.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The last committee recommended the team to expand its human forces as well as to broaden the visibility by participating to more international conferences.

The team has followed these recommendations thanks to the participation to international meetings in China or Germany for instance.

Regarding the human forces, the team relied on one permanent researcher and one permanent engineer as well as on 2 PhD students, two postdoctoral fellows and one assistant engineer (fixed-term contract).

In term of strategy, the team has secured funding (ANR grants, two as leader and one as partner, one grant from ARC) for a total of 1.14 M€.

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

EVALUATION

Overall assessment of the team

The overall assessment is very good to excellent in view of the size of the team.

The team has robust expertise at studying and deciphering the function of the ALPK1-TIFA immune complex in immunity to infections. It has published excellent research articles in specialized journals and reinforced its national and international network of collaborators. It has also secured national grants.

Strengths and possibilities linked to the context

During the evaluating period, the team identified ADP-Heptose from bacteria as the critical ligand for the ALPK1-TIFA pathway. The group published 5 original articles (including in excellent journals such as PloS Pathogens, EMBO Reports, Gut Microbes, etc.) and 1 review with students being very well represented on the important places (first or co-first author). The strength of the team is its expertise on the discovery of the ALPK1-TIFA biology as well as on the characterization of the microbial components that trigger the activation of this emerging innate immune pathway.

The raising of national funds for 1.14 M€ (two ANR grants as leader, one as co-leader, one project from ARC on cancer) as well as the development of international and national networks with Spain and Germany notably are excellent for the last 5 years.

The team leader has been invited to various conferences, including the prestigious World Microbe Forum in 2021. Regarding outreach activities, the team, among others, has now integrated into the various supports of sharing knowledge such as the “la fête de la science” and the ”apprenti chercheur” events that occur annually.

Weaknesses and risks linked to the context

The size of the team is very small.

Despite the robust expertise of the team at working on ALPK1-TIFA pathway, it suffers from the very strong international competition on this specific area of research.

Analysis of the team's trajectory

The team will merge with another one of the institute, which aims at creating a stronger group in terms of science, funding, skills (medical, university, tenured researchers and engineers...). In this context, the team trajectory is not analysed here.

RECOMMENDATIONS TO THE TEAM

The team is planned to merge with another team, so no recommendations are given.

Team 5: Host-Virus Interactions

Name of the supervisors: Ms Clarisse Berlioz-Torrent & Mr Stéphane Emiliani

THEMES OF THE TEAM

The main focus of the team is to study cellular and molecular mechanisms of host-virus interaction. The overall goal is to gain insights into molecular mechanisms underlying viral pathogenesis.

The scientific activity of the team for the reporting period has been mostly developed around four themes: 1) characterize the molecular features of HIV-1 latency in cellular reservoirs carrying replication-competent, silent viruses; 2) map the molecular events controlling HIV-1 expression at transcriptional and post-transcriptional levels; 3) elucidate mechanisms of HIV evasion from restriction factors; 4) characterize cellular proteins pivotal for SARS-CoV-2 virions morphogenesis.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team received a few recommendations during the previous unit assessment including (i) increasing the number of publications also through writing of reviews, (ii) increase visibility of the team by participation to conferences and (iii) reduce the number of projects within the team and focus on objectives where relevant results were obtained. The assessment also commented on the need of integrating efficiently new members into the team.

Although the team's report does not specifically comment on previous recommendations, the following was noticed:
The number of publications remained the same as in the previous reporting period (16 original articles and 3 reviews); this number is appropriate to the team composition and the quality is excellent. 19 oral presentations and 27 posters were presented to national and international conferences; considering the reduced traveling due to the pandemic, the team has worked hard to improve its visibility. Four main projects were carried out: three of these projects were interconnected dealing with mechanisms of HIV-1 latency and expression and strategies used by HIV-1 to counteract host restrictions factors. The team also spent time on SARS-CoV-2 by pinpointing cellular factors essential for virus morphogenesis.

A huge work has been made at the unit level to ameliorate working environment. Thus, although not directly addressed in the report, the team has worked to fulfil 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	2
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	**6**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	1
Post-doctorants	2
Doctorants	5
Sous-total personnels non permanents en activité	**10**
Total personnels	**16**

EVALUATION

Overall assessment of the team

The overall assessment is excellent.

The scientific work conducted by the team is of excellent quality, with several important publications and findings carried out in a highly competitive research field. The team constitutes an attractive working place for young investigators, with excellent contributions to research education. A strategy is in place for future work on emerging viruses. The team was involved in several research activities contributing to society.

Strengths and possibilities linked to the context

The ultimate goal of the team is to identify strategies to control and eradicate virus infections. The team has established important national (Institut Cochin, IUH, Institut Pasteur) and international (Radboud University, Université Libre de Bruxelles (ULB)) collaborations, which will facilitate the continuation of their work on HIV life cycle and the development of new research axes on the following topics: emerging viruses, cytokines, autophagy gene expression and transcription, HDV and HBV. The team has published 16 original articles (5 as leader; several in journals of solid reputation including Plos Pathogens 2022, PNAS 2023, Nat. Commun 2022, J. Virol. 2019 and 2022, Nucleic Acid Research 2017), three reviews (Viruses 2017 and 2021, Autophagy 2021) and contributed to one patent.

The team is an attractive working place for young investigators; during the last 5 years 11 postdocs and 8 PhD students were trained by the team. Four PhD students are authors of at least one publication and the remaining students are still working on their PhD program. The proportion of young investigators from foreign countries was approximately 20%. The team members have been invited to several conferences (e.g. 6th international conference of retroviral integrase 2017; 4th EU4HIVCURE 2018) and have been the organizers of three ANRS symposia on HIV reservoirs, post-intranuclear steps of HIV life cycle and HIV transcription. The team leaders served in the editorial boards of journals Retrovirology and Frontiers in Microbiology and participated as members in advisory committees of FROM scientific council and ANRS Host/Virus Interactions. The team has been supported by national grants (four from ANRS 1271 k€, one from FRM 100 k€, three from Sidaction 314 k€) for more than 1.6 M€. When including ITA/postdoc/doc salaries and operating costs, the overall budget for the team from 2017 to 2022 is 3,211 k€.

The team has participated as co-inventor in a patent. The team has organized several laboratory open houses in 2021 (information to general public on SARS-CoV-2) and 2022 (visit by benefactors of Sidaction to Institut Cochin), participated in public debates on HIV and gave talk at the international festival "Pint of Science" (2022).

Weaknesses and risks linked to the context

During the last 5 years, the team has productively worked on SARS-CoV-2 and HIV. The decreasing level of funding related to these two viruses represents a threat to the activity of the team. The plan is to initiate new projects outside the HIV field and to focus on emerging viruses and cellular mechanisms potentially affected by these viruses. It is noticed that collaborations with biotech-companies are missing, which should not be the case considering that the identification of molecular players involved in HIV-1 latency and transcription could lead to therapeutic intervention.

Reallocation of a permanent researcher (CRCN, CNRS) will lead to loss of important competence for the team. The team has had an excellent level of funding but there can be a risk to rely only on national granting agencies.

Analysis of the team's trajectory

The team's trajectory represents a logical continuation of the excellent work previously conducted by the team. Three detailed projects are presented in relation to task force and granting agencies:

1. Understanding how premature transcription termination enforces HIV latency (in collaboration with researchers in Belgium (ULB) and financed by a collaborative grant ANRS 2023-2025);

2. Studying the regulation of viral and cellular transcriptomes through HIV infection (supported by ANRS 2020-23 and Sidaction 2022-2024);

3. Identifying virulence and restriction factors that control HIV release and infectivity (supported by ANRS 2021-2024).

The topics of the trajectory represent very "hot" subjects of current HIV-1 research as it would be important to identify strategies to eliminate latent HIV-1 reservoirs also through forced transcription of latent HIV-1 reservoirs. The topics of the team's trajectory have an excellent academic value for novel knowledge and belong to a very competitive field, which in theory could lead to HIV elimination, with substantial savings for the health care system worldwide. The committee perceives that international collaborations with excellent scientists operating in Europe and US could be further developed.

From 2025 the team will comprise 5 permanent staff members (including 3 researchers and two engineers). The recruitment of young investigators to the team is anticipated. The collaboration with clinical units will be further developed to perform translational projects.

RECOMMENDATIONS TO THE TEAM

The level of funding could be increased by applying to international sources, including the European Commission and the NIH.

Considering the molecular studies on HIV replication cycle, it should be possible to attract the interest of biotech companies for collaborative studies and grants.

More emphasis should be given to the recruitment of investigators from countries outside France.

In view of the competitive field in which the team is operating, it would be important to establish more international collaborations.

Team 6: Genomic and signaling of endocrine tumors

Name of the supervisor: Mr Jérôme Bertherat

THEMES OF THE TEAM

The team investigates the molecular mechanisms responsible for the tumorigenesis of adrenocortical and pituitary tumors in order to understand endocrine tissue differentiation and physiology, and to study oncogenesis. The main aims are to describe a better classification for the diagnosis and prognosis of these tumors, and to identify key signaling components to be targeted for treatment.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The main recommendations in the previous report are related to the limited access to bioinformatic resources, the number of international postdocs and the interactions with socio-economic partners.

Concerning the bioinformatic resources, the institute is currently implementing a bioinformatics platform with dedicated space and human resources. The director highlighted the strong input of the team for the implantation of this service in and for the institute.

The team succeeded in attracting experienced postdocs, one of whom was recently recruited by the team as permanent investigator by Inserm. This success will foster the abilities of the team in basic research.

Although the team has significantly improved its overall communication and although the members of the team are involved in interactions with society at different levels to disseminate knowledge, collaborations with R/D remain to be developed. Recent studies describing new markers and pathological mechanisms will probably be helpful towards this goal.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	4
Personnels d'appui à la recherche	6
Sous-total personnels permanents en activité	**16**
Enseignants-chercheurs et chercheurs non permanents et assimilés	5
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**10**
Total personnels	**26**

EVALUATION

Overall assessment of the team

The overall assessment is outstanding.

The team continues to have an impressive publication record. Their visibility at the national and international levels in the field of adrenal diseases is well established with a leading position in the discovery of novel adrenocortical disease-causing genes and biomarker identification. There is an excellent articulation between the clinic and experimental research, excellent integration in national and international networks, ability to recruit Inserm investigators and a very good funding ability from national and European organizations and from charities.

Strengths and possibilities linked to the context

During the 2017-2022 period, the team continued to investigate the molecular mechanisms underlying the pathogenesis of endocrine tumors, mainly adrenocortical and pituitary tumors. The classification of these tumors and the identification of their distinctive molecular signatures, thanks to the thorough analyses of their transcriptomes are reported in several publications of the team in high profile journals. This constant and excellent scientific production attests for the notoriety and know-how of this team in the molecular characterization of different subtypes of endocrine tumors. Among the overwhelming publication list of the team, two outstanding publications in Cancer Cell and JAMA Oncol highlight again the top-level achievements of this team in genomic studies during the period of assessment. This knowledge of the team members was recently summarized in an authoritative review in Endocr Rev. with the PI as first author. The team members published 70 articles as first or last authors and a total of 399 articles, including many clinical studies and observations. This high number of publications underlines the capacity of this team to interact with other teams within the institute but particularly outside in national and international hospitals and research centers.

The team also produced a high number of reviews (79). The international recognition of the team is also attested by the numerous invited conferences (30) and communications, some of which in international renowned manifestations. It should be noted that most of the top-level scientific achievements are related to the genomic and clinical studies of the team members, the production related to the genes and pathways identified through transcriptomics analyses are not of the same level and will certainly be fostered in the next years. The recruitment of two Inserm researchers in the last years and the relevance of the critical genes identified represent strong assets to achieve this goal likely during the next contract. This will also increase the visibility of different researchers of the team.

In the last 5 years, the team has secured reasonable finances (between 200 and 750 k€ each year) in order to ensure the feasibility of their projects. The team members are part of 5 ANR projects, including two as principal investigators, and received financial support as a FRM (Medical research foundation) team from 2019 to 2023 for their work on the genes identified as regulators of cortisol deregulation. The team has also obtained European grants within the framework of adrenal tumor networks. Individual fundings were also obtained by the team. These grants allowed the recruitment of 5 postdocs, 6 techs and 11 PhD students.

One remarkable achievement is the training of students with 11 Masters and 7 PhD theses defended during the last term, each having published at least 2 publications.

Besides their scientific activities (research, editorial research, fund-raising, etc.), several members of the team and in particular the team leader hold important responsibilities in the hospital such as the coordination of the national reference center for rare adrenal diseases, the coordination of a research council of a group of hospitals in Paris or activities of an association for adrenal patients. Members of the team organized several meetings (Journée Klotz, Dreyfuss, etc.), are involved in national or international committees for evaluation of research and contribute to guidelines of national and international scientific societies where they regularly sit in their executive committees such as the European Endocrinology Society.

Members of the team are also involved in educational activities for medical and scientific students, but their involvement in the administration and tool implementation for different courses taught is not mentioned.

The team members are continuously developing their communication skills by interacting with media (Lay-public debates, interviews for TV), leading a chair of IA for Health for their University and generating videos for patient care. These skills will undoubtedly lead to further interaction with socio-economic partners.

Weaknesses and risks linked to the context

The team made its major scientific achievements in genomics of adrenocortical tumors. Therefore, there is an unbalance regarding the impact of the publications, although also of good quality, related to the axis of functional characterization of the newly identified genes.

Although the team has strong involvement in biomedical research, there are no patents or interactions with R/D companies. The identification of new markers and potential therapeutic targets, and access to patients should in principle facilitate these interactions and make the transfer to the clinic feasible.

The thematic on pituitary tumors is under-described and represented in the overall description of the team research although the team published a major paper on this theme. This could be a point of dispersion if this thematic is not well integrated among the research axes to develop in the future.

Among the high number of publications of the team, some (9) were done in collaboration with teams of the institute. This collaboration could also benefit to other aspects of the projects.

Analysis of the team's trajectory

The team is planning to use more sophisticated omics technologies to analyse the heterogeneity of cell populations within endocrine tumors. They aim also to use formalin-fixed, paraffin-embedded samples instead of frozen tissues, and new technical protocols in order to analyse larger cohorts and to obtain better characterization of tumors. They also plan to integrate proteomic and steroidomic analyses to the samples in order to refine the current molecular classifications of adrenocortical tumors. This part of the project is a logical continuation of the ongoing research project started some almost 20 years and should not present any major difficulty. The team also mentions the exploration of the mechanisms of response and resistance to antitumor and antihormone treatments which represent an ambitious aim that shouldn't be taken at the margin.

The second axis is dedicated to the functional characterization of the genes responsible for adrenocortical tumorigenesis in adrenal physiology and pathology. Using conditional transgenic mice models, the aim here is to determine the role of the genes identified in the differentiation and secretion of adrenocortical cells. In addition, the team will study the signaling pathways involving the genes of interest in an attempt.

The team will continue to use its networks and their highly suited tissue libraries to obtain high quality biological samples of endocrine tumors, which represent the essential substratum for their research project as it was proved in the past. The leading position and the expertise of the researchers in omics studies should allow the team to continue to produce major findings with excellent scientific production in this field of research. The functional characterization of the genes responsible of adrenocortical disease and the signaling pathways they regulate may shed new light on the pathophysiology of these tumors and could have important implications for the development of novel diagnostic and prognostic markers as well as valuable therapeutic targets. This is a very comprehensive and ambitious project led by an excellent team whose notoriety and visibility warrant again significant achievements during the next contract.

RECOMMENDATIONS TO THE TEAM

The project is ambitious and has many complementary aims. Many omics studies and animal models are envisaged to tackle these aims. Combining forces on few of them could be more fruitful and impactful for the different axes of the project. The team has nevertheless all the competences and the expertise to achieve some of the major goals planed.

The team is encouraged to improve the impact of the studies on the functional characterization of the affected genes identified. The recent recruitment of young scientists using multidisciplinary approaches will probably help in this direction.

Given the numerous competences available within the institute, further collaborations could be highly beneficial to the team, at least for the gene functional characterization axis.

Given the notoriety and expertise of the team leaders and their high profile, applications to international and European, more competitive grants such as ERC grants are to be encouraged.

The trend in student training is excellent and should be maintained with the involvement of as many different supervisors as possible within the team. Qualified supervisors are always needed in a team to envisage its future with serenity. This point is not discussed in the report but is probably among the priorities of the team.

The team should improve its interactions with biotech and industrial partners by performing more translational research which should lead to the filing of patents and subcontracting of these patents. The team has improved its communication toward the social media which should help to attract socio-economic partners in the future. The team leaders should probably sensitize the researchers to intellectual property and to interaction with innovation offices in Inserm and Cochin hospital for the translation of their research findings into different clinical tools.

Team 7: Mucosal entry, persistence and neuro-immune control of HIV and other viruses

Name of the supervisors: Ms Morgane Bomsel & Mr Yonatan Ganor

THEMES OF THE TEAM

The themes of the team during the last reporting period were focused on three intertwined axes: "HIV mucosal immunity", "neuroimmune control of HIV and mucosal viruses" and "mucosal entry and persistence of HIV and SARS-CoV-2". The latter topic was introduced during the SARS-CoV-2 pandemic.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has addressed the provided recommendations, which included to increase dissemination and training activities, expand the number of staff members and consolidate original findings in other cellular systems. They participated in educational and dissemination activities. Training activities were expanded and a large number of PhD students (10) and postdocs (2) were recruited and trained. The absence of permanent-staff technicians underlined in the previous report remains.

The team discovered an additional productive HIV reservoir in megakaryocytes, in addition to their seminal discovery of macrophages being a cellular reservoir for replication competent HIV-1 virions. The studies utilized clinical samples from patients' cohorts.

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	2
Personnels d'appui à la recherche	1
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	5
Sous-total personnels non permanents en activité	**6**
Total personnels	**11**

EVALUATION

Overall assessment of the team

The overall assessment is excellent to outstanding.

Several articles that have a major relevance in the search for HIV-1 cure and vaccines have been published in journals of high impact. Not many groups worldwide can claim the discovery of two new cell types that are HIV-1 reservoir. Important contribution has been also made to the SARS-CoV-2 field. The collaboration with biotech partners continues and several patents were deposited. A large number of young investigators were successfully trained by the team.

Strengths and possibilities linked to the context

The topics addressed by the team are highly relevant to life science research in Europe. The team employs a multidisciplinary approach and has access to mucosal/genital tissues through clinical collaborations.

The team published 30 original articles (7 by team members alone and 23 in collaboration with French (Hospital Raymond Poincaré; Hospital Saint-Louis) and international (Münsler University; New Jersey Medical School) groups, and 3 reviews; 22 invited oral (IAS Conference on HIV Science 2019; International Congress on Mucosal Immunol 2022; etc.) and 8 poster presentations were given. Younger collaborators published several articles as first/co-author. Several of the publications are of outstanding quality and published in important journals (Gut 2017; Nature Microbiol. 2019; Sci. Translational Med. 2020; Nature Comm. 2022). The major scientific achievements by the team are the discovery of two major HIV reservoirs in tissue macrophages and bone marrow megakaryocytes containing replication competent HIV-1 virus (Nature Microbiol. 2019; Sci. Translational Med. 2020; Nature Comm. 2022); in addition, megakaryocytes can also be infected by SARS-CoV-2 thus producing virus-infected platelets (Cell Mol. Life Science 2022).

The activities of the team are attractive to funding agencies and young investigators. The team received grants from French organizations (one from FRM 400 k€, four from Sidaction 277 k€, three from ANRS 310 k€, three from ANR 260 k€, one from SATT-Ile de France/ERGANEO 15 k€) for a total of 1,262 k€. A grant from ANRS allows the purchase of a CCD Camera for BSL-3 lab. The team leader was awarded the prize from the Line-Renaud Gasté Dotation Fund-FRM in 2021 for her work on mucosal acquisition and protection against HIV and SARS-CoV-2 infections. The team leaders were invited speakers at several international conferences and co-organized five international congresses.

6 PhD students completed their PhD thesis, 4 PhD students are currently working on their PhD; 2 postdocs were enrolled.

Three patents were deposited in 2020; the team collaborates with a Swiss company, Mymetics for the development of a prophylactic mucosal HIV vaccine; in another project, the team collaborates with a French company (Synsight) to develop novel HIV/HSV antiviral medicines. In several contexts, the team has shared knowledge with the general public: for instance, the team leader was highly involved in media communication during Covid-19 pandemic.

Weaknesses and risks linked to the context

The lack of permanent engineer/technical staff is a risk moment for this ambitious team.

Insufficient laboratory space is a limitation to the expansion of this team.

Analysis of the team's trajectory

The trajectory is in line with the work previously conducted by the team.

The persistence of HIV in the novel cellular reservoirs for the virus described by the team will be further studied. Tissue macrophages carrying latent, replication competent HIV-1 virions, may preclude virus eradication. The role of infected megakaryocytes and HIV-containing platelets in HIV-1 infected patients with immunological failure will be investigated. Megakaryocytes (and platelets) will also be at focus in studies aimed at assessing if this cell type forms a viral reservoir in patients with long term Covid and if their biology (with special attention to the serotonergic machinery) is altered by SARS-CoV-2 infection. A program to define biomarker of Long Covid is also discussed with clinical units treating these patients.

The antiviral and immunogenic properties of the recently identified peptide P7, isolated from potent HIV protective IgA of an exposed but seronegative individual (ESN), will be characterized. Recently work by the group showed that Calcitonin Gene Related Peptide (CGRP) inhibits HIV-1 and HSV infections (Mucosal Immunol.; PNAS); novel non-peptide small-molecules agonists of the CGRP will be studied in collaboration with a biotech-company (Synsight) as topical microbicides with antiviral properties.

The composition of the team is adequate to conduct the proposed work, but it is important to recruit technical help. Some grants (from ANRS MIE, Sidaction) are already available up to 2024. The work with be conducted in collaboration with several academic and industrial partners.

The trajectory described has the potential to generate outstanding science and training for young investigators and patents on novel antiviral products.

RECOMMENDATIONS TO THE TEAM

The important topics addressed by the team have the potential to lead to international grants; applying for grants from international funding agencies is recommended.

Action should be taken to secure a permanent staff engineer/technician.

Team 8: Mitochondria, Bioenergetics, Metabolism and Signalling

Name of the supervisor: Mr Frédéric Bouillaud

THEMES OF THE TEAM

The team works on the relationship between energy metabolism and higher integrative traits at the cellular or whole organism levels, in the context of several pathologies. The team has a strong expertise in mitochondrial biology and bioenergetics, applied both to rare mitochondrial diseases, to epidemic metabolic diseases (obesity, T2D and NAFLD), and to cancer development. The past topics of the team were mainly focused around UCP2 and hydrogen sulfide (H2S). Linked to the retirement of both experts of these topics, the team will be managed by 2 new co-directors and the research focused on metabolism and cancer.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The last report of the team mainly recommended that 1) the team continues to maintain its high production but promotes more popularization; 2) to maintain their expertise in functional studies of metabolism despite the retirements of some experts; and 3) to maintain its own profile and focus on areas for which their expertise is recognized even though they perhaps do not yet have fully obtained the functional recognition they may deserve.

Point 1: the team maintains a good ongoing publication rate (with 58 original publications compared to 63 in the previous report). However, the number of publications with PI of the team as lead author could be improved (between 1 and 4 depending of the PI for 2017-2021). In addition, few efforts were made towards popularizations despite 1 article in Sciences et Avenir.

Point 2: Despite the 2 retirements of experts of mitochondria and bioenergetics and the future retirement of the team leader in 2025, the team has continued to develop functional studies around mitochondria metabolism, and the next team will also continue to perform fluxomic analysis and metabolomics.

Point 3: the research topics of the team have evolved thanks to the joint effort of two team members toward metabolic reprogramming and cancer. Importantly, the team developed more translational studies with i) analyses of fatty acid oxidation and mitochondrial bioenergetics in normal, steatotic or NASH fresh liver biopsies from morbidly obese patients who underwent bariatric surgery, and ii) metabolomic and lipidomic analyses of plasma from obese patients with and without NAFLD. In the future, this effort will be pursued with the culture of human 3D tumoroids and the arrival of several clinicians in the team.

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

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

EVALUATION

Overall assessment of the team

The overall assessment is excellent.

Strengths and possibilities linked to the context

The team has a unique expertise in quantitative assessment of mitochondrial bioenergetics and energy metabolism fluxes, which lead to several collaborative works with 11 other teams of Cochin. The team is also involved in the local METABOL'IC platform of Cochin Institute dedicated to metabolic measurements from cell to small animals. The team has animated several workshops around the measurement of mitochondrial functions and is strongly implicated in the MeetOChondrie French network. The team was reinforced by the integration in 2019 of a researcher with an ERC starting grant, extending the expertise of the team in cancer and energy metabolism and enriching the technical expertise of the team with omics analyses.

The team maintains a good ongoing publication rate, with 7 reviews and 58 original articles, some of them in excellent journals (Nat Comm, J Clin Invest, Diabetes, Gastroenterology, Hepatology, J Hepatol). The publication output of the team is rather well balanced between team members. Importantly, the complementarity of team members is attested by 15,5% of publications being co-signed by at least 2 PI of the team.

The team has an excellent fund raising with several international (n=2, ERC starting grant and H2020 grant) and national grants (n=10). Particularly, the team was successful in the obtention of grants from charitable organizations (n=12; 3 ARC, 2 ligue contre le cancer, 1 AFM, 2 Cochin grants and 1 SFD) and from the pharmaceutical industry (n=2) (total amount of total amount of 2,45 million euros). The obtention of contracts is well balanced between team members.

The reputation of the team is excellent at both national and international levels. Team members have been invited to 8 international (ETN-H2020 Foie gras Network school, Word congress on hydrogen sulfide in Biology & Medecine) and 2 national (Réseau MeetOchondrie) conferences. One patent on H2S was obtained and 2 declarations of invention have been submitted and are currently under review. All team members participate to transversal actions in research, such as scientific committee (ANR committee, Hcéres committee), research steering bodies (CNRS national committee, INRAE AlimH departement committee), editorial responsibilities or organization of meetings or network schools (ETN-H2020 Foie gras Network school). In addition, several members participated to the scientific animation of the French network "MeetOchondrie" and participated in the organization of annual colloque in 2017 and 2018 and thematic days in 2019 and 2023.

The training capacities of the team is excellent with 8 PhD students (for 6 HDR), 3 postdoctoral researchers (1 foreign) and 6 undergraduates. The ratio between PI with HDR and PhD is good, and 2 accreditations for HDR were obtained over the period 2017-2022. Some members are involved in teaching activities (UE physiopathologie métabolique de DCEM1, Master 2 Endocrinologie et Métabolisme) even if no university members are present in the team. The team has regularly hosted middle and high school students for short-term stays in the laboratory.

Weaknesses and risks linked to the context

The team saw its workforce decrease with several retirements (2 PI) and mobilities outside the team (2 technical staff).

After discussion, it remains unclear for the committee whether the approaches of fluxomics/metabolomics that will be used in the future project are mastered by the PI and performed in Cochin Institutes or whether they will be performed through external collaborations.

The majority of the publications of the team are collaboratives works (intra and extra Cochin institute) and few articles have PIs of the team as lead authors (27%). Furthermore, research valorization activity and contribution to society remained weak. Lastly, linked to the large use of omics analyses in the future, the team is lacking a biostatistician.

Several of the grants are finished or will finish in the next years. The last international funding was obtained in 2017.

Analysis of the team's trajectory

The team has undergone profound changes in the past period (2017-2022): 2 mobilities, 2 retirements and 3 arrivals, which influence the evolution of the team. The direction of the team of F Bouillaud (retired in 01-2025) will be continued by R Dentin & MC Alves-Guerra and the scientific topic will be recentralized around the themes of the 2 co-directors: the crosstalk between metabolism and cancer.

This new Team "Metabolism, Immunity, Cancer & Therapies" will dedicate its activity to fundamental and translational research in cancer to decipher the mechanisms involved in the crosstalk between energy metabolism, immunity and cancer. The team will be smaller than in the previous contract (5 permanent members including 3 PI and 1 PU-PH). Importantly, the team will be reinforced by the arrival of clinical researchers from the Cochin Hospital (Medical Oncology and Biochemistry Department) and previously members of the URP 4466 team enriching the research program with clinical investigations in human oncology. By combining multi-omics experimental approaches to recognized expertise of the team in energy metabolism, the team propose to explore how metabolism shapes the crosstalk between cancer cells and the tumor immune environment and subsequently promotes tumor development and resistance to treatment. The final goal is to identify novel metabolic pathways and targets for pharmacological or nutritional intervention that could improve the efficacy of existing therapies, such as immunotherapy.

The project is divided in 4 axes:
- How metabolic reprogramming favors cancer initiation and development;
- Identification of metabolic therapeutic targets to reduce cancer progression;
- Metabolism, tumor immunity and response to immunotherapy;
- New therapeutics to overcome drug resistance.

One strength of the team is its multidisciplinary, as they propose to combine basic science to mathematical modeling in order to predict pathological phenotypes of cancer cell metabolism and to test new therapeutic strategies, and another one is the use of sophisticated technics such as fluxomic and metabolomic analysis, single cell transcriptomic analysis, culture of 3D tumoroids. However, it is unclear whether all these technics are mastered by the PI of the team (in particular fluxomics and metabolomic analysis) and performed in Cochin Institute platforms or if it depends of collaborations of external platforms.

Currently, the track record of publications of both co-directors as lead author is quantitatively low, even if it is of an excellent level (1 Cell Report in 2017, 1 Nat Comm in 2018 and 2023 for one director and 1 Cell Rep in 2019 and 1 J Immunol in 2022 for the other one). Therefore, the team has to confirm in the next years that all its members can achieve high-level collective work on the new proposed research topic.

RECOMMENDATIONS TO THE TEAM

This is a strong team with an excellent reputation and expertise. The team maintains a good production despite several retirements, but the original publications with PI as lead author could be increased.

As the team begins a new scientific shift with new co-directors, attention must be paid in i) maintaining expertise in mitochondria and bioenergetics, ii) attracting people expert in metabolism (for fluxomic and metabolomic analyses, recruitment of a researcher able to bring analytical expertise and considerations of thermodynamical aspects for the study of metabolic flux would be a strong asset for the proposed project of the team.), iii) increasing publications as lead author and continuing to publish at a high level while having other administrative responsibilities and iv) to make the connection with new oncology clinicians a reality.

As the strategy of the team will be more focus on omics analyses, we could recommend to reinforce the team with biostatisticians.

Team 9: Vascular Cell Biology in Infection Inflammation and Cancer

Name of the supervisor: Ms Sandrine Bourdoulous

THEMES OF THE TEAM

The team's programme focuses on vascular biology in the context of infection and inflammation. A particular focus is the blood-brain barrier, and the infection biology of *Neisseria meningitidis*. The team leverages an interdisciplinary approach exploiting some unique human models as research models. The team endeavours to translate the fundamental discovery science into health applications. In particular, developing therapeutic compounds against type IV pili of *Neisseria,* and a potential factor that may prevent endothelial dysfunction during sepsis.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was recommended to engage with the public, to increase the number of postdocs, and to concentrate their research efforts in few projects given their size. In this period, the team contributed to Science Day and produce videos and tutorials showcasing their research, and hosted high school students. The research projects were more focused in three areas (cancer, meningococcal adhesion, and new therapeutics) with outstanding publications. The size of the team has not changed significantly and no postdocs were recruited.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
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	**4**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**6**
Total personnels	**10**

EVALUATION

Overall assessment of the team

The overall assessment is outstanding.

Outstanding team internationally recognized by the work on N. meningitidis and original research models. The team has maintained an outstanding pipeline of publications in high-impact journals. It is worth noting the excellent training capacity of the team. It has secured national funding including charity-supported projects. The team demonstrates an outstanding activity in terms of patents.

Strengths and possibilities linked to the context

The team is internationally recognized in the area of the research (17 invitations to international meetings and seminars to the team leader, and 18 oral presentations to the rest of the team), and has done some seminal contributions during this period, in particular related to type IV pili of *N. meningitidis*. Overall, the team maintains an outstanding track record marked by the number of high-profile publications (2 Nat. Comm., Nat. Microbiol., 2 PNAS, 2 PLoS Pathogens among a total of 15 and 4 reviews). The number of publications is commensurate to the size of the team.

The team demonstrates an outstanding record in securing intellectual properties based on the research results with six patents filed over the period.

The team demonstrates an excellent capacity to train early career researchers, reflected by the contribution of the trainees as first authors to the high-profile publications (5 of them).

It is worth noting the contribution of the team to the international Covid-19 research efforts. This is another indication of the relevance of the research area for a number of diseases, and the ability of the team to deploy their expertise and models.

The team has secured national funding (ANR, FRM and regional grants) and is part of a Labex network. The team leader contributes to the management of Institut Cochin and has received coveted distinctions in 2020 and 2021, and her work was recognized by CNRS Excellence award since 2018.

Weaknesses and risks linked to the context

The team may be small to deliver the ambitious research programme in a very competitive area of research. The funding at the international level is not evident.

The team has managed in an outstanding way the patenting and the publication of research, however the translational potential might become a weakness if the efforts to pursue this avenue may detract capacity from the outstanding basic research work.

Analysis of the team's trajectory

The planned projects build up upon the outstanding recent research of the team. The three main projects, NEUROPROTECT, MenVir, and EVCARD, are internationally competitive, EVCARD being the most novel project. However, it is likely that the other two projects will progress faster resulting in several high-quality publications. The focus on the interface between blood-brain barrier and viral infections is an excellent opportunity to expand the team's findings to other infections models. While the approaches and models indicated are sensible and sound, the team may benefit by considering scRNA seq approaches (this is particularly relevant for endothelial cells), and integrating spatial information in their analysis (for example tissue mass cytometry). Another area of interest for the team will be to collaborate with vascular physiologists to further investigate aspects of vascular function leveraging functional approaches.

RECOMMENDATIONS TO THE TEAM

The team needs to carefully plan how to increase its size to be in a position to follow in-depth the findings of their recent work. The size of the team is becoming a barrier to increase the impact of its work, and to make a step change in the research programme.

The recruitment will dictate the ability to deliver the ambitious and exciting projects. In case of any challenge, it is recommended to prioritize the *Neisseria*-related projects.

The team needs to carefully consider the pathway to translational research and whether this a priority path for them in terms of generating spin-out company.

While maintaining the national funding, it is recommended that the team leader focuses on securing international funding.

Team 10: Mucosal Microbiota in Chronic Inflammatory Diseases

Name of the supervisor: Mr Benoît Chassaing

THEMES OF THE TEAM

The scientific objectives of the team are mostly related to the evaluation of the deleterious effects of food emulsifier uptake. The team shed light to the cross talk between intestinal microbiota and the host due to reduced efficiency of mucus layer protective wall exposed to dietary emulsifiers. It also explored personalized medicine and nutrition approaches due to the knowledge of microbiota inter-individual variation.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No recommendation has been addressed for this team in the previous report since it was only created in 2018.

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	0
Sous-total personnels permanents en activité	**1**
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	**6**

EVALUATION

Overall assessment of the team

The overall assessment is outstanding.

The team obtained outstanding results published in numerous top-quality journals (Gastroenterology, Gut and Lancet), obtaining wide appeal for the public interest. The team leader's international recognition is underlined by the number of scientific conference invitations and the breakthrough of the team research into general dissemination journals.

Strengths and possibilities linked to the context

The scientific production of the team is extremely relevant in a specific and innovative field of investigation. It consists of 76 research articles, of which the team signed 16 as first or/and last author, and 23 reviews (19 signed as first and/or last author) or commentaries during the last 5 years.

The team can count on 3 postdocs and 2 PhD students, these last were able to obtain a total of 8 scientific publications, underling the ability to be extremely productive. The quality of the manuscripts is often outstanding published by high-ranking journals including Gastroenterology, Gut and Lancet. The techniques mastered by

the team allowed collaborations with external groups further highlighting the international reputation of the team. The main field of collaboration is represented by the possibility to culture intestinal microbiota using the Simulator of the Human Intestinal Microbial Ecosystem. International collaborations include the Kyoto Prefectural University of Medicine, the University of Pennsylvania, the Georgia State University, Montreal University and numerous others. Some ground-breaking discoveries significantly impacted the scientific and general opinion regarding the link between nutrition and chronic inflammation. General articles were dedicated to the team's results by The New York Times and The Guardian.

The numerous invitations of the team leader to international meetings and seminars (Spain, USA, Canada, Sweden, Belgium, UK, Austria, Norway, Czech Republic) highlight the international interest towards the team's field of investigation.

The team has been extremely successful in grant application, including ERC – Starting Grant (2019 – 2024, 1,850 k€), ANR (2022 – 2025, 540 k€), The Bill and Melinda Gates Foundation (2020 – 2022, 600 k€) and several others including the ANR – PRR Antimicrobial resistance that will grant team support in the next future (2021 – 2027, 3,000 k€). The team obtained more than 3,000 k€ from 2017 to 2022 and will be financially well supported until 2024.

Weaknesses and risks linked to the context

No major weakness is pointed out.

The growth of younger members of the lab and their road toward independence is perfectible.

Analysis of the team's trajectory

The team will relocate in 2024 at Institut Pasteur.

RECOMMENDATIONS TO THE TEAM

No recommendations are provided since the team will relocate in 2024.

Team 11: Epigenetics and nuclear organization in recombination and development

Name of the supervisor: Ms Julie Chaumeil

THEMES OF THE TEAM

The research focus of the team is to understand how genome/nuclear organization and conformation impact (i) gene expression during hematopoiesis, (ii) the process of V(D)J recombination, and (iii) the process of X chromosome inactivation. The team aims to study how defects in these mechanisms may lead to cancer and immune-related diseases.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team does not appear in the previous report. The team was created in 2016 when Dr Julie Chaumeil obtained an ATIP-Avenir grant. Dr Chaumeil obtained her HDR in 2022.

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	1
Sous-total personnels permanents en activité	**2**
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	**2**

EVALUATION

Overall assessment of the team

The overall assessment is very good.

The team has implemented sophisticated expertise in single cell 3D DNA/RNA-FISH and high-throughput chromosome conformation capture techniques. This remarkable effort helped the team to develop a number of national and international collaborations and be very successful in obtaining funding through partnerships. The team performance has been excellent as demonstrated by a recent publication in Science Advances and has great potential for future high impact contributions.

Strengths and possibilities linked to the context

The technological expertise developed by the team is clearly its strongest asset. Dr Chaumeil implemented single cell 3D DNA/RNA-FISH and high-throughput chromosome conformation capture techniques that allow her to establish fruitfully collaborations within the Cochin Institute's teams/facilities (3 publications with Imag'IC and 1 with Genom'IC) but also at the national and international levels (7 external collaborations).

This ATIP-Avenir team obtained additional funding through 3 partnerships at the national level (Plan Cancer, ANR, INCa) and from the ARC Foundation raising more than 600 k€ since 2017. The team recently published a high impact collaborative study in Science Advances in 2022 signing as co-senior author. The other five publications are signed as co-author but the team produced a review paper and has apparently several manuscripts in the pipeline. The team has been involved in teaching at the License and Master levels. The team has mentored one postdoc.

Weaknesses and risks linked to the context

The team size is small and has the ambition to tackle numerous projects in different competitive fields. Given its workforce it is difficult to remain competitive as a leader in all those topics at the national and international levels. The team is engaged in many partnerships which is excellent but dilutes its leadership. The team only presented a poster at an international meeting and has no activity as speaker through invitations and at meetings.

Analysis of the team's trajectory

The merging of the team with team 28 is the perfect next move as the two teams will complement each other and increase the workforce and may represent opportunities to develop innovation outputs. However, the proposed plan with the three axis appears very ambitious for the size of the future team and will likely rely on collaborative efforts.

RECOMMENDATIONS TO THE TEAM

An effort should now be made to play a more prominent role in the leadership on the projects which would in turn help gain in visibility for recruitments and speaker invitations to meetings. One way to go is to focus and push hard on one research topic to establish oneself as an international expert on the topic.

Now that the team PI obtained her HDR, recruiting PhD students through European networks would be a good way to reinforce the workforce of the team.

Team 12: Pulmonary and Systemic Immune Responses to Acute and Chronic Bacterial Infections

Name of the supervisor: Mr Pierre-Régis Burgel & Mr Frédéric Pène

THEMES OF THE TEAM

This team is specialized in bacterial infections of the respiratory tract and the mechanisms of defense against these infections. Its work focuses on two areas: immune responses during chronic bacterial infection in cystic fibrosis and bronchiectasis, and the mechanisms and consequences of sepsis-induced immune dysfunction (SIID).

The team operates on a continuum between fundamental science and clinical research, with a focus on two research axes. Firstly, they delve into immune responses during the chronic infectious phase in cystic fibrosis and bronchiectasis. This axis is further divided into two parts: the study of lymphoid neogenesis induced by bacteria and the phenotypic and functional heterogeneity of neutrophils in cystic fibrosis. The second axis examines the mechanisms and consequences of immune responses triggered by sepsis, and it is subdivided into three parts. This includes investigating the repercussions of sepsis in tumor development, understanding the role of antigen-presenting cells in the pathophysiology of SIID, and studying the impact of primary insults on lung defenses and of alveolar macrophages during this process.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous committee recommended giving priority to the most innovative aspect of the project and being mindful of international competition, particularly in areas such as epigenetics. The project should have revolved around the unique cohort of meticulously phenotyped patients and the top-notch clinical samples, establishing them as the project's cornerstone. In light of the achievements during the period, it appears that this was not the path chosen by the team.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**8**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	0
Sous-total personnels non permanents en activité	**2**
Total personnels	**10**

EVALUATION

Overall assessment of the team

The overall assessment of the team is very good to excellent as evaluated through the connection between experimental and clinical research. The very good scientific level and productivity are fulfilled by national grants funds.

Strengths and possibilities linked to the context

The human workforce of the team is led by clinician-scientists from pulmonology and critical care medicine backgrounds. All permanent researchers are professors and MCU, no full-time research scientist is represented in the team and only one technical personnel is permanent.

The solid reputation of the team is acknowledged through many expertise duties. Team members are engaged in editorial responsibilities as chief or associated editors in Respiratory Medicine and Research, European Respiratory Journal and Journal of Cystic Fibrosis. They participate to the Science Councils of the European Respiratory Society, Vaincre la Mucoviscidose association and in several research steering committees and learned societies, such as the French Cystic Fibrosis Reference Center network, Translational Research Committee of the French Intensive Care Society, French National Professional Council in Intensive Care Medicine and French Society of Pneumology. The visibility of the team can be positively evaluated considering the fact that members have been invited to present their research in 46 oral presentations, 31 of which were conducted in international meetings. On top of that, team members held chair positions in several French meetings: Congress Committee of the French Intensive Care Society, Annual national congresses "Réanimation" e-congress COVID-19 of the French Intensive Care Society. The team has been distinguished through the attribution of the Mid-Career Gold Medal by the European Respiratory Society in cystic fibrosis to the team leader in 2022. During the past period, 3 doctoral theses and 2 HDR (Habilitation à diriger des recherches) have been successfully defended.

The team has gained recognition through its success in competitive calls with significant fundings reaching about 1 M€ over the period, mainly provided by national agencies and charities. The PIs are coordinators of 2 ANR grants for a total amount of 370 k€. The team secured several foundation grants, among which Fondation Sauver la Vie, Fondation du Souffle, ARC, Vaincre la mucoviscidose (150 k€), Foundation 1O1. Funding (20k€) from Idex Université de Paris was obtained as well as from national and european learned societies, Société de Réanimation de Langue Française and European Society of Intensive Care Medicine (total 35 k€). The team benefit from Inserm to fund a doctoral fellowship (Poste d'Accueil, 100 k€).

The team has shown a very good level of scientific productivity. Between 2017 and 2022, they authored a total of 35 original articles, consisting of 12 dedicated to basic/translational research (1 of which were entirely from their own laboratory, 4 with internal collaboration, 7 with external collaboration) and 23 clinical articles (with 15 originating from their own lab). Out of these, 10 articles were co-authored by PhD students, with 5 of them serving as the first author (2 translational/scientific papers). Furthermore, the team contributed to 4 book chapters and produced 7 reviews, with one of the reviews being authored as the first author by a PhD student.

Concerning the networking with non-academic world, the team is mainly engaged in interaction with the French CF patient Association (Vaincre la Mucoviscidose). Although no industrial funding has been reported, team members conduct research activities with companies: prospective study to assess the performance of a point-of-care multiplex immune assay (BioMérieux), collaboration with the BioAster start-up that develops microfluidic devices. The team contributes to the dissemination of their research activities to society since members of the team participated to several TV or radiophonic programs about COVID-19 and cystic fibrosis and regularly hosts secondary and high school students.

Weaknesses and risks linked to the context

The team lacks permanent basic researchers as well as permanent technical personnel and there is a shortage of PhD students, which makes it difficult to publish in generalist high-ranked journals. Moreover, team members contribute very little to international conferences, especially students. All significant funding sources originate from French organizations. The team has little or no interaction with industry.

Analysis of the team's trajectory

The team members will merge with team 40, specialized in the study of neutrophils under physiological and pathological conditions. The project will therefore focus on the cellular and molecular mechanisms involved in systemic inflammation, capitalizing on their longstanding collaboration in cystic fibrosis research. This collaboration has recently yielded significant success in revealing the pivotal role of neutrophils in acute respiratory distress syndrome triggered by severe SARS-CoV-2 infection.

The future team's trajectory is proposed to be centered around three main objectives.

Aim 1 will delve into the role of PCNA in regulating neutrophil functions, encompassing the investigation of molecular and structural aspects of the PCNA-S1008 interaction in COVID-19 patients' neutrophils, profiling the PCNA interactome through proteomics in these patients, and exploring potential molecules with therapeutic promise. Furthermore, the team explores the partnership between PCNA and NAMPT, associated with the N1 to N2 transition in cancer, in lung cancer patients and murine models, collaborating with colleagues in Germany and Cochin Hospital.

Axis 2 will focus on studying long-lasting bacterial infections in the airways of patients with cystic fibrosis and bronchiectasis. By using the experience of both teams in handling mice models and patient samples, they want to understand how certain proteins in neutrophils work and see how drugs that target CFTR affect people with cystic fibrosis.

Axis 3 will explore how sepsis-induced alterations in the intestinal microbiota and gut epithelium may impact airway epithelium functions and contribute to compromised lung defenses.

This project amalgamates both fundamental and translational research to identify innovative therapeutic strategies.

RECOMMENDATIONS TO THE TEAM

The fusion of the team 12 with team 40 is an excellent decision as it will help strike a balance between clinical and fundamental research aspects. The new team should prioritize the pursuit of international funding and the attraction of candidates for recruitment into public research organizations and hiring permanent technical personnel. During the oral presentation, the team communicated the successful recruitement of a permanent scientist at INSERM who joined the team in October 2023.

Team 13: Cancer and Immune Response

Name of the supervisor: Mr Emmanuel Donnadieu

THEMES OF THE TEAM

The team works in the field of immuno-oncology, focusing mainly on T cell regulation and CAR-T cell production. Over the years the team has developed original mouse models and human experimental systems to dissect the interactions between T cells and cancer cells in the tumor microenvironment.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations were focused on the quality of the scientific production, better attraction of students and postdocs and better identification of project leaders within the team.

Based on the self-assessment document, the team has improved all aspects mentioned above.

Over the period of evaluation, the team has published 15 articles signed as first and/or last author in journals with excellent scientific reputation. The team has hired 5 postdocs and 9 PhD students. Each PI in the team is in charge of clearly identified projects with complementary expertise in human and mouse experimental systems.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**4**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	2
Doctorants	5
Sous-total personnels non permanents en activité	**9**
Total personnels	**13**

EVALUATION

Overall assessment of the team

The overall assessment is excellent to outstanding.

The excellent scientific contributions as well as technical breakthroughs in imaging of T cell activation, have made the team internationally recognized in the field. Given its expertise in cancer therapy and in particular in CAR-T cells, the team had an outstanding capacity to raise funds from national and international agencies and from private companies. The publication track record is excellent.

Strengths and possibilities linked to the context

The team works on long-standing central questions in onco-immunology, namely those that relate to the characterization of positive and negative mechanisms leading to an effective anti-tumoral immune response (including why T cells are frequently incompetent in colonizing and eliminating tumors, or how T cells and macrophages crosstalk in a manner that can be exploited therapeutically). The excellence of the scientific contributions of the team results from significative fundamental discoveries, e.g. the recent demonstration that TGFβ limits IFN-induced tumor regression promoted by pharmacological STING activation in spontaneous mammary tumors, as well as from technical breakthroughs in imaging of T cell activation.

The team has a good balance in human resources, with 4 permanent staff (3 researchers + 1 engineer) and 9 non-permanent staff (including 2 postdocs and 5 PhD students). The team has been reinforced in 2019 by a researcher (Inserm CRCN), contributing to strengthen the ability to produce CAR-T cells and assess their functions in mouse models. In the evaluation period, the team has recruited 5 postdocs and 9 PhD students (4 of which have defended).

The solid reputation of the team is acknowledged through many expertise duties. The team leader is engaged in editorial responsibilities as associate editor in The Journal of Immunology and topic editor at Frontiers in Immunology. The team members participate to national and international research steering committees, like Fondation de France "Cancer resistance to treatments", Fondation Association pour la Recherche contre le Cancer, Institut Pasteur external evaluation committee, AACR Combination Therapies Think Tank, Ligue Nationale Contre le Cancer, and local grant evaluation committees (University of Paris, Institut Cochin) and actively act in the "Adoptive Cell Therapy" working group of the French Society of Cancer Immunotherapy.

The visibility of the team can be positively evaluated considering the fact that members have been invited to present their research in plenary sessions or after abstract selection in national and international conferences, like International Cancer Immunotherapy Conferences, IO summit, EHA, Gordon conference, Collège de France. The team leader has organized 5 international meetings, including an European Association for Cancer Research, and a French Society of Cancer Immunotherapy annual workshop on adoptive cell therapy (College de France).

The team is internationally recognized in the field of onco-immunology. The team has strengthened its expertise in cancer immunotherapy by reorienting part of its activity towards the development and analysis of CAR-T cell functions. This choice was wise and has enabled the team to integrate into national and international consortia (most notably the inter-continental Cancer Grand Challenges NexTGen consortium, but also multicentric european projects, such as H2020 CARAT, IMI T2EVOLVE, and Era PerMed OptiCAN, and also at the national level: SIRIC-CARPEM, HTE PROGRAM), leading to an impressive ability to raise funds in recent years (868 k€ in 2021; 1 153 k€ in 2022). For example, International and European contracts have been obtained from NCI (UK), Horizon 2020 and MSCA, European Science Foundation, ARN ERA and DFG Funds. National funds have been raised from Inserm plan Cancer, INCA, PIA programs, and charities, ARC, Ligue contre le cancer, LLC.

The team has contributed to 50 peer-reviewed publications, including 15 articles in excellent journals led by team members - for which team members have signed as first and last authors (e.g. PNAS 2018, Cancer Immunol Res 2021, Elife 2021, Nat Commun 2019, Haematologica 2022). The remaining 35 articles were the result of the participation of the team in collaborative efforts with other teams within the unit or with external collaborators. All doctoral students who have completed their thesis figure as authors in published and submitted publications. The team has developed substantial and productive interactions with industrial partners. A partnership for the monitoring of HLA-G CAR T cells in human tumor explants has been established with Invectys, the amount of the contract is of 151 k€ and includes a Ph.D. student Cifre salary. Contracts with Roche-Genentech (197 k€) and Tollys (15 k€) have been engaged to evaluate new immune checkpoint combinations on non-small cell lung tumor biopsies and to detect p-IRF3 in FFPE tumor sections, respectively. In addition, 3 patents have been filled since 2017.

The team participates to the diffusion of scientific knowledge toward general public during the annual one-day manifestation "Feast of Science".

Weaknesses and risks linked to the context

Although overall scientific output of the team has improved during this evaluation period, a stronger dynamic was expected and should be an aim for the future, given the number of permanent scientists and secured funding. Lack of sufficient number of technicians and engineers for the size of the team has been recognized as a problem that needs to be tackled. The publication track record, although of high quality, could be improved.

Analysis of the team's trajectory

The team has strengthened its scientific production in recent years and consequently its international visibility. Moreover, it smartly reoriented part of its activity towards the development and analysis of CAR-T cell functions, which led to the team integrating different research consortia and showing a remarkable ability to raise funds. The team leader will move to another research structure in 2025/2026 and the team will be reorganized around the current PIs and a new PI who will join the team. The focus of the restructured team (to be renamed "Cancer Immunotherapy and cell reprogramming") will largely remain on tumor immunity and cancer immunotherapy. The team has delineated its scientific plans, which will make use of the expertise and interests of the 3 PIs, into two main research vectors: 1) To decipher the mechanisms of tumor progression and immune suppression, and 2) To identify immune components that may be exploited for therapeutic purposes and to test innovative therapies (namely related to epigenetic reprogramming of CAR-T cells, and inhibiting RINF or IL4L1). It is the impression of the committee that the team's goals, although well-defined and based on the recognized expertise of each PI, could be more ambitious, and better explore new research avenues and potential synergies arising from common interests between the three. This would most likely benefit the overall ability of the team to increase the impact of its research.

RECOMMENDATIONS TO THE TEAM

The team leader will move to another research structure and the team will be reorganized around the current PIs. Given that the current team leader is expected to leave the team in 2025/2026, it is of utmost importance that the new team leaders anticipate funding research needs that will allow them to fulfil their scientific goals. It is also important that the team tries to raise its publication output. For this, integration of more technicians and engineers may be critical, so that researchers do not need to spend as much time with non-scientific tasks. Perhaps more importantly, the team should attempt to articulate their future research program in a manner that is more integrated even if that implies exploring new topics that can arise from the common interests to the 3 PIs and not solely those that are within their "confort zone".

Team 14: Normal and Pathological Hematopoiesis

Name of the supervisor: Ms Michaela Fontenay

THEMES OF THE TEAM

Team 14 is specialized in the physiopathology of myelodysplasia (MDS) and acute myeloid leukemia (AML) exploring their molecular mechanisms through preclinical models and human samples aiming to find innovative therapeutics.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The main weaknesses highlighted in the last evaluation were the imbalance between the number of medical staff and scientists, the lack of recruitment of young scientists, particularly with a specific expertise on the topic, and the lack of visibility to the general public. The team has since recruited a CRCN Inserm and it is now composed of 3 PU-Ph, 2 MCU-Ph and 2 CR.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	**13**
Enseignants-chercheurs et chercheurs non permanents et assimilés	6
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	7
Sous-total personnels non permanents en activité	**15**
Total personnels	**28**

EVALUATION

Overall assessment of the team

The overall assessment is excellent to outstanding.

The team is internationally recognized in the field of acute myeloid leukemia and myelodysplastic syndromes, as evidenced by its high-level publications and the recognition of its members through invitations to conferences and membership of learned societies. The team's translational research is based on excellent complementarity between its medical and basic research staff, enabling research to be carried out from the patient's bed to the bench and from the bench to the clinic.

Strengths and possibilities linked to the context

The team operates at the intersection of clinical and basic science disciplines. The distribution of permanent and non-permanent positions is well-balanced, with 13 permanent members and 15 non-permanent members. However, when compared to the hospital-university staff, the team's contingent of basic scientists remains relatively small.

The team's research is organized around three primary areas: hematopoietic stem cell (HSC) biology, the pathophysiology of acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS), and the exploration of metabolic pathways in AML. Team members' expertise is adapted to the scientific and technological context (experts in mouse models, metabolism, genomics, bioinformatics, flow cytometry, cell biology and biochemistry). The institute provides all the necessary technical platforms (animal house, FACS, microscopy and bank of Biological resources which may help the team to validate on patient samples their initial data obtained on cell lines. The team benefits from an exceptional network of international collaborations. These collaborations include esteemed institutions such as Dana Farber and the National Institutes of Health (NIH) in the United States, as well as institutes in Japan and European countries, including Italy, the Netherlands, and France (specifically CRCT and IRSD in Toulouse, and Institut Jacques Monod in Paris).

Additionally, the team actively participates in French and European consortia (SFH, GFM, GDR, Micronit, EHA, MDS-RIGHT, i4MDS) and reviews grants for organizations like EHA (European Hematology Association) and ARC (Association for Cancer Research).

The team obtained a total of 2.7 million euros between 2017 and 2021. Most of this funding comes from European institutional sources (as partners in H2020), French sources (such as ANR JCJC, ITMO, SIRIC, LabEx), and associative sources (having received the LNCC and FRM labels). Approximately 10% of the funds come from industrial sources, and the team is affiliated with the Institut Carnot Opale.

Team 14 has demonstrated outstanding track records in terms of scientific productivity. Between 2017 and 2021, they authored a total of 152 original articles, including 110 devoted to basic/translational research (comprising 32 from their own laboratory, 6 in collaboration with colleagues of the Cochin Institute and 72 in collaboration with external partners). These publication journals consist of various titles such as Blood Journal, Haematologica, Leukemia, and the British Journal of Haematology. They are specialized journals with a notable impact on publications in the field. The team also published 42 clinical articles (26 involving external collaborations including New England Journal of Medicine). Notably, 92 of these articles were co-authored by PhD students, including 20 as first author. In addition, the team contributed a chapter to the WHO classification book and produced 23 reviews, 6 of which were co-authored by PhD students. Team members were invited to present their research at 8 conferences (including ESH lectures). Moreover, two team members have received the "Elsevier Innovation Prize" for the years 2020-2021.

During this period, 16 doctoral theses were defended, under the supervision of 10 different thesis supervisors. In addition, the team actively participated in educational activities, both at academic (M1, M2) and clinical level (ESH, MARIH, Hematology Day, DES). Furthermore, the team has established strong interactions with patient associations such as "Connaître et combattre la myelodysplasie". The team is involved in the EuroBloodNet network to explain the pathophysiology of this disease and have also participated in meetings on health democracy, where both patients and researchers discuss the consent process. All these achievements demonstrate the team's excellent reputation at national and European level.

Weaknesses and risks linked to the context

The number of industrial contracts represent only 10% of the team resources but recent participation in the Institut Carnot Opale should help weave this network with industry.

The team would benefit from refocusing its activity on fewer research axes or recruiting more full-time scientists.

Even if the team has recruited a CRCN the ratio basic scientists/medics is still low and will be lower in few years.

Furthermore, all oral presentations were given by PU-PH. It would be beneficial if students also gave presentations, and not just posters, at national or European conferences at least.

Analysis of the team's trajectory

The team has refocused its research on 3 aspects: the metabolic adaptation of AML/MD, the post-translational mechanisms involved in the inefficient erythropoiesis of MDS, and targeting the tumor microenvironment. The projects are solid, based on the expertise already in place in the laboratory; one small downside is that the immunotherapy part, although of good quality, is difficult to link to the other projects. The number of people involved in each project needs to be taken into account, as it may seem insufficient in some areas.

RECOMMENDATIONS TO THE TEAM

The team must continue its excellent work, trying to recruit a young CR and translate its basic research data into preclinical applications. The team should also encourage students to participate in the meeting through oral communication.

Team 15: Phagocytes and Cancer Immunology

Name of the supervisor: Ms Julie Helft

THEMES OF THE TEAM

The research led by the PI focuses on deciphering how mononuclear phagocytes (macrophages and dendritic cells) control and regulate adaptive T cell immunity with a focus on tumor immunology. In 2017, after spending 9 years in the US and UK, the PI has been recruited as a "Chargée de Recherche" at Inserm in France and started a research group in the immunology department of Institut Curie, Paris. There, she developed projects on the development and function of tumor-associated phagocytes in breast cancer. She published 3 studies as a senior author: in Immunity (2020), Cell (2022) and in Nature Cell Biology (2023). The team, Phagocytes and Cancer Immunology was created in September 2021, following an open international call for new team leaders at Institut Cochin in 2020.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Not a team before.

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	0
Sous-total personnels permanents en activité	**1**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	0
Sous-total personnels non permanents en activité	**2**
Total personnels	**3**

EVALUATION

Overall assessment of the team

The overall assessment is outstanding.

Despite the recent creation and the still small size of the team, the PI has made important contributions on the role of tumor-associated macrophages in tumor immunity and immunotherapy, with an outstanding scientific production. In particular she identified a FOLR2+ tissue-resident macrophage population with good impact on patient outcome (Cell 2022) and reports cancer-induced distal reprogramming of myelopoieseis of the bone marrow (Nature Cell Biology 2023). In 2023, the PI was awarded the ERC consolidator grant by the European Research Council.

Strengths and possibilities linked to the context

The team has an outstanding performance in term of attractiveness:

The team leader has built a solid network of collaborators in France and abroad (UK, USA, Singapore, Japan, Israel, etc.). She published 3 papers as a senior author in major journals in the last 4 years: Immunity (2020), Cell (2022), and Nat Cell Biol (2023).

The team leader has been repeatedly invited as plenary speaker in international conferences (x4: PIO, CIMT, ITOC, Keystone Symposia), as keynote speaker in 2 scientific retreats and 4 national symposiums and as invited external speaker in French research institutes (x6).

The team leader expertise is solicited by French and European funding agencies (ERC, ANR, etc.) and by peer-reviewed international high impact journals (Nat Immunol, Science Immunol, Nat Comm, etc.). She participates regularly to PhD (x7) and HDR committees (x3).

The team leader organized various workshops (x2) and international meetings (x3) including: DCBIOL (Marseille 2017), EMDS (Marseille 2019), CFCD (Paris 2021, Bordeaux 2023). JH is also the treasurer of the "CFCD" since 2018. The team has hosted national and international PhD students and postdoctoral fellows (5 nationalities) supported by competitive fellowships from French doctoral schools, and associations/ foundations.

During the period from 2017-2022, JH has received 884 k€ euros in funding mainly as coordinator from: ANR Jeune Chercheuse (ANR JCJC, 179k€), Fondation ARC (100 k€), Ligue Contre le Cancer (85k€), I Curie (80 k€), INCa (440 k€). In 2023, JH was awarded the ERC consolidator grant. This grant will fund her research for the next 5 years.

The scientific production is outstanding, the PI published 11 original publications during the period including 4 signed at leading positions (first, last or co-last positions) including 11 prestigious reviews. Three articles were internal to the team (Immunity 2020, Cell 2022 and Nature Cell Biology 2023), 10 research report were published in collaboration with the Institut Curie (3 different teams) and 4 publications were produced through external collaborations. The team published also 4 papers among which papers in Cell, Cancer Immunol Res. It is of note that one PhD student is first author of the Nature Cell Biology (2023) and 2d author of the Cell publications (2022). One postdoctoral fellow and one bioinformatician scientist are co-first authors of the Cell publication (2022).

The contribution of the research activities of the team to the society is also significant. Indeed, the team has filed an international patent exploring the therapeutic benefit of targeting FOLR2+ macrophages. The PI received a "booster grant" from Fondation Carnot to generate the first proof-of-concept experiments. In 2021, t patent has been presented to Argobio Studio, a start-up dedicated to novel therapeutics.

The team has also been active by presenting the work to the lay public charity members of Institut Curie (2018), participated in the "Fête de la Science" open doors event at Institut Cochin (2022), and welcomed students through the "Apprentis chercheurs" association.

Weaknesses and risks linked to the context

There is no real weakness. The small size of the team may represent a weakness as the scientific expertise will rely on the PI herself and an ITA. A potential threat is the issue of space in Institut Cochin since the team will increase in size. At the moment, offices can only accommodate 5 persons but will comprise up to 10 persons in January 2024. The team needs more senior scientist/personnel participating in the lab management and perpetuating the lab expertise.

Analysis of the team's trajectory

In 2025, the team will be composed of the team leader (CRCN Inserm), 3 PhD students, 2 postdoctoral fellows, 1 Bio-informatician and one technician (ITA CNRS). The team has also been approached by a PUPH (Vice Doyen de l'UFR de Médecine de l'Université de Paris), who wishes to integrate the team together with a PhD student for the next Inserm mandate to develop a project focused on the role of dendritic cells in the Langerhans Histiocytosis disease.

The team will pursue its identification of a FOLR2+ tissue-resident macrophage population located in perivascular regions in close contact with CD8+ T cell and with good impact on patient outcome (Cell 2022). CD8 T cells engage in long-lasting interactions with FOLR2+ macrophages in human breast cancer.

The lab has developed a research program to address the hypothesis according to which FOLR2+ macrophages locally shape the compartment of tumor-infiltrating CD8+ T cells. Mechanistically, they will address if FOLR2+

macrophages spark local CD8+ T cell responses directly, by interacting with T cells or indirectly, by fostering lymphoid aggregate formation including perivascular lymphoid aggregates (PVLAs) and tertiary lymphoid structures (TLS). They will explore innovative immunotherapy approaches targeting FOLR2+ macrophages to promote tumor-specific T cell responses.

The program is divided in 3 axes:
Axis 1. To characterize the FOLR2+ macrophage-perivascular niche: this will involve tissue-imaging and an unbiased high-dimensional analysis of T lymphocyte states and niche cellular components.
Axis 2. To evaluate the role of FOLR2+ macrophages in controlling CD8+ T cell responses against tumors. This will be performed in vivo in mice using mice selectively deficient in FOLR2 in Macrophages through a double conditional control of the DT receptor under the Folr2 and Csf1r/MCSF-R promoters (Folr2iCre x Csf1rlox-STOP-lox-DTR).
Axis 3. To decipher the role of FOLR2+ macrophages in the organization and maintenance of tumor associated lymphoid structures. They will target in mouse model the lymphotoxin beta receptor (LTbR) in FOLR2 TAM.

The team leader got the ERC consolidator grant to pursue this project. The project is clearly detailed, with all technologies and model well described. They already have developed and validated a new mouse strain (Folr2-IRES-iCre: Folr2iCre strain) Folr2iCre mice expressing the CRE recombinase under the promoter of the Folr2 gene. They will be crossed to the transgenic Csf1rlox-STOP-lox-DTR mice.

Altogether, the team has the financial and human resources and expertise to conduct this project.

RECOMMENDATIONS TO THE TEAM

This an outstanding team. No specific recommendation, except to keep focus on the original projects, especially if the team is joined by the PUPH researcher.

Team 16: Dendritic cells, immunostimulation of the viral and tumoral microenvironment

Name of the supervisors: Ms Anne Hosmalin & Mr Rémi Cheynier

THEMES OF THE TEAM

The team encompasses immunologists and medical researchers working on a wide range of topics related to dendritic cell functions. They study immune control of viral infections, in particular HIV-1, SARS-CoV-2, yellow fever and JC virus, as well as cytokine functions and their potential therapeutic uses. A new checkpoint inhibitor of melanoma is under investigation, IL4-I1.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous committee made a few recommendations to the team. The first recommendation was to continue to focus on the publication of results in renowned journals. The performance of the team in the current period has followed this recommendation notably through their publications in Critical Care and J. Immunol. The second recommendation was to take care of having a clear and focused research direction. During the current period, the team has continued to explore different and remote research topics (melanoma, HIV, IL7, SARS-CoV-2, yellow fever, IL4I1…), which are handled by several subgroups in the team.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	3
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**14**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**4**
Total personnels	**18**

EVALUATION

Overall assessment of the team

The overall assessment is excellent.

The team has made outstanding contributions to the field of immunology. The team had excellent to outstanding success in raising funds to support research. The team has a very good to excellent publication record with 57 publications, of which 20 are first or last author. In terms of training through research, the team has a very good to excellent output with 9 PhD students trained. The team has excellent to outstanding international visibility through participation in major congresses and scientific societies.

Strengths and possibilities linked to the context

The team has successfully combined basic and clinical research, as evidenced by the patient cohort (INTESTIPAX, MYELOID-COVID, IMMUMELA, ENZYMELA and ANRS-Immunovir study) and the scientific articles generated during the reporting period. It has a very good to excellent publication record and published 57 scientific articles, 20 of which as first and/or last author. Most publications are in medium- to high-profile journals including J. Immunol. Critical Care and Front. Immunol.

The total production is divided equally among the different members and includes the team leaders, researchers, PhD students and technical staff. All PhD students who defended their thesis during the evaluation period published at least one article, but more often between 2 to 6.

The team has an excellent to outstanding success in obtaining grants through competitive calls. During the period 2017-2022, the team raised 1.9 M€ from 11 national grants (ANR, ANRS, AVISEAN, INCA PLBIO) of which 9 as coordinators, two private industry grants (SILab, ViiV healthcare) and 14 grants from patient associations or scientific societies ("Fondation pour la recherche médicale", "Ligue de recherche contre le cancer", "Association pour la recherche sur le cancer", etc.). Team members put together applications for the unit and obtained grants to fund state-of-the-art flow cytometers, including spectral and acoustic flow cytometers (ANRS, SiricCarpem, ITMO Cancer, 550 k€).

The team has excellent attractiveness and scientific reputation, as evidenced by numerous participations and invitations to congresses and academic and international meetings: 19 presentations during the evaluation period, 14 chairs in congress for one team leader. In addition, an EMBO workshop was organised at the Institute (2019) and another in Shanghai. (2018). PhD students have presented their work at congresses (posters and oral communications) and several have been involved in the functioning of the Doctoral School and two were president of the JECCO (Young Institut Cochin researchers). The team's researchers are members of numerous academic associations and steering committees: the team leader was president of the Coordination Action 31 of ANRS, member of the board of the Federation Biogée and the Fondation ACTERIA, the team co-leader is member of the steering committee of the Infectious Disease Models and Innovative Therapies (IDMIT) infrastructure at CEA. The team was involved in the management of the unit; the team leader was Director of International Affairs and member of the Direction board and became Director, Immunology and Immunopathology IHM, Université Paris-Cité..

Weaknesses and risks linked to the context

Two teams merged in 2017 leading to the formation of the "Dendritic cells, immunostimulation of the viral and tumoral microenvironment" team. The team consisted of up to 14 scientists, including medical (3) and basic researchers, who formed many subgroups. There has been a multiplication in the number of remote topics because of the size and composition of the team.

Three postdoctoral researchers had no publications accepted as first author at the end of their contract: two because of late start of the ENZYMELA cohort due to the Covid crisis, the other one has three posters as first author.

The main weakness of the team is the retirement of both team leaders, which will lead to the dismantling of the team, even though the repositioning of subgroups has been considered and planned.

Analysis of the team's trajectory

The team will be discontinued, so no trajectory is given.

RECOMMENDATIONS TO THE TEAM

The team will be discontinued, so no recommendations are given.

Team 17: Mucosal Inflammation and Immunity

Name of the supervisor: Ms Molly Ingersoll

THEMES OF THE TEAM

The team Mucosal Inflammation and Immunity, headed by M Ingersoll, was created in Sep 2021, following an international call from I Cochin in 2020. Prior to September 2021, Dr Ingersoll headed a group at the Pasteur Institute.

The team is interested in understanding mucosal immune responses in the bladder in response to infection and cancer immunotherapy. They are investigating the innate immune response to infection at early bacterial exposure and adaptive immune response months after infections.

As uropathogens are increasingly multidrug resistant, their work focuses on immunomodulation to develop non-antibiotic-based immunotherapies for urinary tract infection.

The team is also interested in understanding the mechanisms of action of immunotherapy for bladder cancer.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was created during the present evaluation period.

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	0
Sous-total personnels permanents en activité	**1**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	1
Post-doctorants	2
Doctorants	3
Sous-total personnels non permanents en activité	**7**
Total personnels	**8**

EVALUATION

Overall assessment of the team

The overall assessment is excellent to outstanding.

This recently established team performs original research on mechanisms at the bases of bladder pathology, with broad applications to mucosal immunity, antimicrobial resistance, infection and cancer.

Considering the relatively small size, the team has had an excellent to outstanding scientific production with several original observations published in top-ranking specialty journals.

Strengths and possibilities linked to the context

The team Mucosal Inflammation and Immunity is a young team created in September 2021, following an open international call for new team leaders at Institut Cochin in 2020. Prior to September 2021, Dr Ingersoll headed a group at the Institut Pasteur.

The team has an outstanding performance in term of attractiveness as judged by its international recognition as illustrated by the number of invitations to present at seminars and conferences (>60), the funding level (see below), the number of foreign applicants (the team is only 30% French) and quality of its collaborations (Singapore, Switzerland, USA, UK, Sweden, as well as France) supported with personnel exchanges and the participation in thesis defenses in all over Europe (n=10), Australia (1) and France (10).

The team is well funded, in the period from 2017-2022, the team leader has received 1,820,000 euros (including an American research foundation for Bladder Cancer, 2 collab with a Swiss company, 4 ANR of which 2 as coordinator) and is funded until at least December 2026.

The establishment of the team at Institut Cochin offers opportunities for new collaborations internal to the institute (teams 22 and 10), and access to qualified staff in the technological core facilities.

Post-doctoral fellows and students from the team have several publications: a PhD student graduated in 2020 has published 6 articles including 3 as 1rst author (1 original, 2 reviews). A second year student is 1rst author in a review and a Post-doctoral fellow published 5 articles including 2 as 1st author.

The team is rather small but the research subject is a unique niche, with broad applications to mucosal immunity, antimicrobial resistance, infection and cancer. Compare to its size the team has an excellent publication level with several original observations in recognized specialty journals (Sci Immunol. 2023, ACS Nano 2021, Sci Adv. 2020, J Immunol. 2020, JCI Insight. 2019) and reviews in Nat Rev Urol. (2018, 2019, 2020, 2022, 2023). In particular the team identified the importance of sex differences in urinary tract infection with a key role of IL-17 and in T cell infiltration in bladder tumor-bearing mice. They further described the role of distinct resident macrophage subsets and Tissue-resident memory T cells in mucosal immunity against recurrent urinary tract infection. The team is also involved in vaccine strategy allowing to preserve bacterial antigenicity. In total, the team has published: 11 papers internal to the team but no papers with external collaborations.

Interaction with the clinic is mentioned with the access to cohort of bladder cancer patients. As the team gains recognition, they are now contacted by groups seeking to collaborate, including companies having products for bladder diseases. The team has been supported by a private research foundation (Albert Institute for Bladder Cancer Care and Research). The team has no patent but has collaboration with a Swiss company (Collaborative Research Agreement, OM Pharma) to understand the mechanisms of action of a commercially available drug to prevent recurrent urinary tract infection. All research tools produced by the team are available and their marked UPEC strains have been disseminated all over the world for research use. The team participated to several lay public activities for science dissemination (I Cochin open doors, Pint of Science, YouTube "tête-à-tête").

Weaknesses and risks linked to the context

Beside the expression of scientific independence, the move to the Institut Cochin was in part motivated by the objective to strengthen the link with the clinic but the strategy to reach this objective may need to be consolidated. The originality of their work in mouse with the developed models would really benefit from complementing lines of investigation in human.

The small size of the team may clearly represent a weakness as the scientific expertise will rely on none permanent members, the recruitment of at least one permanent researcher and/or Lab manger will be critical. To overcome this weakness, actions are ongoing with a seignior postdoc in the team currently applying for a permanent position in CNRS/Inserm.

The team space is also a threat and there is a need to increase lab space.

The objective is to develop innovative immunotherapy solutions for multidrug resistant uropathogens however the team has generated no patents in this area, a step that will be needed to reach the stage of clinical application.

Analysis of the team's trajectory

With current funding in place, the team should be 2-3 postdocs, 2-3 PhD students, an engineer, a technician, and master's students. Visiting PhD students will be encouraged.

For the next two years, the team will continue to build on knowledge they have developed, including the immune response to urinary tract infection (UTI), the influence of sex as a biological variable in immunity, the role of macrophages and T cells in bladder immunity, and the response to nonantibiotic based therapy or immunotherapy.

This continuation is logical however the described approaches for most of these objectives are quite generic and do not really allow a precise evaluation, furthermore there is, a priori no description beyond the next years.

RECOMMENDATIONS TO THE TEAM

The team needs to develop a strategy of recruitment for scientist and lab-manager and in parallel obtain from Institut Cochin the space needed for their development.

The strategy of the team to develop more translational research in human may need to be consolidated.

To reach their objective to develop innovative immunotherapy solutions for multidrug resistant uropathogens the team will need to generate patents that will be required to reach the stage of clinical application.

Team 18: Functional Pharmacology and Pathophysiology of Membrane Receptors

Name of the supervisors: Mr Ralf Jockers & Ms Julie Dam

THEMES OF THE TEAM

The overall theme is G protein-coupled receptors (GPCRs) pharmacology (and more recently leptin receptors), their biology and therapeutic potential in obesity and type 2 diabetes (T2D), as well as other metabolic diseases including a link to the pathophysiology of Alzheimer disease. The group utilizes expertise in BRET, TR-FRET technologies, and biosensor development. During the Covid pandemic the team has explored the novel actions of melatonin and its derivatives in the context of COVID-19 infection.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The number of PhD students supervised in the group has grown to 9 over the last 6 years, addressing one of the recommendations originating from the previous review.
The team had been further recommended to increase the diversification of their research themes, beyond melatonin receptors. This has been achieved by the team, which has diversified to a new receptor (leptin) as well as novel connection to diseases. It appears this effort may have somehow overshoot, leading to a very diversified portfolio (six project lines), especially in terms of the wide array of diseases being addressed (from diabetes to Alzheimer's disease). The panel advises in favour of prioritising two or three lines, possibly pivoting on intramural collaboration with any of the Cochin teams addressing metabolic disorders.

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	5
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	**6**
Enseignants-chercheurs et chercheurs non permanents et assimilés	4
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	**7**
Total personnels	**13**

EVALUATION

Overall assessment of the team

The overall assessment is excellent-outstanding.

Strengths and possibilities linked to the context

The research group's publication record has a principal focus on Melatonin Receptors, a traditional area of expertise of the team, now extended GLP1R, the orphan GPCR (GPR50) and an incursion in molecular studies

about Covid-19 cellular entry via ACE2 receptors. This approach heeded the recommendation to diversify the repertoire of GPCRs made in the 2017-18 review.

The team has had an output of 43 primary research manuscripts, an average of 7 (rounded by defect) primary research manuscripts per year. Of these, an average of 2 manuscripts per year over the whole team are in prestigious journals, such as Nature Communications or Nature Metabolism.

The team's commitment to collaboration and interdisciplinary research is commendable. The organization of international conferences and active involvement in networks and institutions showcases the team's dedication to fostering scientific cooperation. Examples are the i-GPCRnet International Research Network or participation in COST Action 18133.

The teams has been able to secure substantial funding (3.2 M€) in the last funding period, meaning 530 k€ of funding per year, averaging to 88 k€/year for each of the 6 permanent members of the team. The group has a broad portfolio of projects funded by national and international funding agencies (ANR, Horizon2020), as well as by the private sector (since 2017, 4 industrial contracts were established (Servier, Sanofi, Calixar)).

The diversity of research topics within the group reflects their ability to address a wide range of scientific challenges, increases the resilience of the team, and addressed positively the recommendation from the previous funding period. However, the diversification process may have somewhat overshoot (please see Weaknesses and risks).

Engaging graduate and undergraduate students in research activities is a positive aspect of the team's work. The number of PhD students supervised in the group has grown to 9 over the last 6 years, again addressing one of the recommendations originating from the previous review.

The group has a good number of international visiting researchers (9 international visiting students, PhD students, postdocs and scientists), and is able to maintain its average size (~15) thanks to effective recruitment of 9-10 non-permanent researchers.

Weaknesses and risks linked to the context

While the scientific output is robust, and the number of publications large, for a team of average size 15 working on 6 major project lines this may create an issue of dispersion of energy, limiting what could potentially be a higher impact in each of the specific lines.

The group conducts several 'platform' activities, e.g. screening gene mutations via high-throughput plate reader assays exploiting, for instance, their biosensor palette. In this context, maintaining a technological edge to remain highly competitive appears important, either by a strong integration with the technology platforms (e.g. the microscopy platform) or by external collaborations with groups developing new methods.

The absence of a permanent engineer or lab manager is indicated as a cause for loss of technical know-how. While this aspect is appreciated, and it would be beneficial that a permanent lab technician be hired, nonetheless it would be helpful for the team to delineate and implement strategies for retaining such know-how: albeit not involved in day-to-day technical activities, the permanent staff (6) should be able to appropriately train non-permanent members of staff, avoiding or at least minimising knowledge drain.

Analysis of the team's trajectory

The research group has demonstrated consistent growth and achievements over the years. They have made significant contributions to the fields of receptor biology, GPCRs, and therapeutic potential in obesity and type 2 diabetes. The group's research trajectory reflects a commitment to excellence and innovation, as seen in their recent work on the orphan GPCR and the role of melatonin in COVID-19. Their ability to adapt to emergent research areas, and establish international collaborations has contributed to their success.

RECOMMENDATIONS TO THE TEAM

Implement a prioritisation and focusing strategy over the next evaluation period, ideally pivoting on intramural collaborations.

Explore investing in developing novel technologies: given the competitiveness of the research field, approaches need to be pursued by the team to maintain a technological edge over competitors addressing similar topics.

Address Technical Support Needs: Devise a plan for know-how preservation even in the absence of a permanent technician.

Team 19: Biology of Plasmodium Transmission

Name of the supervisor: Ms Catherine Lavazec

THEMES OF THE TEAM

The team studies the biology of sexual stages (gametocytes) of the major human malaria-causing parasite *Plasmodium falciparum* and its impact on erythropoiesis.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations of the previous report were the following:
- The recruitment of more PhD students and postdocs to compensate the small size of the team: during the reporting period, 1 postdoc and 6 PhD students have joined the team and 3 have completed their PhD;
- The lack of European grants and industrial funding: the team has secured national funding (ANR, CNRS, Labex, etc.) over the reporting period but still neither European grants nor industrial funds have been obtained.

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	1
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	**3**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**4**
Total personnels	**8**

EVALUATION

Overall assessment of the team

The overall assessment of the team is excellent to outstanding in terms of invitations to congresses.

The team has advanced expertise in the biology of Plasmodium and erythropoiesis with several national and international collaborations. The scientific production is excellent to outstanding regarding the small size of the team. The capacity to raise grants is excellent to outstanding. The attractiveness regarding PhD training is excellent: three students have completed their PhD thesis; all are co-authors in published studies. 3 PhD students are still in the team.

Strengths and possibilities linked to the context

The team has an excellent to outstanding publication record in *Plasmodium* and erythropoiesis with some published in well-known journals (e.g. Blood, Scientific reports, eLife, Nature Medicine); 21 publications and 7 reviews were published over the reporting period; this is remarkable regarding the small size of the team.

The team has excellent complementary scientific skills on the one side on parasitology and on the other side on erythropoiesis; complementarity works really well.

The team notoriety at the national and international levels is attested by the four international PhD students/postdocs (Ivory Coast, Italy, Brazil, Greece). In addition, the team hosted four visiting students or visiting scientists from international laboratories (Cagliari, Canada; Abidjan, Ivory Coast).

The team is involved in training through research (1 postdoc, 6 PhD students and 8 undergraduate students).

The team is part of two Labex (*Parafrap* and GR-Ex) and has an excellent to outstanding funding ability from national organizations for a total of 1,040 k€ (FRM: 448 k€; "Fondation de France": 120 k€; ANR: 101.8 k€; CNRS: 70 k€; Labex GR-Ex: 298 k€; Labex Parafrap: 185 k€, etc.).

The team has developed several collaborations at the national (CNRS Montpellier (student exchanges, 2 grants, 3 publications); CNRS Roscoff (1 grant, 1 publication), Cimi Paris (4 publications), IRD Paris (student exchange, 2 publications), Erytech Pharma (1 service contract, 1 publication)) and the international levels (Ivory Coast (student/postdoc exchange, 1 grant); Italy (postdoc exchange, 1 grant, 1 publication); Spain (student exchange, 1 publication); Germany (student exchange, 3 publications).

The reputation of the team leader is outstanding in the field. She was invited to give 13 seminars at main conferences in the field such as Gordon Research Conference "Red Cells", Newport, USA (2017); ASTMH Annual Meeting, Washington, USA (2019); Gordon Research Conference "Malaria", Les Diablerets, Switzerland (2021, cancelled); Singapore Malaria Network Meeting, Nanyang University, Singapore (2022); Gordon Research Conference "Red Cells", Newport, USA (2023) or was invited to renowned Institutes: Melbourne University, Australia (2017); Instituto de Medicina Molecular, Lisbon, Portugal (2018); 38e Congrès de la Société Française d'Hématologie, Paris, France (2018); Heidelberg University, Germany (2018); London School of Hygiene and Tropical Medicine, London, UK (2020); University of Pennsylvania, Philadelphia, USA (2021); Swiss Tropical & Public Health Institute, Basel, Switzerland (2021); European School of Hematology, Paris, France (2023).

The team leader has organized two international conferences: Conference on Plasmodium vivax Research, Paris 2019, EMBL conference: Biology and Pathology of the Malaria Parasite 2021.

Weaknesses and risks linked to the context

The size of the teams is still small, although they were able to attract several PhD students and postdocs.

The capacity to raise funding at an international level is not yet demonstrated.

Analysis of the team's trajectory

The team's trajectory is well described and focuses on the interactions of *Plasmodium falciparum* gametocytes with erythroid cells.

3 main axes are described:

1) the characterization of erythroblast infection by *Plasmodium falciparum*;

The feasibility of the project is in part supported by one grant from the Labex GR-Ex and one International Emerging Action from CNRS;

2) the elucidation of how *P. falciparum* infection affects erythropoiesis; this is partly funded by one grant from the Labex GR-Ex and one from the Labex Parafrap;

3) the elucidation of how *P. falciparum* parasites modify the mechanical properties of infected erythrocytes; this is partly funded by ANR and the "Fondation de France".

Altogether, all aspects of the project are strong and well thought in terms of funding.

RECOMMENDATIONS TO THE TEAM

The team needs to continue its excellent scientific output.

The team should put efforts in attracting talented postdocs so that they can compete for researcher positions in order to increase the team's workforce.

Team 20: Immunology of diabetes

Name of the supervisor: Ms Agnès Lehuen

THEMES OF THE TEAM

The team has focused on immunology and genetics of metabolic diseases (type 1 diabetes, type 2 diabetes, obesity, liver diseases associated with metabolic diseases) based on their expertise in the immunological mechanisms of autoimmune and inflammatory diseases, through mouse models, human genetics and access to cohorts of well-characterized patients.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations of the past evaluation in 2019 were that the team should continue to maintain their level of excellence. It was also suggested to strengthen the collaboration of the different team leaders to address issues related to genetic regulation of MAIT cells and ILC. The team was also encouraged to work toward licensing their patents.

The team was suggested to maintain its organization and life in order to secure the level of excellence they have reached. Regarding the scientific strategy it was recommended to continue to understanding the functional and pathologic reciprocal role of distinct immune cell types in T1D i.e. pDCs and neutrophils, with special reference to the study of MAIT cells and ILC in the pathological cascade. Similarly, it was recommended to clarify the relationship of MAIT cells and ILC in the pathogenesis of low grade inflammation in T2D. These approach for T1D and T2D would clarify the phenotype and functions of these immunotypes under distinct milieu.

Overall, the team has addressed the recommendations of the previous report and will continue to maintain their level of excellence in understanding the functional and pathologic relationship between distinct immunotypes in T1D, pDCs, neutrophils, with special reference to the role of MAIT cells and ILC in the pathological cascade. Further the team will continue to unravel the role of MAIT cells and ILC in the low grade inflammation underlying T2D.

The team has realized important interactions with industries (big pharma and biotech-companies) therefore It would be important for its scientific output to continue to work toward licensing their 5 patents. The team has continued to maintain a high level of organization and internal collaboration.

The team should hire more postdoctoral fellows to develop its research.

Due to permanent staff retirement it would be important to clarify the PI responsible for scientific and administrative supervision of the team's activities.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	4
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	**12**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	13
Sous-total personnels non permanents en activité	**15**
Total personnels	**28**

EVALUATION

Overall assessment of the team

The overall assessment is outstanding.

The team has outstanding recognition, reputation, and scientific production in the field of the immunology of diabetes with very good interactions with the non-academic world.

Strengths and possibilities linked to the context

Team members are strongly involved in European scientific research community. They are experts in immunology and genetics of diabetes and metabolic diseases through international collaborations. This is shown by 2 European Reserch Council grants (Exant and Innodia), two international ANR grants with Germany and Switzerland, two European Grants from European Foundation for Study on Diabetes (EASD) and an International Juvenile Diabetes Foundation (IJDRF) grant (with two Finnish laboratories as partners). The team outstanding expertise is demonstrated by regular presentations to international meetings and conferences (95 presentations in total over the team period of evaluation). The team received 38 regular invitations to international meetings including 23 conferences in Europe, i.e. Cell Symposia (Basel), Agean Conferences in Autoimmunity and on Immuno-Metabolism (Greece). The team was awarded 12 projects funded by competitive grants (national/international, see above). Funding acquisition covered the salaries of 5 postdoctoral fellows, 7 PhD students and 7 engineers. Five PhD students were awarded PhD fellowships from the French Ministry of Research and Inserm-MD-PhD program.

Ten international and European meetings were organized including the EASD annual meeting (2017-2022) in Oxford, meeting on unconventional T cells in Oxford (2019) and Goteborg (2021). Team members are involved in several international/European committees such as EASD scientific committees including the jury for EASD prize, French speaking Foundation for Research in Diabetes (FFRD), European Society for Pediatric Endocrinology (ESPE). Team members are involved in master programs hosting European students as well as European research teaching programs and have participated to 11 PhD thesis defenses in European universities. The laboratory hosted 10 foreign/European students and fellows through international fellowship programs.

The team was awarded as Foundation for Medical Research (FRM)-labelled team and has been selected to be part of the Inserm network on Microbiota (PTM) and of Paris-Toronto University network.

60 publications were produced over the last 5 years including in highly cited journals as first/last author or collaborator including Nature Immunology, Nature Communication and Nature Medicine. The diffusion of the results of the team is also achieved through review articles published in leading journals at the request of their editorial boards (14 reviews including one in Nature Reviews in Immunology and an editorial in Nature Immunology).

Due to its regular recruitment of PhD students, fellows and engineers, the team has maintained a high level of scientific production through excellent supervision of young researchers, students and young engineers in their projects. The high motivation of all team members is also achieved by encouraging them to present regularly their projects and results not only internally but also at national and international meetings including European conferences Cell Symposia (Basel), Agean conferences in Autoimmunity and on Immuno-Metabolism (Greece). Altogether, this allows young researchers and engineers to produce a good level of scientific production (18 original articles and 9 reviews signed as 1st or 2nd author). Lastly, the team obtained the recruitment of a postdoc to an Inserm permanent position in the team.

The team members regularly write highlights addressed to sponsors, donators, politicians and patients. Research dissemination is realized to communicate to patient's associations i.e. Aide aux Jeunes Diabétiques (AJD) which granted research grants and FFd participating in the life of the association. The team interacted closely with several industrial partners (big pharma and biotech-companies) throughout its consortia. The team obtained 5 international patents. The team participates in 15 national and international industrial expert boards, including scientific committees to support the implementation of clinical trials in diabetes (phase 2 and phase 3). The team also developed new scientific collaborations outside of diabetes field, and discussions are on-going to attract investors.

A member of the team is fellow of the Royal Academic of Medicine of Belgium.

Weaknesses and risks linked to the context

An absence of postdoctoral fellows has been noted.

Analysis of the team's trajectory

The team has longstanding experience in investigating the innate and adaptive immune system in the development of metabolic diseases using human samples from well characterized cohorts of patients and original mouse models.

The team has merged and collaborated with another research group on genetics of diabetes at Cochin four years ago. Within the team, the subgroup which focused on the characterization of antigenic epitopes recognized by autoreactive T cells in T1D will end due its leader's retirement. Conversely, the clinical Department of Pediatric Endocrinology and Diabetology will merge, bringing a high level of expertise in translational research in pediatric endocrinology and diabetology and new functional approaches. The new team will jointly focus its research projects on the study of mechanisms involved in frequent metabolic and endocrine disorders, to discover new biomarkers and develop innovative therapeutic strategies.

The roles of innate and adaptive immune systems in diabetes and obesity, and on the genetics of diabetes and endocrine dysfunctions will be deepened by investigating Mucosal-Associated Invariant T (MAIT) cells, which are unconventional T cells abundant in gut mucosa but also in liver, fat tissue and inflamed tissue such as the pancreas in T1D. In T2D and obesity, MAIT cells produce inflammatory cytokines in adipose tissue, ileum and liver and they participate in adipocyte dysfunction and liver damage highlighting a deleterious crosstalk between MAIT cells and macrophages. The impact of patients and mouse microbiota on MAIT cells will be evaluated in vitro by coculture experiments, as well as in vivo (gnotobiotic mice inoculated with human stool samples). Microbiota from patients and mouse models will be analyzed by metagenomic, metabolomic and bioassays (TLR ligands). The ultimate goal is to understand the mechanisms involved in MAIT cell alterations and functions in metabolic diseases to develop therapies targeting MAIT cells directly or through nutritional interventions modifying microbiota.

The team's genetic research will try to clarify the underlying genetic diversity in diabetes etiopathogenesis, both T1D and monogenic forms through multidisciplinary approaches, in order to address specific questions that are not efficiently investigated by largescale classical genetic studies of multifactorial diabetes. After the identification of several novel genes responsible for syndromic monogenic diabetes since 2000, and shared genetic factors between different diabetes forms, monogenic and multigenic, the next challenge, will be to identify monogenic forms of diabetes that may not be necessarily clinically atypical, including in patients with autoimmune diabetes. Strategies include population-based studies (populations with high prevalence of consanguinity, predicted to result in increased prevalence of monogenic recessive forms of diabetes) and studying patients with immune/autoimmune features, as well as subgroups of patients with likely monogenic diabetes affecting immune mechanisms. Genetic studies will allow to adapt the patient's treatment to the molecular mechanism of the disease and foster new interactions on genetics, immunology and functional analyses on diabetes and endocrine disorders in particular through the collaboration with Polak's group.

RECOMMENDATIONS TO THE TEAM

The team performance requires collaboration among its members to connect the different research objectives.

Further the team performance could benefit from the enrolment of young postdoctoral fellows and permanent staff to pursue all different research objectives.

Team 22: Regulation of T-cell effector functions

Name of the supervisor: Mr Bruno Lucas

THEMES OF THE TEAM

The research themes developed by this team are focused on the cellular mechanisms that control the tolerance and activation of T lymphocytes under normal or various physio-pathological conditions. Over the period of evaluation, the team has centred their researches on the effect of aging on T cell ontogeny as well as the impact of adjuvant supplementation on T cell effector functions in the context of cancer. To do this, the team is using established preclinical models to study T cell subsets and anti-cancer responses.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations to the team in the previous evaluation campaign were focused on:
1) the need of developing further international collaborations to improve the overall international visibility of the team, but this is still appearing as a weakness;
2) increasing the number of PhD students and postdocs with expertise in transcriptomics.

During the period of evaluation, 3 PhD theses were successfully defended in the lab and 4 PhD theses are in progress. Two postdoctoral fellows have also been hired with the expertise needed to drive the team's projects forward. The team benefits from the excellent genomic/transcriptomic core facility present at IC.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**8**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**4**
Total personnels	**12**

EVALUATION

Overall assessment of the team

The overall assessment is excellent.

This team works on long-standing and central questions in T cell-biology, particularly in relation to anti-tumor responses and, more recently, aging. During the evaluated period, the team had an excellent publication track record, raised substantial funding and is actively involved in promoting the permanent researchers and young scientists of the team. The team leader is actively involved in the governance of France's national research institutions.

Strengths and possibilities linked to the context

The workforce present in the team is well adapted to the research activity since the permanent staff is composed by 3 permanent scientists, 2 engineers and 1 assistant-engineer. The team benefits from the excellent genomic/transcriptomic core facility present at Institut Cochin.

The team helped promote the IC visibility and foster collaboration agreements by organizing a symposium in 2021 bringing together various players from the private research sector to present the various technologies and services offered by the IC core facilities: "Innate T cells: from basic research to therapeutic applications". The scientific reputation of the team is also recognized by editorial responsibilities held by the PI as associate editor in Frontiers in Immunology and by reviewing activities of the researchers in international journals. The team members sit in scientific committees of several funding agencies, at the national (ANR, FRM, Ligue, ARC, ARSEP, AFM) and international levels (UK: "Medical Research Council"; Portugal: "Fundação para a Ciência e Tecnologia"). Being involved in national research institutions, the team leader has a global and in-depth vision of the latest biology research and technological advances that could benefit the team and the institute Cochin.

The team leader is actively involved in the governance of France's national research institutions. Notably, he has been deputy director of the Institute for Biological Sciences (INSB) of the CNRS in charge of Immunology, host-Pathogen interactions and inflammation and co-directed the ITMO I3M between 2013 and 2019. The team leader leads a CNRS national consortium GDR to bring together the innate T cells community. Lastly, the team leader is awarded by the CNRS since 2010 for its Scientific Excellence.

The team hosted a significant number of students during the evaluated period. Three PhD theses were defended, 4 PhD theses are in progress and 17 undergraduate students from Licence-3, 8 Master-1 and Master-2 performed their internship in the laboratory. Two PhD students succeeded in competitive calls for fellowships from Inserm and 2 postdoctoral fellows have been recruited thanks to one ANR JCJC (250 k€) and a grant from GHU Saint-Anne (55 k€).

The team has been regularly supported by public grants mostly at the national level, the total amount of funds raised by the team since 2017 is about 1,8 M€. In addition to the ANR JCJC already mentioned, the team appears as partner on an ANR grant shared with team 26 of Institut Cochin and received 100 k€. Two contracts were financed in the PIA context: Labex Who I am? (120 k€) and Idex UP-Cité (18 k€). All the 11 contracts obtained from private foundations are coordinated by the team: 4 grants LCC (total 174 €), 4 grants ARC (total 270 k€), 2 grants FRM (total 730 k€) and 1 grant from the Fondation du rein (30 k€). A private funding of 20 k€ was raised from Gefluc (Group of French Companies in the Fight against Cancer).

The team has published 21 articles in journals of excellent scientific reputation: Nature communications, elife, The Journal of Immunology, Journal of Autoimmunity, Arthritis and Rheumatology and the Lancet Respiratory Medicine. Members of the team were first/last author in about half of these publications. Many articles published in collaboration are with other teams of the Institut Cochin, highlighting the synergistic dynamic driven by the team. All PhD students, who have completed their training (3), figure as a first author within the published and submitted publications.

Weaknesses and risks linked to the context

Although the team has many national collaborations, the permanent researchers have limited international visibility (few participations in international meetings) which may impact on the success of grant applications and on the possibility of publishing in journals of high reputation.

As identified in the SWOT by the PI, the team may have too many collaborations and research projects that may hinder their priority projects in a very competitive field.

Analysis of the team's trajectory

They will pursue 3 objectives:
- Aim 1: Ontogeny and functions of peripheral regulatory CD4 T cells;
- Aim 2: T-cell aging and exhaustion;
- Aim 3: Regulation of anti-tumor responses.

Overall, the trajectory is very clear in terms of scientific questions, tools, models and collaborations to address them, and demonstrated feasibility.

As the field of T-cell aging is highly competitive, the team should remain focused on the questions and interesting observations it has recently made, in order to rapidly imprint this area of research.

RECOMMENDATIONS TO THE TEAM

The committee encourages the team to continue the excellent work it has developed over recent years and recommends that its members attend conferences to disseminate their research and improve the overall international visibility of the team. Attention has to be driven to keep focus on their expertise (Treg) and acquired results.

Team 23: Neuromuscular Development, Genetics and Physiopathology

Name of the supervisors: Mr Pascal Maire & Mme Athanassia Sotiropoulos

THEMES OF THE TEAM

The team is interested in the molecular mechanisms underlying muscle development, adult myofiber diversity, plasticity and metabolism as well as muscle stem cell biology.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous Hcéres report made several recommendations to the team of Pascal Maire and Athanassia Sotiropoulos. The first was to advertise their science at international meetings and to strengthen collaborations. The performance of this team in the current period has followed this recommendation. The second recommendation was to recruit more postdocs to obtain a critical mass of scientists. This has been partially successful, possibly due to reduced international exchange during the pandemic period. However, the team is on a good way with recruiting new scientists. Furthermore, it was recommended to focus on fewer projects and thus to enhance productivity. Productivity has been significantly enhanced, the number of publications in excellent journals such as Nat. Comm. has increased. However, the spectrum of projects is still broad which also has advantages for the new research plans. During the current period, the team has continued to explore different research topics which seem to be well connected and profit from each other.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**7**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**4**
Total personnels	**11**

EVALUATION

Overall assessment of the team

The overall assessment is excellent to outstanding. The Maire team has an outstanding publication record and an excellent record in training of PhD students. External funding appears very good, and the team has excellent international visibility. This group is an international leader in the field of muscle developmental biology.

Strengths and possibilities linked to the context

The Maire/Sotiropoulos group is internationally well recognized as a strong group in the field of skeletal muscle development and plasticity. This is documented by the relatively high number of excellent and prominent publications, invitations as invited speakers to international and national meetings and participation in other academic events. There are10 presentations during the evaluation period. There are 4 patents and industrial contracts. In addition, the PhD students from this group have presented more than 20 posters at various congresses, and they have participated in the organization of the graduate program and the muscle group, which is organized by the institute. A.S. has been appointed as director to set up and develop the French reference center for 3R principles in animal research, and the group has also participated in the organization and teaching at the first international course on techniques in immunology in 2018. The team researchers are members of scientific committees in France, such as the scientific committee of the French Association against Myopathies, and contribute to activities of science organization with a member of the unit sitting in the board for a master at University of Paris Cité.

The Maire/Sotiropoulos team has an excellent publication record with 41 publications, 13 as first or last author publications and 28 articles from external collaborations. The team has made several important scientific discoveries that have been published in prominent international journals. Among these is the finding on the role of SRF in controlling satellite cell fusion with myofibers through the maintenance of the actin architecture, published in J. Cell Biology in 2018, work on single nucleus RNAseq and FISH to identify coordinated transcriptional activity in mammalian myofibers, published in Nature Commun. in 2020, which constitutes a major technical breakthrough for the field. In the same year, they filled a major gap in current knowledge how SIX-1 and SIX-4 homeoproteins regulate PAX-7-positive progenitor cells during fetal myogenesis (Development), and in 2022 they characterized a fast Myh super-enhancer that controls adult muscle fiber phenotype. This work has also been published in Nature Comm (2022).

The group has been very successful in collaborating with external groups and contributing to various aspects of muscle physiology. This includes work on the metabolic requirements for adult muscle adaption during exercise, work on the signalling pathway for insulin-independent glucose uptake in skeletal muscle, the pathways in stress responses that initiate muscle stem cell activation and hypertrophic growth. In particular work on metabolic pathways in muscle of healthy individuals, diabetic patients and during aging appear highly original and interesting and a good basis for the next years in which the research line of the Viollet group needs to be integrated.

Research output is divided among the different members and includes the directors, researchers, PhD students. All PhD students who defended their thesis during the evaluation period published at least one article, more than half of the PhD students had two publications and more. During the evaluation period 7 PhD students finished their training and 2 PhD students started in 2022.

Weaknesses and risks linked to the context

Work in the Viollet group has so far not changed focus towards muscle biology and appears broad, requiring a new focus. Despite the excellent work of the Maire- Sotiropoulos group, external funding is low, in particular through participation in international consortia and from international (EU) sources.

The group has been joined by new MCU workers. The number of first and senior publications from these scientists has been relatively low so far. However, the chances for very good and excellent publications on the basis of this additional expertise in this group is very high if these new researchers are well integrated.

Analysis of the team's trajectory

In the next funding period, the team will fuse with the Viollet group and integrate a researcher who is an expert on metabolic mechanisms. Thus, the experience of the Viollet team in signaling pathways in diabetes and obesity will be integrated, which is obviously a great chance to move from developmental aspects towards metabolic and pathophysiological contexts of muscle fiber physiology, plasticity and pathophysiology. The four aims proposed for the team's trajectory are based on previous successful work of these groups, and in principle appear highly attractive and straight forward. For aim 1 on motoneuron myofiber diversity, the team proposes to use reporter mice for FACS isolation or motoneuron nuclei, in order to map transcriptomes of motoneurons with those of connected muscle fibers, and to see how motoneuron plasticity guides adaption of myofibers in various contexts. This is state of art and highly attractive. The group has good strategies and promising preliminary data that show feasibility of this approach. Aim 2 on muscle atrophy and hypertrophy appears as a highly interesting and timely topic and integrates the expertise from the Viollet team. Also aim 3 on the role of muscle as a secretory organ that is involved in endocrine and paracrine signaling in response to various environmental conditions appears highly important and very interesting.

Aim 4 focuses on the generation of a single cell atlas of motoneuron-myofiber interactions. This appears as a highly challenging but also highly attractive enterprise. This project offers the opportunity to be expanded within the frame of an international team, after attracting funding, for example for an EU-network. The same is also true for aim 4b on the ex vivo model of myofiber contraction specialization, for which this team has ideal expertise.

RECOMMENDATIONS TO THE TEAM

The team should further develop strategies to integrate various expertise and strengths from all team members towards a joint research profile, to address new scientific questions for which the existing expertise in particular in the area of muscle adaption to aging processes and pathophysiological metabolic conditions can optimally be included. The participation in international networks and consortia is encouraged, in particular for aim 4a, but also for other aims, in order to further improve access to funding possibilities.

Merging the Viollet group to this team appears attractive on the basis of previous work of both groups. Integrating expertise on metabolic pathways to muscle physiology and pathophysiology could not only be a basis for further successful publications and international visibility, but also for fundraising to maintain high levels of visibility in a highly competitive international research field. It is recommended that also the postdoctoral scientists and lecturers contribute to the design of such research lines. Expansion of ongoing collaborative projects with other groups in the areas of sports physiology, and the involvement of muscle pathophysiology in other human diseases is highly encouraged.

Efforts to attract junior researcher PhD candidates and postdocs from other countries should be expanded.

The international visibility of MCU researchers is outstanding and there are high chances that it can be further expanded to the field of muscle metabolism in other diseases and aging. The researchers that are joining this group should be encouraged to contribute to the muscle research field and to apply for independent funding, to contribute review articles in international leading journals and to participate at national and international meetings.

The further contribution of Athanassia Sotiropoulos to the scientific leadership for this group is highly recommended.

Team 24: T-cell tolerance, biomarkers and therapies in type 1 diabetes

Name of the supervisors: Mr Roberto Mallone & Ms Sylvaine You

THEMES OF THE TEAM

The team by Mallone-You works in the field of T cell tolerance, biomarkers and therapies for Type 1 diabetes (T1D).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team Mallone/You has increased independence and scientific production in top journals as first/last author with increased potential for the future due to research funding acquisition and possibility to attract PhD students and postdoctoral fellows.

The team has increased interaction with the non-academic world and society since the previous evaluation.

The team has increased organization and life since the previous evaluation in order to secure the level of excellence they have reached. The team has increased its potential in understanding immune-endocrine interactions also by fusing with another group.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	4
Personnels d'appui non permanents	3
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**11**
Total personnels	**16**

EVALUATION

Overall assessment of the team

The overall assessment is outstanding. The scientific production, reputation and visibility of the team Mallone/You are excellent. The translational relevance of the team activity is realized through a strong synergy with clinical units within the Hospital and participation in clinical trials. Contribution to society, economy and non-academic world is excellent through interaction with patients' associations and industrial partners and press/media communication to general audience.

Strengths and possibilities linked to the context

In the past 5 years 2017-2022, the team included 18-20 people with 4 permanent, 8 PhD students, 8 postdoctoral fellows, 5 clinical research assistants and 11 technicians/engineers.

Contribution is highlighted by the capacity to attract qualified national and international members from 11 different nationalities. A satellite lab was launched in the Indianapolis Bioscience Research Institute through a 3-year start-up grant. Attractiveness is also demonstrated by 57 talk invitations (48 delivered by Mallone and 9 by You) to national and international conferences and 9 presentations delivered by PhD students. Visibility is also demonstrated by the organization of 3 international conferences (i.e. IDS 2023 Paris), membership of steering boards, academic activities as jury of PhD students (4 from abroad) and medical students, Institutional activities i.e. member of Inserm Scientific commission N° 5), on average 30 reviews /year of international grants from important organizations and Foundations, article reviews (approximately 17/year) in highly cited journals, invitations to write review articles as opinion leaders in T1D immunology. Attractiveness is also demonstrated by research funding acquisition of approximately 5M euros from national, international foundations, charities, industries (Novartis, Provention Bio), active patient cohorts, associated biobanks and T1D clinical trials, integration in EU INNODIA and international networks (nPOD, JDRF working group).

The team leader and several members of his group have been publishing in specialized top journals (Diabetes, Cell Metabolism, Frontiers Immunology, etc.) during the period of evaluation demonstrating strong expertise and successful scientific achievements in continuity with the previous evaluation period. The team produced 50 articles published in international journals, including 28 original articles and 22 reviews. Of these, 24 articles originated from the laboratory (first or last author) and 26 from collaborations. PhD students produce from one to four papers. The production has translational relevance with three patents filed by Inserm-Transfert during the 2017-2022 period although not licensed yet. The scientific production is proportionate to the research potential of the team. Further the new team Mallone/You has increased visibility due to increased independence than in the previous contract.

The unit stands out by the quality and quantity of its non-academic interactions as demonstrated by funding support from several national and international charities supported by patients and industry, e.g. with Novartis and Provention Bio. The team is moreover part of several international research networks (www.jdrfnpod.org and INNODIA, www.innodia.eu), which features a strong direct participation of patients and their families. A dynamic clinical activity is realized through the coordination of 4 multicentric patient cohorts with associated biobanks and by participation in different therapeutic trials sponsored by academic or industrial partners. Further R. Mallone is member of the Data Safety Monitoring Board of the two international trials in Type 1 diabetes.

Team scientists are also regularly solicited by biotech and pharmas for expertise and advisory tasks on new T1D treatments or biomarkers to predict or monitor clinical efficacy and by patient associations to present the latest results of their own research or to explain recent advances in the field. The team also contributes to press articles in magazines, and radio broadcast. The team has regularly hosted middle and high school students for short-term stays in the lab usually coordinated by PhD students with an interest and passion for teaching.

Weaknesses and risks linked to the context

No licensing of the patents recently obtained.

The number of permanent staff and postdoctoral fellows at 31/12/2022 is low.

There is still lack of bioinformatics expertise since the previous report.

Except for Cell metabolism, Diabetes there are no publication in outstanding journals such as Nature, N Engl J Med as first/last author.

Analysis of the team's trajectory

The presented team trajectory is feasible and excellent. For the next years the team Mallone/You will continue to build advanced knowledge in the field of immune-endocrine cross talk in T1D leading to deeper understanding of the disease etiopathogenesis, exploring the existence of an autoimmune T cell phenotype. This will lead to the development of novel immunotherapeutic strategies. Collaboration and merging with another group will reinforce expertise to address new challenges in translational research and opportunity to file and license new patents. The highlighted trajectory will also lead to enhance funding support from industries, eventual ERC support and encourage the opportunity of permanent staff appointments and further increased visibility of the team.

Fusion with another team will certainly increase the opportunity for academic and industrial collaborations at international level and the potential to attract successful research funding. The collaborative effort with the start-up EndoCell will produce complementary expertise of beta cells and autoimmunity with significant translational relevance.

RECOMMENDATIONS TO THE TEAM

The research production by Mallone-You team is excellent and with high translational significance and potential due to interaction with clinicians and pharmaceutical companies. The team is expected to continue to publish in highly ranked journals in the field of T1D pathogenesis, biomarkers and immunotherapies.

Attention could be payed to attract full-time young scientists and enroll permanent staff.

In the future the translational input of the team is expected to lead to licensed patents and patent development.

Team 25: Retrovirus, Infection and Latency

Name of the supervisors: Ms Florence Margottin-Goguet & Ms Claudine Pique

THEMES OF THE TEAM

The team focuses on the interactions between HIV and HTLV1 retroviruses with their cellular environment, at the fundamental, translational and clinical levels in order to better understand retroviral restriction, escape, tumorigenesis and latency.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the former evaluation were: 1. *The excellent scientific production in the last funding period needs to be continued. More resources should be acquired through both national and European funding programs to maintain basic research that can then be evaluated by the clinical team in patients. Outreach activities, especially in the review processes of journals and foundations should be increased. 2. The team gender balance should be maintained in the future. 3. With the identification of FAM as a new HIV restriction factor, no indication so far that HTLV-1 is affected by FAM and an ambiguous role of SAMHD1 in HTLV-1 infection, the two subgroups have even further drifted apart. The synergies and rationale to study HIV and HTLV-1 in one team should be strengthened, by for example exploring a role for FAM during HTLV-1 infection. If this cannot be achieved and no further funds can be acquired for the proposed HTLV-1 research, the two team leaders might consider working only on the proposed HIV studies and the characterization of FAM and its mechanism in HIV suppression.*

Following the former committee's recommendations, the team maintained the high visibility of its research in terms of publications and obtained competitive national grants (ANR, ANRS, FRM label, MSD Avenir Foundation). The team leader's scientific reputation was reinforced over the period by participation in several national (Pasteur, SIDACTION, ANRS, CNRS) and international boards (FNRS), and one of the team's leader was winner of the international prestigious KT Jeang Retrovirology Prize in 2022. They increased their participation in editorial boards (PLoS Pathogen, Retrovirology, Frontiers in Microbiology) and grant evaluation.

In terms of strategy, the committee suggested to increase synergy between the HIV and HTLV subgroups; this was not followed since no shared publications have been obtained over the period.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	3
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	6
Sous-total personnels permanents en activité	**12**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**7**
Total personnels	**19**

EVALUATION

Overall assessment of the team

The overall assessment is excellent to outstanding.

The team has had an excellent publication output, with excellent to outstanding publications led by team members. The team has been able to secure excellent to outstanding competitive national funding until 2025. However, international participation in networks and grant programs is missing. Training and participation in education programs are excellent to outstanding. The team has outstanding international visibility through organisation and participation in major conferences and scientific societies. Dissemination to the society and innovation are very good.

Strengths and possibilities linked to the context

Over the period, the team was able to maintain its publication standard, with an excellent publication output in terms of impact of the discoveries published and the recognition by the pairs. Both team leaders and the clinical group leader have a solid reputation in the field. The team published 21 articles led by team members in journals highly recognized in the field. Indeed, articles on HIV restriction factors and latency, led by the team members and published in Nature Communications (2022) and Nature Microbiology (2018), are highly cited by their peers. For the HTLV-1 topic, the results obtained on the role of oncoprotein Tax were published in excellent speciality journals (PLoS Pathogen 2017 and Journal of Virology 2020) with team members as leading authors.

For the clinical subgroup, 16 papers (1 Journal International AIDS Society, 1 eBioMed, 1 Micron Spectrum, 1 Clinical Infectious Disease) were led by the group, among them the Journal International AIDS Society paper (2019) on HIV DNA dynamics in HIV controllers has a solid reputation in the field.

The team members were also co-authors in 9 excellent to outstanding fundamental collaborative works (Nature Communications, PloS Pathogen, Leukemia, Blood, etc.) and 48 clinical works (AIDS, Clinical Infectious Disease, Journal Clinical Virology, Leukemia, etc.), showing the capacity of the team to share their expertise, tools and clinical samples with a broad scientific community. They have established strong collaborations with essentially French labs (Centre International de Recherche en Infectiologie, Cochin Institute, Pasteur Institute, IDM–T - CEA, SC-10 Bicêtre).

Grant leverage is very good to excellent. It was rather low from 2018-2021 (80 k€ per year), but in 2022 the team was very successful and obtained funding for a total of 750 k€. Funding relies essentially on the National French AIDS agency (ANRS 7 grants over the period) and AIDS charity (Sidaction 2 grants) all as PI. Recently, the HIV subgroup renewed its FRM label, which is a competitive foundation funding, this grant is running until 2025. Of note, the clinical subgroup obtained a MSD Avenir Foundation grant for clinical trials. The subgroup leader coordinates the analysis of two ANRS national cohorts (ANRS CO6 PRIMO, ANRS CO21 Codex).

In 2022, the HIV subgroup leader obtained the international prestigious KT Jeang Retrovirology Prize, as a sign of recognition of the quality of the research performed by the team. The subgroup PIs are editorial members for PLoS Pathogen, Retrovirology and Annual Review of Virology, participated in international board committee's (Fond National Recherche Scientifique, Belgium) and in the organisation of conferences (International Conference on Human Retroviruses, The Conference on Retroviruses and Opportunistic Infections (CROI), and were invited to present their works as speaker in more than 20 events, which is outstanding for the period.

The team leaders are part of national evaluation committees (Pasteur, ANRS, Sidaction, ANRS cohort steering committee) and institutions as "chargé de mission" (CNRS).

Training trough research is outstanding with 7 PhD candidates that defended their PhD with an average of two papers as leading author and one review. 3 PhDs are ongoing. 4 postdocs were also hosted in the lab over the period.

Weaknesses and risks linked to the context

There is only one co-publication between subgroups and no one with the clinical team, showing the absence of a common project in the team that is built on juxtaposition of expertise but lacks from an integrative spirit. The lack of international funding and participation in European or international research consortia is a weakness. This is contrasting with the important recognition of the research performed by the team in the community.

Moreover, the funding obtained was in its vast majority obtained from the national AIDS agency and one AIDS charity institution, this might be a risk.

The team was leading only 4 international reviews (Current Opinion in HIV and AIDS, Retrovirology, Frontiers in Microbiology), which is low for a team counting 7 tenured senior and junior researchers.

For innovation and tech transfer, two patents are listed but none of them went to a licence.

In the same line, attractiveness of the team to foreign PhD candidates and/or postdocs is weak, with only 1 PhD candidate over 10 being from abroad (Lebanon). The team is not part of a Marie Skłodowska-Curie Innovative Training Network or any EU-PhD co-fund program that might bring some international spirit in the team.

Only two international collaborations (Université Libre de Bruxelles (Belgium) and University of California, San Diego (US)) and no collaboration outside Paris are listed.

Analysis of the team's trajectory

The trajectory proposed is excellent and realistic. It aims to refocus all subgroups activities on HIV latency. Joint effort on this central topic will help to be competitive in ambitious grant applications. However, neither specific actions nor a clear plan are described to convince the committee that common synergistic actions will be performed in the near future. Funding is secured until 2025, which is a good point; however new grant opportunities have to be considered to maintain the high level of expertise and quality of the research performed. Obtaining funding for the screening to identify new restriction factors might be risky in regard of the high competition, even at the national level, on this field.

RECOMMENDATIONS TO THE TEAM

The team should strengthen their interactive collaboration between sub-groups, to address new scientific questions. The participation in international networks and consortia is encouraged to have access to new funding possibilities.

Merging the forces of the two sub-groups working on fundamental research questions is encouraged in order to put all the efforts on the HIV model. This will increase their success in fund raising, and present an important workforce to keep attractiveness and appeal in this competitive field. The committee encourages the recently recruited young researchers to participate in this joint effort, although their research topic specificity has to be preserved.

The committee considers that the clinical research team is not yet really integrated, except for sample sharing. This subgroup appears standing by the other subgroups. It is now time to imagine and apply for funding of a common ambitious translational/clinical research project federating all research aspects of the team on HIV latency, reservoir and cure.

The capacity to attract junior researchers, PhD candidates or postdocs from abroad should be reinforced, this could be done by participating and presenting the results of the team in major conferences of the speciality and being invited to present in renowned international institutes. Creating fruitful collaborations with teams in the US might give access to NIH funding.

International visibility could be improved, especially for the junior investigators, by writing reviews for international high-profile journals.

Action for dissemination to lay public should be encouraged in the team.

Team 26: Receptor Signalling and Molecular scaffolds

Name of the supervisor: Mr Stefano Marullo

THEMES OF THE TEAM

The group Receptor Signalling and molecular scaffolds has a focus on signalling processes associated to G protein coupled receptors, with a focus on mechano-activation of receptors as well as the role of beta arrestin in the nucleus. Recent inroads into anti-inflammatory compounds have allowed a currently very successful Spin-off.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report (2019) had highlighted that the number of publications per team member could have improved. The publication output has remained in line with that of the previous report, albeit the focus of the team has shifted significantly to the IP valorisation of a newly-developed anti-inflammatory compound. The establishment and successful fundraising for the spin-off company ALLSPIM addressed any concerns from the previous evaluation about contacts with the non-academic world. The team had been encouraged to support PhD students in publishing their research outcomes more, which now appears to have been achieved since 3 PhD students who defended their thesis published 4, 2 and 1 article respectively.

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	3
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**7**
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	**10**

EVALUATION

Overall assessment of the team

The overall assessment is excellent to outstanding.

The team has conducted overall excellent to outstanding research and technology transfer activities over the current evaluation period. Several key scientific projects have been concluded with high impact publications, and the ALLSPIM start-up has successfully secured almost 13M€ to date. Since the PI is retiring (emeritus) a satisfactory transition has been agreed upon for the remaining members of the team, who will be joining the team 30.

Strengths and possibilities linked to the context

The team possesses a strong level of scientific expertise, particularly in the fields of GPCR functions, regulation, and signalling pathways. Their research projects reflect a dedicated focus, allowing them to make valuable contributions in these domains. The identification of a novel anti-inflammatory compound (2,4-D) and its potential applications in immune-mediated inflammatory diseases is a notable achievement, positioning them for further advancements in the field.

The team has published in top quality journals, such as Nat. Communications and Oncogene, completing several ongoing projects.

The team's success in valorization efforts through the creation of the ALLSPIM start-up and the development of 2,4-D demonstrates their ability to translate research into potential solutions with societal and economic impacts. The availability of funding and industrial partnerships enhances the prospects of successful research commercialization.

ALLSPIM R&D project obtained additional funds from the Nexbiome Company. Moreover, for the RHU-6 project we are preparing on inflammatory eye diseases, industrial partnerships have been established with IrisPharma, Olink and Fareva Companies.

Team members actively participating in international conferences, holding editorial roles, and receiving invitations to present highlight the team's attractive scientific reputation. These engagements not only contribute to their visibility in the academic community but also foster potential collaborations and opportunities for future growth.

Group leader was invited to 15 international conferences in the past 10 years. Other team members invited to several international conferences. Organized 2017 GPCR congress in Paris.

The lab has trained 5 PhD students and 5 postdocs.

Diverse funding sources, including grants and collaborations with industrial partners, showcase financial stability and a robust research support system. The group has obtained 7 grants from sources such as ANR, FCRF and ARC, either as lead or partner. ALLSPIM - has collected over 13 M€.

Weaknesses and risks linked to the context

The team's limited engagement with the general public and limited involvement in societal debates represent a weakness.

Analysis of the team's trajectory

Not applicable.

RECOMMENDATIONS TO THE TEAM

Not applicable.

Team 27: Robustness and evolvability of life

Name of the supervisor: Mr Ivan Matic

THEMES OF THE TEAM

The team studies replication errors and DNA damages that contribute to the evolution and adaptation to stress conditions of bacteria.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team joined the unit in 2019.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	7
Sous-total personnels permanents en activité	**11**
Enseignants-chercheurs et chercheurs non permanents et assimilés	5
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	**7**
Total personnels	**18**

EVALUATION

Overall assessment of the team

The overall assessment is excellent.

The team has an excellent publication record, based on work that is very well funded. Team members are regularly invited to conferences and two postdocs are part of the team, indicating a very good to excellent attractiveness. The arrival of new members further shows the strength and attractiveness of the team and will provide opportunities to conduct high-impact research.

Strengths and possibilities linked to the context

The stability of bacterial genomes and their evolution through replication and DNA repair errors are timely subjects and important to understand the adaptation of bacteria to stress condition and the evolution of antibiotic resistance.

During the reporting period, the team published 14 original articles with 6 first and/or last authorships. The publications were in high-profile journals of general interest, such as PNAS, Scientific Reports, Science Advances, mBio and Nucleic Acids Research. One article was selected as Nucleic Acids Research breakthrough article. The PI and members of the team published 8 review articles as first and/or last authors, of which some are in top-

standard journals such as Annual Reviews in Microbiology, Current Biology, Molecular Cell, Nature Reviews in Microbiology, and one book chapter.

The PI has been elected member of Academiae Europaeae.

At the end of the evaluating period, the team hosted 2 postdocs and one graduate student.

Funding is excellent with several grants during the reporting period, including 3 ANR grants of which one as coordinator (181 k€, 432 k€, and 317 k€, respectively), one ANR JCJC grant (346 k€), one grant "Domaines d'Intérêt Majeur - Malinf, Île-de-France" (77 k€), one grant Labex Who Am I? (120 k€), "Initiatives d'excellence" (Idex) (40 k€), one project "Emergence - Mairie de Paris" (180 k€), one Idex grant University of Paris, one from FRM charity (170 k€) and one industrial contract with Amabiotics (117 k€).

The PI and team members were invited for 13 seminars of which 5 outside of France (Belgium, UK, Estonia, USA, Switzerland), 28 invited oral presentations. The PI was chair of the Gordon Research Conference on Molecular Mechanisms in Evolution, Stonehill College, Easton, MA, USA, 2019, and co-chair and invited speaker at an international conference (Federation of European Microbiological Societies (FEMS) Summer School for Postdocs; Split, Croatia, 2022).

Weaknesses and risks linked to the context

The team has no European grants.

Team members are not fully involved in science communication to the large public.

At the end of the evaluating period, the team had only one HDR, limiting the hiring of graduate students.

Analysis of the team's trajectory

The arrival of new members will strengthen further the research. Several timely projects will be carried out, including the exploration of barriers to horizontal gene transfer, the connection of bacterial growth and antibiotic resistance, or the use of mini-guts within the ANR funded project DREAMS to identify the evolution of antibiotic resistance in different diet-exposed gut microbiota.

RECOMMENDATIONS TO THE TEAM

In view of the excellent publication record and the interesting topic, the team should apply for international funding (e.g. HSFP fellowships, ERC grants).

Team members should be more active in science communication to the large public.

The team should increase the number of HDR holders.

Team 28: Epigenetics, DNA replication and Cancer

Name of the supervisor: Mr Benoît Miotto

THEMES OF THE TEAM

Research of the team is to understand the epigenetic control of DNA replication in mammalian cells and how defects in these processes may lead to diseases. The team also has a specific interest in understanding the molecular basis of Meier-Gorlin Syndrome.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team responded well to the previous report recommendations. The team kept a focus on the Meier-Gorlin Syndrome, presented regularly at conferences although mostly locally and nationally, they increased team size including supervision of a postdoc and a PhD student, and decided to join forces with team 11 for the next term.

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	3
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**4**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	**1**
Total personnels	**5**

EVALUATION

Overall assessment of the team

The overall assessment is excellent.

The team is now consolidated and running smoothly, with an excellent research program and national recognition. The team was successful in obtaining grants, established national and European collaborations, published regularly research and review papers, participated in networks of excellence, and successfully mentored students. Overall, this dynamic team had an excellent output.

Strengths and possibilities linked to the context

The team has developed excellent expertise in genomics and cell biology approaches through strong collaborations with several teams (teams n°14, 23, 30) and facilities: PIV, Mouset'IC, Proteom'IC and Genom'IC facilities. The work on the Meier-Gorlin Syndrome is exciting and very promising and received labels from 'Filière de Santé Maladies Rares' OSCAR. The team has now access to unique mouse model and human cells derived from patients (iPS, lymphoblastoid cells and fibroblasts) to study the molecular basis of the disease. The team contributed new knowledge on the function of the ZBTB38 transcription factor and its regulation by the

deubiquitinase activity of USP9X through 4 publications authored by team in specialized journals and one in NAR in 2018. The team discovered a non-metabolic function of HK2 in cancer (NAR 2022,) opening new research avenues to the team in the study of cancer cell migration and the regulation of stemness.

The human workforce is adapted to the activity of the team since the permanent members are 3 scientific researchers, among whom an Inserm recruitment in 2021 and 1 engineer.

The team was very active in communication, presenting posters (27 poster communications) and giving oral presentations (15 presentations), but mostly at the national level. Two team members have been awarded prizes from "Les Entreprises Contre le Cancer" in 2019 and 2022. The visibility of the team can be recognized by the participation of members to different networks: Labex "Who am I?", the French DNA replication network, and the "filière santé maladies rares" OSCAR. The PI took part to 3 PhD defense committee, 1 HDR defense, 1 concours lecturer at university, 2 panels for promotion to professor level and 3 panels for ITA promotion. In the perimeter of the unit, the PI sits in the scientific committee of the Genom'IC platform.

The team successfully mentored a postdoc (now permanent at Inserm since 2021) and a PhD student (NAR 2022 first author publication).

The team secured 765 k€ of funding since 2017 and coordinates all grants which aimed to finance research activities and salaries for short-term engineer contracts. The EU grant AssemblePlus raised 5 k€, the national ones (Inserm nouveaux entrants et Plan Cancer) about 200 k€ and the participation to the Labex "Who am I?" the sum of 25 k€. A total of 7 grants have been obtained from charities and foundations, among which Ligue contre le Cancer-Paris (40 k€), FRM programme amorçage (300 k€), Fondation Maladies Rares (51 k€) and ARC (50 k€). Private funds from EDF (25 k€) sustained a project related to radiobiology.

The team has a very good publication record over the period with 11 publications, 3 reviews, and 4 manuscripts on the go including 2 pre-prints in bioRxiv and 2 manuscripts under review as first and last authors.

The team contributed to teaching at the License and Master levels at University of Paris and to reach out to the general public (Writing for "Bulletin de veille scientifique", participation in the « Fêtes de la sciences, visits in primary/elementary schools, and interviews).

Weaknesses and risks linked to the context

At this stage and in light of their efforts, the team now deserves encouragements. However, following up on too many fronts might dilute visibility on the international scene.

Analysis of the team's trajectory

The merging of the team with team 11 is a great idea as the teams will complement and reinforce each other. The proposed plan with the three axis that include (i) epigenetic regulation of mammalian genome dynamics (ii) analysis of the impact of defects in DNA replication factors and (iii) role of epigenetics in cancer initiation and progression, is well implemented with a special interest on the establishment of the mouse model for the Meier-Gorlin syndrome.

RECOMMENDATIONS TO THE TEAM

Becoming internationally recognized should now be the aim of the team which is within reach after merging with team 11. The suggestions to reach international recognition level are to focus the research plans to a limited number of topics and to join European and International networks to attract students and postdocs.

Team 29: Biology of Phagocytes, Infection and Immunity

Name of the supervisor: Ms Florence Niedergang

THEMES OF THE TEAM

The team has a long-standing expertise in the biology of professional phagocytes. They investigate the molecular mechanisms regulating phagocytosis, internalisation and trafficking of phagosomes in physiological and pathological (mainly infections) conditions using primary cells and cutting-edge experimental approaches.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The committee did not report any weakness in the previous evaluation and suggested to focus on fewer, more promising objectives with a clear funding strategy. The team is now focusing on the molecular mechanisms of phagocytosis by professional phagocytes and the impact of infections by HIV and respiratory viruses on these processes.

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

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

EVALUATION

Overall assessment of the team

The overall assessment is excellent to outstanding as for the management duty.

The scientific production of the team is excellent with several research articles published in high-impact journals including Nucleic Acids Research and EMBO Reports. The attractiveness is outstanding with numerous invited talks, the recruitment of PhD students and postdocs and the development of projects at the interface between cell biology, immunology and infections that allowed the team to secure several research funds.

Strengths and possibilities linked to the context

The main research interests of the team are the study of the cellular processes involved in phagocytosis, from the formation of phagosomes at the plasma membrane to the intracellular phase of phagosomes inside cells. This is important in the context of cellular homeostasis and in the regulation of innate and adaptive immunity. In this latter case, the team investigates how pathogens take over this pathway to invade and proliferate in host cells. Studies on host/pathogen interactions are mostly focused on viral infections (HIV and other respiratory

viruses). Co-infections of phagocytes by viruses and bacteria (Salmonella) are also investigated. Emphasis is given on the development of new imaging and transcriptomics approaches.

With 11 research articles, 4 reviews and 3 book chapters as main author (first author and/or corresponding author) in relatively high-ranking journals (e.g. Nucleic Acids Research, EMBO Reports), the production of the team is excellent.

The national and international visibility of the team is outstanding as demonstrated by 26 presentations at national and international meetings, including 9 invited talks by the group leader at Gordon Research Conferences and EMBO workshops among others. The team is also highly involved in outreach activities including the organisation of national and international meetings, open science days, TV and radio appearances and a social media project for science communication.

Attractiveness is highlighted by the recruitment of 2 international postdocs (UK and Australia), 3 PhD students (1 from Italy, 2 from France) and 1 assistant professor.

The development of independent research axis allows permanent staff to diversify, secure fundings and develop cutting-edge approaches to address their scientific question. The team has raised 1.7 M€ from ANR (1.2 M€), FRM (300 k€), ANRS (100 k€), Sidaction (40 k€) among others, with 9 grants coordinated by team members. Collaborations with pharmaceutical companies and the hospital is also stimulating patent applications and three patents have been filed during the reporting period.

Weaknesses and risks linked to the context

A potential risk is that the new position of the team leader as head of the Institute might impact the research axis she coordinates in the team. However, adequate measures have already been deployed.

Analysis of the team's trajectory

The composition of the team will evolve during the next mandate, also anticipating the retirement of a senior staff scientist. A clear project is presented, which is in alignment with the research avenues currently explored by the team. The development of new, promising technologies should lead to important new findings.

RECOMMENDATIONS TO THE TEAM

The committee encourages the team leader to delegate functions to other staff scientists in the team to reduce the risks associated with time management at a minimum.

Team 30: Genomics and Epigenetics of rare tumors

Name of the supervisor: Mr Éric Pasmant

THEMES OF THE TEAM

The team focusses on the genetics and epigenetics of rare tumor-predisposition syndromes, with a particular focus on neurofibromatosis type 1 (NF1) and type 2 (NF2) as well as Schwannomatosis. Recently, the team has extended its research interest to DNA polymerase proofreading-associated polyposis (PPAP). The current research activities of the team address (a.) the underlying genetic and cellular mechanisms driving these rare proliferative disorders, and (b.) identifying pharmacological and genetic strategies to facilitate future therapeutic targeting of these tumors.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In the previous report, the committee recommended on the scientific production and activities to continue producing high-quality science. Furthermore, the team was encouraged to put more emphasis on projects that address biological questions at mechanistic level to stimulate senior/corresponding author publications in high impact journals of team members. Finally, an increase in the international visibility and impact on the community was recommended.

The current report demonstrates that the team has continued at high level to produce high-quality science (during 2017-2022 team members contributed to 347 original research articles (mostly clinical) and 15 reviews in peer-reviewed journals. In addition, the team leader is co-corresponding author of a high impact publication in PNAS (PNAS, 2019) which provides mechanistic insight into the role of PRC2 in NF-1-associated malignant peripheral nerve sheet tumors (MPNST). Beyond the impressive publication record, the team also increased the international visibility and impact on the community by co-organizing the 1th World Congress on Neurofibromatosis in Paris, 2018. Concerning the team´s organization and life the committee recommended to recruit additional researchers to the team. In line with this recommendation, the team successfully applied for competitive grants and received funding for a postdoc position and an engineer. Finally, concerning the scientific strategy and projects it has been recommended to study the candidate genes/modifiers identified in the syndromes studied (by unbiased NGS approaches), at latter stage at the mechanistic level. The team has successfully performed such mechanistic analysis on MPNST (PNAS, 2019).

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	4
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	**12**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**3**
Total personnels	**15**

EVALUATION

Overall assessment of the team

The overall assessment is excellent.

The team has excellent scientific production and third-party funding. The team is internationally recognized and has established a strong network facilitating excellent-outstanding interaction between clinics and basic research.

Strengths and possibilities linked to the context

The team is well-recognized for the expertise on neurofibromatosis at national and international level. Accordingly, members of the team received numerous invitations (n=33) as invited speakers or chairmen at national and international conferences, and the team co-organized the 1th World Congress on Neurofibromatosis in Paris in 2018. All members of the team participate in peers reviewing for numerous international scientific journals (AJHG, EMBO Rep, JAMA Derm. etc.). The team leader serves as editorial board member of *Frontiers in Genetics* and *Genes*, and is involved in numerous national committees (Inserm, ARC Foundation) for research evaluation.

The quality of the hosting policy is for example reflected by the first author publication of a postdoc of the team, in a high-ranking international journal (PNAS, 2019). The team has successfully obtained substantial funding by different national and European funding agencies with an overall funding amount of 1.2 M€ in the period from 2017-2022. Funding was used for 2 postdoc fellowships, one of them after one year of funding obtained a permanent CRCN position at Inserm. In addition, the team trained numerous master students (n=14) and PhD students (n=5) in the period between 2017 and 2022, further illustrating its attractiveness. The team also expanded its collaborations by novel Cochin internal partners, numerous national ones and international collaborations (MSKKC, USA and in Cardiff, UK).

The team has contributed in the last 5 years to the current understanding of the genetics of the rare tumor predisposing syndromes NF-1, NF-2, PolE-associated cancers and related tumors and cancers. The overall publication (n=362; 28 original research articles, 12 editorials or reviews, 334 hospital activity-linked papers) output in the period between 2017-2022 of the team has been excellent. In addition, the team also clearly follows translational/clinically relevant research aspects, for instance by having demonstrated that POLE proofreading mutations are a predictive biomarker of immune checkpoint therapy response (Cancer Discov, 2022). The team is highly interactive at the national and international level and has published 4 papers together with Cochin internal partners (teams 6 and 14), 8 with external national partners (Curie, Paris; Paris Est University; Université "Paris Cité", etc.) and 4 papers with international collaboration partners (MSKKC, USA and in Cardiff, UK).

Since the team is largely consisting of clinician scientists with activity in the hospital in oncology and genetics, the team shows very strong interaction with the hospital. Team members are frequently involved in clinical trials such as UNICANCER 2017 anti-PD1 for rare cancers, PAOLA-1 (phase III: Olaparib vs. placebo in ovarian cancers), RIPH2 TCF trial (midgut cancers), RAR-Immune (Phase III: Nivolumab-Ipilimumap vs. placebo in sarcoma). In addition, the team is involved in national and international networks such as ClinGen NF Variant Curation Expert Panel, French Sarcoma Group, European Group FOSTER, ESMO, ASCO, and the French National Academy of Pharmacology. Finally, team members are members of different scientific societies (e.g. National Association of Molecular Genetics Practitioners, etc.).

In addition, the team aims to commercialize their research in diagnostics and tumor targeting. In this regard, the team owns a European patent on the "use of inhibitors or aryl-hydrocarbon receptor for treating soft-tissue sarcoma and preventing neurofibroma growth and/or transformation". Furthermore, the team interacts with the French biotech company PEP-Therapy to develop therapeutic approaches on the treatment of NF-2 mutated cancers.

Several members of the team are heavily engaged in teaching and training activities (350h/year) at different levels and faculties at the Université Paris Cité.

Weaknesses and risks linked to the context

Although the team operates at a very high level and has successfully obtained significant funding in the period between 2017-2022, in relation to its current number of permanent positions (n=12), an increase in the number of third-party funded positions (n=3) would be desirable.

The team works very successfully at the interface between clinics and basic science, and therefore their research findings contain high translational and clinical potential, which appears to be currently not fully developed. In this regard, a few more cooperation with partners from pharmaceutical industries might be explored.

The overall scientific production of the team is very high (n=362), with most of the publications being hospital activity-linked papers (n=334), and 28 original research articles and 12 editorials/reviews. The number of first/last author publications of team members in high-ranking journals could be still increased to deepen the impact of their research.

Since the team is largely consisting of clinician scientists with activity in the hospital, the team has excellent-outstanding professional interactions with the hospital and patients. If it is intended, we encourage to even broaden these activities by participation in lay public activities for science dissemination, since the research topic "rare inherited diseases" is of pivotal interest for the public.

Analysis of the team's trajectory

The trajectory of the team is built on its already existing strength and excellence and in linking clinics and basic research. From 2025 the team will be constituted by 13 permanent members, including 3 researchers, 5 teaching researchers and 1 engineer.

The teams is planning to continue the study of rare hereditary tumor/cancer syndromes evoked by mutation of NF1, NF2 and POLE, and is going to expand its current portfolio also to mutations in tumor suppressor PTEN and to its regulation by posttranslational modifications. The latter will be conducted by an experienced scientist that recently joint the team. Beyond continuing their research on identifying modulators of NF1 and NF2-linked tumorigenesis, the team will also develop research activities in functional signalling and molecular targeting of rare tumors, eg. by performing functional CRISPR/Cas knock-out screens and high-throughput screens using drug libraries in order to identify synthetic lethal interactions with NF1 and NF2 mutations. Although the research plan on PTEN appears to be very ambitious and in part risky, we encourage the team to explore this research direction. However, regular analysis of the project progress in relation to the invested input and the expected results is recommended for the PTEN project.

RECOMMENDATIONS TO THE TEAM

This is an excellent team showing an excellent level of productivity, excellent-outstanding interconnections with the hospital, and high national and international recognition. We recommend that the team continues with producing high quality science at the interface between clinics and basic research. The trajectory illustrates that the team´s research activities will continue to move on into the direction of mechanistic and functional analysis. We strongly encourage the team to exploit this research direction, which is expected to further increase the scientific and clinical impact of their work, and the potential to valorise findings.

Team 32: Iron and Immunity

Name of the supervisor: Ms Carole Peyssonnaux

THEMES OF THE TEAM

The research team adresses the organ specific regulation of iron metabolism by hepcidin ferroportin mainly focussing on the intestine and on skin. Genetic and epigenetic control of iron uptake and release as well as pharmacologic intervention affects cell turnover and can be exploited for therapeutic purposes. This is a promising approach and also affects the crosstalk of epithelial cells with immune cells, which is being studied by the research team. In addition, the team also studies the intracellular transport of iron by serotonin, which also controls cellular iron metabolism and is an attractive pharmacological target.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The research team has considered the recommendations of the previous evaluation very well and improved their outreach activities by participation in science fairs and by presentation of their research in the media with their participation in radio shows. The team is also participating in teaching activities and has recruited a visiting professor to further enhance their portfolio and scientific output. Also, scientifically all previous recommendations were fully addressed and the research group is now on a promising track to further act as leading group in the field of iron metabolism.

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	2
Personnels d'appui non permanents	1
Post-doctorants	1
Doctorants	4
Sous-total personnels non permanents en activité	8
Total personnels	13

EVALUATION

Overall assessment of the team

The overall assessment is excellent.

This team is excellent with respect to the publication track and the international visibility. The ream rates excellent with respect to funding and research trajectory.

Strengths and possibilities linked to the context

The "Iron and Immunity" team and the team leaders are well-established and internationally recognized group, who has made seminal contributions to understanding of systemic and tissue-specific regulation of iron metabolism. As documented by the outstanding track record of the group, this research has led to the development of novel ideas and insights, where the role of the hepcidin-ferroportin axis in the physiology of the skin and intestine are major original experimental observations with far-reaching implications. Informed by their fundamental studies on constitutive hepcidin knock out mice and in close collaboration with other team members at the Institute Cochin this work has been translated to seminal work on skin diseases and intestinal disorders with great success. The high potential of this work is also documented by the successful filing of 4 patent applications that demonstrate the strong translational aspect of their work on hepcidin with outstanding commercial potential.

Beyond hepcidin, the group has also successfully identified the complex hormonal cross-talk between serotonin and hepcidin in the control of endocrine and intestinal disorders. Also, these studies are of outstanding translational potential and highlight the broad scope of the group, who is on a promising research track to improve currently available therapies for skin diseases such as Psoriasis, inflammatory bowel diseases and metabolic disorders not only with iron-directed therapies. The team has published 90 articles (75 original articles + 15 reviews) in international, peer-reviewed journals including a significant number in top journals (Science, JCI, Leukemia, Blood, Gut, JEM). Members of the groups hold key author positions in all the top articles published in Science, Journal of Clinical Investigation and Cell reports, where corresponding and senior author positions are held by group members.

Other strengths of the team are (i) the excellent structure of the research team with Professors, visiting professors, postdocs PhD- and master students (increase in team size) (ii) the excellent productivity of the team in novel research areas, where the team are world leaders and (iii) the strong interdisciplinary connection with other groups and research areas at the institute Cochin. The academic grant leverage was also excellent with a total sum of 1 864 720€ (2 FRM grants, 2 x ANRC grants as partners, as well as CNRS grants including "prematuration and valorisation" grants that clearly highlight the team's activities with respect to their potential to 'valorise' their research).

The team also excels in their teaching activities with their affiliation with the doctoral program at the ED 562 – BioSpc and Learning Planet Institute. Université Paris Cité, Inserm. The team is currently composed of 14 members. The training activities are documented by the fact that they have trained 3 postdocs, 7 PhD students, 5 master and 3 internship students. Four theses are currently in progress and all PhD students who defended their thesis published at least 2 articles.

The team also has excellent international visibility, because of their cutting edge science. This is documented by a total of 68 conference invitations (including presentations at international conferences such as the European Iron Club in Oxford 2022, the Conference of the European Hematology Association 2022, the Redox Medicine Conference in 2022 and the Targeting Mitochondria conference.

Weaknesses and risks linked to the context

Weaknesses that were identified during the evaluation include the lack of European funding and the team's limited understanding of the exact cell biological mode of action of hepcidin-mediated dysregulation of organ homeostasis.

Another weakness is the ambitious phase I clinical trial in beta-thalassemia patients as currently limited information on clinical involvement is available. It appears that inclusion of patients with the target disease would render this a Phase II clinical trial.

Analysis of the team's trajectory

The team proposes to apply their research findings on the role of the hepcidin and ferroportin axis as central regulator of iron and immunity in 2 distinct disease areas, which are clinically highly relevant and represent an area of great unmet medical need. Both their projects on the study of hepcidin at the mucosal interface between potentially pathogenic bacteria and the role of hepcidin in disorders of keratinization as well as inflammatory skin diseases are based on sound hypothesis and explore well founded research tracks. The idea to utilize modified lactobacilli to express human hepcidin for the treatment or prevention of inflammatory bowel disease is highly innovative and should be explored. The proposed methodologies with transgenic mouse strains that specifically express or lack hepcidin in certain cell types and the planned use of neutralizing antibodies are very appropriate and timely.

The second research trajectory aims at understanding the functional interaction between serotonin and iron metabolism in a wide variety of disorders is highly innovative and involves up-to-date methodology and research concepts (e.g. 'click chemistry'). This research is very likely to provide the basic insights into how serotonin and iron metabolism interact, but is also very likely to lead to the identification of novel therapeutic targets for haematological and possibly neurological conditions. The brief description of their novel findings is exciting and provides a strong rationale to further investigate this outstanding research track.

The team has proposed ambitious goals for the future research directions, which include also the evaluation of innovative therapeutic concepts in animal models of specific diseases. The fact that the team is embedded in a very productive scientific environment will also ensure that different animal models will be employed as critical pre-clinical development steps. Other than that the committee does not see obvious risks or limitations of the research team and their collaborators, the available infrastructure and methodology or the proposed projects. Overall, the team is very well suited to continue their very successful research.

RECOMMENDATIONS TO THE TEAM

The team should use their fundamental insights and their innovative animal models also as tools to address even more basic research questions. This includes addressing if modulation of the hepcidin ferroportin axis modulates iron, cell division in the skin or gut and if hepcidin actually acts via the luminal or via the basolateral surface of intestinal epithelial cells. Also, the link between serotonin and iron metabolism should be brought to the next level by investigating the interaction of serotonin with iron chaperons (PCBP1 and PCBP2).

The team is encouraged to follow and ambitious research plan for the next few years. The selection of collaborators is well balanced.

The team should consider to evaluate the function of recombinantly expressed hepcidin in cell models before going into animal studies when using recombinant lactic acid bacteria.

Team 33: Glucose sensing, Insulin signaling and Glucotoxicity

Name of the supervisors: Ms Catherine Postic & Mr Tarik Issad

THEMES OF THE TEAM

The goal of the team is to characterize the molecular and biochemical mechanisms underlying the control of intermediary metabolism by nutrients and hormonal signals under both physiological and pathophysiological conditions, including type 2 diabetes, insulin resistance, non-alcoholic fatty liver disease and inflammatory diseases.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In the previous report, very few recommendations have been proposed, except for the scientific strategy where the committee pointed a rather ambitious project and suggested to focus their research on the most promising avenues. The role of insulin action in the gut was judged as particularly interesting.

Over the 2017-2022 period, the team clearly focused their research around 3 axes: 1) the contribution of insulin signaling to liver and gut homeostasis; 2) the role of O-GlcNAcylation in hepatic and inflammatory diseases; 3) the tissue specific functions of ChREBP in energy homeostasis. The team performed significant advances in each topic by demonstrating that: 1) insulin signaling in the gut is an indispensable gatekeeper of intestinal barrier integrity and antimicrobial defense, and acts as a safeguard against microbial imbalance and acute infections by entero-pathogens.; 2) O-GlcNAcylation plays a central role in in metabolic diseases, inflammatory processes and in response to various cellular stresses including viral infections; 3) ChREBP acts as a key actor of the inter-organ communication, through the secretion of hepatokines (FGF21) and incretins (GLP-1) ensuring metabolic homeostasis. Therefore, the team managed to bring out original data in these 3 axes in a well-balanced manner.

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

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

EVALUATION

Overall assessment of the team

The overall assessment is excellent.

The team is excellent in regard to scientific reputation, publication record and fund raising and outstanding for its training capacities.

Strengths and possibilities linked to the context

The team has a strong expertise in glucose and lipid metabolism and performs an integrated research at the whole organism levels using original preclinical models. The team is well integrated in the Cochin institute with several collaborative works with other team of the institute. The team is co-founder and scientific advisor of the local METABOL'IC platform of Cochin Institute dedicated to metabolic measurements from cell. The workforce of the team has slightly reduced with the retirement of 1 PI and 1 engineer, but it did not impact the productivity of the team.

The team maintains an excellent ongoing publication rate (n=51), with 11 reviews and 40 original articles, several in excellent journal (Hepatology, J Hepatol, Scientific reports, Cell reports, Nat Med, Nat Com, Gut, J Immunol, JCI Insight). Importantly, half of the publications of the team are led by PI of the team (23 articles on 51, 45%). The other part of the publication is well-balanced between collaborative works with either Cochin Institute or external teams (39% in each case). In addition, the publication of the team is rather well balanced between team members and several articles are co-signed by at least 2 PI of the team. Lastly, all PhD students and postdocs have at least one publication as lead author (9 articles signed in 1st author for 7 PhD students and 5 articles for 3 postdocs).

The team has an excellent fund raising with 1 international (H2020 grant, 230k€), several national grants (n=10 ANR and 3 grant from PIA, 1,4M€) and several grants from charitable organizations (n=9, FRM, SFD, AFEF, Ligue contre le cancer, association Laurette Fugain, around 600k€), even if the team has no grant with industrial partners. The obtention of contracts is well balanced between team members. Several national grants (n=4) run until 2025, allowing the team to begin the future five-year term with peace of mind.

The reputation of the team is excellent even if no member received price over the 2017/2022 period. This is compensated by the fact that i) the team has active national and international collaborations, ii) team members have been invited to 30 conferences and iii) the team has organized on-line international meeting. One patent on novel compound, compositions and methods for treating insulin resistance and one license agreement were obtained over the 2017-2022 period. All team members actively participate to transversal actions in research, such as national and international scientific committee (n=6 in charitable organization), national and international funding agencies, several local duties and responsibilities at Cochin Institute, editorial responsibilities, or organization of meetings.

The training capacities of the team is outstanding with 7 PhD students, 3 postdoctoral fellows including several foreign ones, 19 M2 and 8 undergraduates. The ratio between PI with HDR and PhD is excellent (7 PhD for 6 HDR), and 1 accreditation for HDR was obtained over the period 2017-2022. Some members are involved in teaching activities and the team members regularly participate to public actions, interviews, radio shows. Particularly, several international student fellowship will be obtained to attract foreign students (Marie-Curie, Chinese scholarship council, fellows from Mexico and other local grants).

Weaknesses and risks linked to the context

The team performs excellent research using original mice models but it could benefit to the team to increase their collaboration with other metabolomic/fluxomic platforms of Paris to give a more metabolic dimension than a genetic one to the project, as well as with clinicians to perform more translational research.

The team has an excellent fund raising, but surprisingly no contract with pharmaceutical companies was obtained during the last period while the research subject lends itself to it. The team could benefit to collaborate more with industrial partners in order to increase the valorization of their work. Furthermore, the team must continue to be visible internationally by working to obtain new international contracts.

The workforce of the team has slightly reduced during the last period with 2 retirements. Therefore, the team could benefit to recruit of new young researcher and research assistant, and it is one of the goals of the team which have some candidates.

Analysis of the team's trajectory

The team proposes to continue their projects around their 3 axes (gut insulin sensitivity, O-GlcNacylation, ChrREBP), by focusing on the discoveries performed during the previous contract. Therefore, the team will capitalize on its expertise on these topics, on their developed tools and preclinical models, and on its reputation. There will be 3 axes: 1) Relationship between gut insulin resistance, intestinal barrier function and inflammation; 2) Role of O-GlcNAcylation in hepatic and inflammatory diseases; and 3) Role of ChREBP in the inter-organ network that controls energy homeostasis. There is no doubt that the team will continue to perform very well on these topics, but the risk-taking part of the project as well as the major scientific and technological breakthroughs for the next 5 years should be more emphasized.

Whatever, the research project is excellent and part of the project will be more focused on the gut, in addition to the liver. The team will develop original preclinical models. In the future, the team wants to increase its translational research and includes analysis in human biopsies in all their research projects. Furthermore, the team will also use human gut organoids.

Concerning the interesting new developments in the team's trajectory, the team also wishes to take into account sexual dimorphism in the development of NAFLD and focus its research on O-GlNacylation on a mitochondrial form of OGA.

RECOMMENDATIONS TO THE TEAM

This is an excellent team with a high reputation and expertise, an excellent contribution to national and international networks and an outstanding involvement in training. The committee recommend to the team to maintain this leadership in their work despite 2 retirements, and to success in the recruitments they plan to do. The team uses a lot of original mice models and is involved in the METABOL'IC platform, but the team should benefit from getting closer to other metabolomic/fluxomic platforms from Paris in order to give a more dynamic metabolic dimension to the project. Lastly, the team should benefit to increase their partnerships with both clinicians and industry in order to extend translational research and to valorize it.

Team 34: Bacteria and Perinatality

Name of the supervisors: Ms Claire Poyart & Ms Agnès Fouet

THEMES OF THE TEAM

The scientific objectives of the team are mostly related to the pathophysiology of invasive infections, particularly during pregnancy and neonatal period. The main focus of the group is the *Streptococcus* (Groups A and B) physiological response including host/microbe response, metabolic signatures.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous evaluation suggested to improve techniques such as 3D organoids and immunological aspects for the host-pathogen response. The team has improved the organ-on chip technology although there is still space for pushing this area of investigation to explore the host-pathogen cross talk particularly in the context of M-cells related research.

Dissemination activities to reach general public with different communication strategies has been partially addressed. The participation to the "Fête de la Science" with initiatives specifically targeted to children and their families is an example of excellent science communication to the public. The team shares new published papers through press releases.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	1
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	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**3**
Total personnels	**8**

EVALUATION

Overall assessment of the team

The overall assessment is very good to excellent.

The scientific production consists of 60 manuscripts co-authored by team members, including several in top specialist journals. The international recognition of the team is excellent, as seen by the numerous international conferences invitations as invited speaker. Similarly, funding has been constantly received via several sources. The team was able to recruit one postdoc and four engineers, and supervised 7 PhD students and numerous Master students.

Strengths and possibilities linked to the context

The team is internationally recognized for the important contributions in the field of *Streptococcus* pathophysiology. Team members strongly contributed to clinical studies and more basic science/mechanistic studies. The scientific production was excellent with 60 published studies, 8 as PI and 41 as collaborations on high-rank journals including J. Clin. Invest., Clin. Infect. Dis., J. Biol. Chem. Overall, this interconnection represents a plus for the team. Investigations efficiently combine bench to clinical work with possibility to access clinical samples paving the way to translational applications as demonstrated by the 8 basic science and 10 clinical/medical articles.

Members of the team were invited as speakers or chairs to numerous talks during the last five years, including 11 international conferences (e.g. ISSAD and Lancefield meetings, ESPID, ECCMID, and SEISC). The numerous invitations to national and international meetings highlight the international interest towards the field of investigation and this is highlighted by the involvement of a team member to the organizing committee of the International Symposium on Streptococcus agalactiae Infectious Disease (ISSAD) Global Conference held in London in 2021.

Team members were able to obtain funding as coordinator or partner by e.g. ANR (448 k€, 2018-2022), Inserm (90 k€, 2017-2019), FRM (350 k€, 2017-2022). Team support comes from both public and private grants. The role as a partner is particularly relevant in a structuring project for competitivity funded by the Public Investment bank (Inspire, BPI PSPC, 500 k€, 2018-2024). The unit recruited 1 postdoc and 4 engineers, trained 7 PhD students and 29 students (M1 and M2).

Weaknesses and risks linked to the context

Due to the retirement of one team leader, the team will be profoundly changed with association to a new team. Currently, the complementarity between both is not clear.

Analysis of the team's trajectory

As aforementioned, the team will profoundly change and will include a new team leader not yet internationally consolidated. Despite the current lack of a coherent development plan strengthening both team leaders' scientific production, there is a common ground of interest to be better explored.

RECOMMENDATIONS TO THE TEAM

The team will be included in a new team for the next mandate. Still, some weaknesses should be addressed with a more courageous approach to abandon the established comfort zone and explore other research opportunities. Previous suggestions to develop 3D intestinal models have been only partially explored with a need of increased complexity to address host-pathogen interactions taking also into the equation the role of the immune cells. There is a need to identify fertile niches to grow collaborative network and exploit the team members' talent.

Team 35: Immune cell signalling and retroviral infection

Name of the supervisor: Ms Clotilde Randriamampita

THEMES OF THE TEAM

The themes of the team during the reporting period were focused on signalling pathways in activated T cells by chemokines, upon inflammation and retroviral infection. The team also investigated signalling induced by HIV-1 infection in dendritic cells and macrophages upon cell-to-cell transfer from infected T cells.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has partially addressed the recommendations provided in the previous report. As recommended, they published articles in higher-profile journals (J. Allergy Clin. Immunol.; Cancer Immunol. Res.; 2 articles in PLoS Pathog.; a review in Nature Rev. Immunol.). It was also recommended to organize the team in themes to improve synergies between members in order to increase international visibility. This was only partially done and only few works included contributions of two main researchers of the team as co-authors of original articles (J. Virol.; Front. Immunol.; PLoS Pathog.; J. Allergy Clin. Immunol.), without strong significant team coherence.

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	4
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	**7**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**5**
Total personnels	**12**

EVALUATION

Overall assessment of the team

The overall assessment is very good to excellent.

The achievements are of very good to excellent quality. Several articles were published in leader position in the different topics developed by the team, as well as a review in an outstanding journal displaying competences and visibility. Attractiveness is excellent with several young investigators who were trained by the team, and 2 who obtained a permanent position during the reporting period. The contribution to society is very good with some contributions to debates in society.

Strengths and possibilities linked to the context

The team was composed of 4 researchers and 1 emeritus researcher, who developed independent topics, with contributions of each other's in some studies. They identified the cAMP/PKA pathway as important in T cell

migration upon chemokine stimulation, with potential function in T cell directionality. They characterized the inhibitory mechanism on T cell migration of Fam65b upon its phosphorylation, and linked a mutation in CDC42 to a severe autoinflammatory syndrome, revealing CDC42 connexion between several signalling pathways. The team also identified the modulation of the transcriptional activity of FOXO1 as crucial in the context of T cell infection by HIV-1, and in the generation of new type of CAR-T cells. The team uncovered two sequential cell-cell fusion processes for the high production of HIV-1.

These findings are associated to 21 original articles: 8 with team members as last authors, 7 were in collaboration with platforms or teams from Institut Cochin and 20 in collaboration with external teams (national collaboration with C2N Univ. Paris Saclay, Imagine Institute, Necker Hospital, ENS Saclay; international collaboration with Pasteur Institute of Shanghai (China), EPFL (Switzerland)). The quality of the publications from the main topics of team members is very good to excellent with articles published in high-profile journals and/or well-established ones (J. Allergy Clin. Immunol.; Cancer Immunol. Research; J. Virol.; mBio; 2 articles in PLoS Pathogens).

The team has been supported by grants for a total of 1.5 M€ in the reporting period on a regular basis of more than 200 k€/year. Grants include national ones (e.g. 7 from ANRS, 3 from Sidaction, 1 from ANR, ARC, 1 from "Ligue Contre le Cancer") and international (HIVERA Program, H2020 FOLSMART and for PhD candidates from the Chinese Academy of Sciences (6)). They also obtained grants for valorisation (Inserm Transfert, 40 k€).

The team has trained 9 PhD students (including 3 international PhD students), 5 having completed their thesis at the time of the report (with a mean of publication of 2.7 per PhD student); 5 French and 1 foreign postdocs were also enrolled during the reporting period. Of note, two young investigators got a permanent position during the contract, one as assistant professor (MCF) and one as researcher (Inserm CRCN), and a new researcher (DR2) joined the team in 2022.

The team gave 11 talks in meetings, including five in international ones (e.g. four times in Spring Harbor meeting on retroviruses, USA), and presented four posters.

Activities were supported by two patent applications (on a FOXO1 inhibitor & on the immunostimulatory effect of a drug, both in 2017). One patent is in preparation on the repositioning of a drug to regulate RHOA pathway.

Weaknesses and risks linked to the context

A strong and dedicated synergy between several topics/expertise of the different PIs is not deeply engaged to get papers in very high-profile journals and to get shared high-level grants.

The total number of publications (7), reviews (6), oral presentations (11) and posters (4), in leading position by members of the team, is not so high for a team of 4 full-time researchers (+ 1 emeritus), 9 PhD students and 6 postdocs.

The team will split for the next contract, and one team leader, a researcher and the newly recruited CRCN will leave the lab.

The departure of team members, experts in retrovirology, hampers the team to obtain funding from major national agencies (ANRS) or charities (Sidaction) that were important sources of funding.

The current perspective of absence of postdocs to consolidate the research is a weakness.

Analysis of the team's trajectory

The team is going to change its organization due to the departure of 3 full-time researchers for the next contract, the arrival of a new one (in 2022) with new competences (biophysics), and new team leaders (a previous team member will share the lead with the new coming researcher).

The trajectory is in line with works previously conducted by the remaining members of the team (cell polarity and motility), and the new organization of the team proposes new projects at the edge of biology and biophysics. Projects will pursue on the role of cytoskeleton in controlling specific immune function, with some focus on the role of mechanical forces in tissues and cell biology. Three main axes followed will be: 1/ cytoskeleton in polarity, to investigate signalling involved in the parallelism between cell polarity during motility and in the immune synapse; 2/ cytoskeleton in inflammation, through links with clinicians to determine the molecular mechanisms involved in the control of inflammatory processes via their impact on cytoskeleton, cell morphology and mechanics; 3/ cytoskeleton and lymph nodes, to understand the impact of mechanical tissues perturbations due to the dynamics of microenvironment on B cell activity in antigen capture.

Due to complementary interdisciplinary expertise and available tools for mechanobiology studies, the trajectory described has the potential to generate excellent science in a competitive field of research.

RECOMMENDATIONS TO THE TEAM

The new complementary expertise of team members opens new topics addressed by the team, which have the potential to lead to interesting science. In this new team adventure, it is recommended to involve most human and skill forces on very limited studies (1 or 2) with very high potential (for very high-profile journals), in order to secure the team and long-term access to funding.

It is recommended to exploit biophysics tools and expertise to address highly challenging and relevant biological question(s), and not the opposite, in an international competitive context. Generating preclinical models to study rare disease could also be envisaged to develop potential unique and relevant tools to study autoinflammatory syndrome.

Team 36: Intestinal Self-renewal and tumorigenesis

Name of the supervisor: Ms Béatrice Romagnolo

THEMES OF THE TEAM

The Intestinal Self-renewal and tumorigenesis team focus its activity on the elucidation of the mechanisms underlying self-renewal, with one main activity related to the role of Wnt/ß-catenin signalling in normal intestinal development, as well as in colon rectal cancer and liver cancer. Additional research activities are related to the definition of the proteomic profiling of serrated colorectal lesions, and to the role of autophagy signalling in the normal and pathological intestine.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

NA, the team was established in 2019.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	4
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	**6**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**5**
Total personnels	**11**

EVALUATION

Overall assessment of the team

The overall assessment of the team is excellent.

The major goal of the team is the definition of the core signalling networks supporting self-renewal of intestinal epithelial stem cells, and how these pathways lead to the development of colon cancer. The scientific output has been excellent, thanks to publications in international peer reviewed journal related to intestinal and liver physiopathology but also in high-ranking generalist review journals. The team has also achieved excellent results in obtaining funds from highly competitive entities, both national or regional agencies.

Strengths and possibilities linked to the context

The major goal of the team is the definition of the core signalling networks supporting self-renewal of intestinal epithelial stem cells, and how these pathways lead to the development of colon cancer. The topic is certainly of great interest, as cancer cells impinge prominently on the self-renewal networks to sustain their survival. Also, building upon their previous observations published in 2015 in Nature Cell Biology, the team has determined the central role of autophagy in protecting Lgr5+ intestinal stem cells. These findings, reported in PNAS by the group

in 2020 are enticing, given also the translational potential of this discovery. Related to these efforts, the team has also explored the role of Wnt/ß-catenin signalling in hepatocellular (HCC) carcinoma and colorectal cancer (CRC), which are other areas of great relevance, in particular HCC, which remains still poorly studied. The assessment of the contribution of the WNT pathway, and in particular Axin 1, with the generation of a mouse model, is of great interest and potential impact.

The team is well integrated within the Institut Cochin, where most collaborations occur. From the range of publications, it would also seem that the team is leveraging nicely on the technologies provided by the core facilities of the institute, as attested for example by the proteomic analysis of the rare serrated colorectal lesions, showing a tight integration with the clinical colleagues (which at times could be challenging) and the proteomic facility. One particular strength is the close interaction with the clinic, attested by several papers published with clinical colleagues, and by the strong commitment demonstrated by clinicians and pathologists, in supporting the scientific activities of the group. In addition to the 2 researchers (the group leader and a CNRS scientist), the team hosts two clinicians who promote strong interactions with Cochin's hospital and translational studies. As a general comment, the human workforce is well adapted to the laboratory activity.

The team leader displays large reputation in the field as highlighted by her participation to different national committees (Ligue contre le cancer Grand Ouest, commission ANR section CE14 Physiologie-Physiopathologie, commission Fondation ARC, Membre de l'école doctorale HOB, Université Paris Cité) and her contribution to the organization of an international meeting (Microbiota in Host Health and Disease: from Correlation to Causality: Paris, 2018). A team member occupied an invited editor position from 2021 to 2022 in the review Endocrine-related Cancer; others scientists and clinicians raise editorial responsibilities as reviewers for various international journals (Nature Com., Gut, Cancer Research, Oncol. Immunology, Plos Biology, Plos One, Dev Biol, J Pathol, Virchows Archiv, Gut, Ann Pathol). The attractivity of the team is underlined by the teaching activity (about 114 h), hosting a foreigner visiting scientist since 2021, an international PhD student and a postdoc fellow.

The recognition of the team is circumscribed at the national perimeter as stressed by the invitations and participations to give oral talks in national meetings, 7/8 and 8/9, respectively and by the 5 seminars given in French institutions.

The team has also achieved excellent results in obtaining funds from highly competitive entities, both national or regional agencies. During the 2017-2022 period, the team obtained 13 grants for a total of more than 1.7 M€. Three grants from ANR, INCa, ITMO were obtained in which the team is partner, for a total amount of 447 k€. The PIA programs (Labex and Cancer research) allowed the team to lead 2 grants for a total of 190 k€. Finally, 10 contracts were raised from charities (Ligue contre le Cancer, Gefluc, ARC), among which the team coordinate 9 of them (total about 1 M€).

The scientific output has been excellent, thanks to 20 publications in international peered reviewed journal related to intestinal and liver physiopathology. More specifically, the team led in 8 articles, where team members were first or last authors, among which two articles in high-ranked general journals, i.e., PNAS (2020) and Nat. Comm. (2021). Seven papers were published in collaboration with other teams or facilities of the Institut Cochin. The team members also contributed to 12 articles from external collaborations. The clinicians of the team have been implicated in more than 200 publications related to their clinical research activity and all PhD students of the team published or prepare at least one first authorship paper. Finally, one book chapter and six reviews are part of the scientific production of the team.

There has also been activities towards the engagement of the public, as for example the participation to college student research apprentices programs and to French science festival. They also welcomed members of the Crohn disease foundation (Afa Crohn) to allow their donators and patients to discover the research community.

Weaknesses and risks linked to the context

As acknowledged by the group, and despite clear strengths in the scientific know-how, in the tools developed and in the publication records, the committee would note as potential weaknesses a bit of insularity, as the group has published mostly though collaborations within the institute, with relatively few international collaborations. Engaging collaborators outside the Cochin institute would allow the participation to international grant proposal, enhanced possibility of exchanging ideas and expertise, sharing of technologies potentially not present in the Cochin institute, and finally securing more international grants. Along these lines, despite its high productivity, the group is relatively small, and some more members might foster an even more productive environment.

Analysis of the team's trajectory

Building upon the strong foundations of their previous papers and tools that the team has been recently established, the proposed trajectories align well with the overall themes proposed, and promise to deliver impactful results in the near future. Notably, the findings of some pathways, namely autophagy, as central in several of the processes identified in intestinal stem cell biology, could usher important translational results, that given the strong engagement of the clinicians in the team, could then be swiftly transferred into the clinic.

RECOMMENDATIONS TO THE TEAM

Relying too much on colleagues and expertise within the institute may limit the possibility to tackle more complex and ambitious projects. While there are several collaborations ongoing, mostly with institutions in Paris and Montpellier, more extended partnerships with additional labs would be beneficial. Given the leadership role acquired in the field of intestinal stem cell, and the potential connections with cancer, we anticipate that this engagement should be relatively straightforward.

Team 37: Functional pancreatic beta cell mass in rodent and human

Name of the supervisor: Mr Raphael Scharfmann

THEMES OF THE TEAM

The team works on pancreatic development, beta cell differentiation and function during health and disease (diabetes).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Strengths: Team praised for work on human pancreatic/beta cell development, for the expanding impact that the EndoCbeta cell lines have made in the field (in particular via the spin out EndoCells) and interaction with pharmaceutical companies.

No major weaknesses were noted.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	8
Sous-total personnels permanents en activité	**14**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	2
Post-doctorants	1
Doctorants	2
Sous-total personnels non permanents en activité	**7**
Total personnels	**21**

EVALUATION

Overall assessment of the team

The overall assessment is excellent to outstanding.

The Scharfmann team demonstrates excellence in research and technology transfer, with high levels of productivity, output and impact over the review period. The PI is well known in the diabetes research community with a strong international profile, both for the development, validation and distribution of the EndoCbeta cell lines, and for leading research on pancreatic development, beta cell differentiation and function. An excellent track record of funding, and consistent research outputs demonstrate a well-functioning lab. Strong record in training doctoral students and evidence for public engagement activities. Exciting trajectory with a proposed fusion with the team of Mallone-You to create the "Immune-endocrine cross-talk in diabetes" to investigate the early stages of type 1 diabetes pathogenesis.

Strengths and possibilities linked to the context

The team has an excellent international profile: it is well known in the diabetes research community for the development, validation and distribution of the EndoCbeta cell lines, and for extensive work on pancreatic development and beta cell biology. There have been regular invites to international meetings including the European Association for the study of Diabetes (2019), Islet Study Group (2019) and American Diabetes Association (2023): these are the top international diabetes meetings. There were invited talks with industry, i.e. Astra Zeneca.

The track record in securing research funding has been outstanding over the past 5 years (>3million Euros), ranging from national ANR research grants, through substantial international H2020 funding (including as WP lead) to industrial sponsorship (AZ, Lilly). >1.5m Euros from industrial sponsorship.

There has been a strong record in training doctoral students (5 theses defended in review period).

Excellent track record with research outputs: a consistent level of publications (n=45, of those 24 were internal to the team) in strong, visible and well-respected metabolism journals including Diabetologia, Diabetes and Molecular Metabolism was noted. Many collaborative papers (18 external collaborations, 3 collaborations with Cochin teams) demonstrate a strong profile and international networking. Core research covered human pancreatic development, beta cell modelling and beta cell biology. PhD students trained by the lab have contributed to 24 research publications.

Technology transfer: Successful distribution of beta cell models was developed by the lab (EndoCbeta lines), and patented by Cochin, via the spin out company Human Cell Design, which is an outstanding example of real-world impact and valorisation of academic research. This cell model underpins part of the lab's academic research, as well providing the key platform on which the spin out company is based. The beta cell models provided by human cell design are widely used by the academic, biotech and pharma R&D community (used in >250 publications, and >300 research groups).

Evidence for public engagement, for example holding talks with people living with Diabetes (Diabéte et Méchant; Glucose toujours) and contributing to the production of a cartoon relating to diabetes in Editions Delcourt.

Weaknesses and risks linked to the context

No major weakness. The PI highlights some issues at the Institute: continuity of contracts for technicians/engineers, and challenges recruiting outstanding postdocs (both issues present at other European institutions).

Analysis of the team's trajectory

The proposal is for the fusion of the current Scharfmann and the Mallone-You teams, creating the "Immune-endocrine cross-talk in diabetes" team. This is a positive and exciting idea, coupling the cutting-edge insights of the Mallone-You team into the early pathophysiology of T1D (initiation of pancreatic autoimmune beta cell destruction) with the beta cell biology expertise of the Scharfmann team, including world class in vitro modelling of human beta cells. This proposal will combine two high performing groups, with great potential to generate new insights (and potentially new therapeutic approaches) into Type 1 Diabetes. Descriptions for this merger/fusion demonstrate that planning is underway, with a clearly articulated and credible set of research goals. This combined team is outstanding.

RECOMMENDATIONS TO THE TEAM

The Scharfmann team is well established and performing well, leads by an experienced PI. The proposed fusions with Mallone-You represents a new chapter and new set of opportunities, creating an outstanding research group. The challenge going forward will be managing this merger as efficiently as possible, minimising disruption and building momentum in the combined team. From the self-assessment documents provided it would appear planning for this is underway by both teams. During the presentations from the fused team, all 3 leaders presented and demonstrated a shared vision and strong working relationship, backed up by many years of collaboration. Therefore, the review panel had no concerns about the functioning of this fused team and were excited about its prospects going forward.

Team 38: From Gametes To Birth (FGTB)

Name of the supervisor: Mr Daniel Vaiman

THEMES OF THE TEAM

The team focuses on the holistic study of reproductive physiopathology in humans. This encompasses infertility, pregnancy disorders, and the long-term programming of diseases resulting from in utero exposures. The team's goal is to decipher the molecular aspects of gamete function, genetics, epigenetics, gamete interactions, the effects of endocrine disruptors, and the molecular effects of pregnancy and parturition in both animal and human models.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report mainly recommended improving the team's involvement in socio-economic activities. To a large extent, this has been achieved. Two patent applications are currently in progress, Cifre contracts have been established to finance two PhD students, and a start-up called FREMA has been created.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maîtres de conférences et assimilés	5
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	**18**
Enseignants-chercheurs et chercheurs non permanents et assimilés	5
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	9
Sous-total personnels non permanents en activité	**15**
Total personnels	**33**

EVALUATION

Overall assessment of the team

The overall assessment is outstanding.

The team has had an excellent publication output, receives invitations to national and international meetings, demonstrates success in fundraising, has established international collaborations and relationship with private companies. The team actively contributes to the training of young researchers, and makes efforts to communicate with the general public through various actions.

Strengths and possibilities linked to the context

The laboratory's holistic approach to studying human reproduction makes the team highly attractive. Over the period, the team has published 105 articles in peer-reviewed journals, including 52 in leading positions and 23 reviews, with 14 in leading positions. Among the list of publications in leading positions, many are published in top journals in the field of reproductive biology, such as Hum Reprod Update, Hum Reprod, but also in journals

from other specialities, such as Blood, Am J Hum Genet. In addition, the team has contributed, through collaborations, to important papers in Science, Nat Com, and J Clin Invest.

The quality of the scientific production is also evidenced by the number of invitations to international and national meetings. Three team members are regularly invited to international conferences, with the PI being invited 2-3 times per year. In 2022, the PI chaired and organized ISSHP2022. All team members are regularly invited to national meetings.

The team's involvement in national and international networks, such as iPLACENTA and ANDRONET European COST, as well as their editorial activities, exemplify their expertise. For example, the team leader is the Editor for IJMS, Frontiers in Genetics, Clinical Genetics, Genetics Selection Evolution, and another member of the team has been a guest editor for a special issue of International Journal of Molecular Science titled 'Sperm Adhesion and Fusion.' Team members also have responsibilities in different French institutions, including the French National Consultative Ethics Committee, Inserm CSS3 committee, PHRC-I, and CRC-I evaluation committee. Furthermore, they have received awards, such as the Junior Charles Thibault award from the GDR CNRS "Reprosciences" in 2018 and the award from the European Young Researchers in Andrology in 2019. The team leader received the senior Prix Charles Thibault in 2023.

Another strength of the team comes from the wide expertise of its members. Indeed, the team's researchers have expertise covering both basic and clinical sciences. The team takes advantage of its proximity to the hospital, and the fact that some clinician-biologists are involved in the themes developed by the laboratory.

The team has trained 13 PhD students, with an average of 3 to 5 papers per student and 8 for two of them.

The team is very successful in terms of grant applications, notably a grant from the Bill & Melinda Gates Foundation. During the period, it raised 4.2 million Euros from 29 grants, including 3 international grants, 7 ANR grants, 1 RHU grant, and 18 others. This ensures the continuity of the team and has also allowed the strengthening of bioinformatic expertise, providing additional autonomy to the team.

A new technology, single-cell/nucleus RNA sequencing, has been implemented in the laboratory, allowing the discovery of new biomarkers. These results are on the way to being patented. In the last five years, the team has filed two patent applications, and has set up collaborations with companies that contribute to the financial support of two PhD students through Cifre contracts. Compared to the previous period, the team's involvement with industrial partners and patient associations has improved.

Remarkably, all the projects developed by the team have been successful.

Weaknesses and risks linked to the context

There is no weaknesses.

As is the case with many French research teams, the main difficulty arises from the lack of permanent research support staff (< 0.4 per/researcher).

Analysis of the team's trajectory

The project of the team is a continuation of the previous term. The team's interdisciplinary, particularly the close links between basic and clinical research, allows them to approach the next phase of their projects with confidence, despite the wide range of topics they cover. Insofar as these are in line with a logical understanding of human reproduction, from its beginnings, gamete differentiation, to its end, the birth of a healthy child, and where the team has already demonstrated its expertise, there is no doubt that their scientific output will continue to be excellent.

A significant aspect of the project's appeal lies in its translational nature, spanning from very basic research to clinico-biological applications. The team's combination of researchers and practitioners guarantees the credibility of such a strategy.

RECOMMENDATIONS TO THE TEAM

The team is excellent, and considering that the project is a continuation of previous work, there are few recommendations to be made:
The team need to focus on the recruitment of new researchers.
To enhance the team's level of expertise, efforts should be made to recruit more postdocs.

Team 39: Physiopathology of AMPK and AMPK-related protein kinase in diabetes and obesity

Name of the supervisor: Mr Benoît Viollet

THEMES OF THE TEAM

The themes of team 39 "Physiopathology of AMPK and AMPK-related protein kinase in diabetes and obesity" during the reporting period were focused on the understanding of the roles of AMP-activated protein kinase (AMPK) and salt inducible kinase (SIK), member of the AMPK-related protein kinase family, in various physio-pathological conditions from diabetes to obesity and also cancer, and to assess their utility in diagnosis and efficacy in therapeutics. The team has studied the role of AMPK familly in several type of tissue, such as the liver in the context of hepatic steatosis, or in the skeletal muscle in the context of T2D.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations from the previous report primarily focused on improving the selection of fields to investigate and refocusing activity on a narrower range of strong themes. This consideration has not been completely followed since the team still present its activity around 5 different axes which seems relatively high regarding its size. The team collaborates with several other labs but do not lead most of these projects and the number of publications co-signed as a corresponding author is relatively weak (7 with 4 of them in 2018).

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	0
Sous-total personnels permanents en activité	**2**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	0
Sous-total personnels non permanents en activité	**1**
Total personnels	**3**

EVALUATION

Overall assessment of the team

The overall assessment is very good.

This is a very good team, which is internationally renowned for its research on AMPK in pathophysiological conditions. The team has developed highly relevant biological models to investigate AMPK's function in multiple metabolic organs. However, the team's scientific output is very good, predominantly collaborative.

Strengths and possibilities linked to the context

The renown of the two permanent researchers is undoubtedly a strength for the team, as they are part of an international network of scientists investigating the consequences of AMPK regulation. Within this network, the team has made impressive contributions, with 54 publications to their name. Similarly, the team has collaborated on publications in highly renowned journals (including 2 in Nature Communications in 2022). Regarding the team's involvement in this international network, its researchers regularly organize and participate in international meetings on AMPK (for instance, the 11th AMPK meeting in France held at Evian Les Bains), further enhancing their legitimacy in this field of study.

The team has also attracted and trained 1 PhD student (french) and 1 postdoctoral fellow over the period funded respectively by PhD fellowship from region Île-de-France and an ANR grant.

The team has then the ability to successfully apply for various types of national grants, securing 700,000 euros over the period, and collaborate with several industrial partners such as Sanofi. Contracting with these partners has significantly contributed to the team's funding (180 k€). These industrial contacts are a crucial aspect of the work performed by this team. The team leader is for instance in the SAB of Poxel, for developing of new pharmaceuticals and the initiation of a clinical trial to assess the therapeutic effects of AMPK activators in the context of NASH for example.

The models developed by the team are important to mention. They constitute an exceptional resource for studying AMPK in various contexts, leading to significant breakthroughs in the field, either through the team's own projects or those involving collaborations.

Weaknesses and risks linked to the context

Over the evaluated period, the size of the team was small regarding the proposed ambitious project and the number of permanent staff (2 permanent researcher), postdoctoral fellows (only 1) and PhD students (only 1). The team is also strongly dispersed over several objectives (5 axes are developed).

Overall, the team's size is critical given the intended number of research axes they pursue, and their attractiveness in terms of the number of Ph.D. students and postdoctoral fellows is relatively low.

The team did not manage to secure grant at the European level even if it is balanced by industrial contract. This constitutes a weakness and its correction could favour the acquisition of lead position in the developed projects.

Finally, the ability of the team to be leaders on the developed project is questionable since their work is mainly collaborating and their publications rarely signed as first author or corresponding author (only 4 between 2019 and 2023).

Analysis of the team's trajectory

Regarding the small size of the team, its fusion with the Maire team is relevant. In the context of this merger, former members of the team will focus on studying muscle motoneuron physiology. Their primary role will be in the axis - Muscle atrophy and hypertrophy, where AMPK may play a role in orchestrating the crosstalk between fiber hypertrophy and the metabolic shift towards oxidation during overload-induced hypertrophy of skeletal muscle.

RECOMMENDATIONS TO THE TEAM

The team is encouraged to develop a strategy that harnesses the diverse expertise and strengths of its members to establish a cohesive research profile. Substantial efforts are anticipated from the former members of Benoît Viollet's team at this level to seamlessly integrate the themes of the merged team and actively contribute to their advancement.

This strategy should empower the team to address emerging scientific inquiries by fully utilizing the existing expertise. Active participation in international networks and consortia is highly recommended, and relevant members of the international networks integrated by Benoît Viollet and Marc Foretz should be actively engaged.

Team 40: Immunopathology and neutrophil dysregulation in pulmonary and systemic inflammation

Name of the supervisor: Ms Véronique Witko-Sarsat

THEMES OF THE TEAM

The team focusses on the biology of neutrophils in systemic inflammatory disease. The team studies neutrophils in autoimmune vasculitis and pulmonary inflammation associated with cystic fibrosis.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team followed the former committee's recommendations focusing on higher profile publications.

The team reduced the number of Master students trained to preserve research time of senior staff as proposed in the previous report.

In term of strategy, the former committee recommended to pursue the development of small molecules as new therapeutic approaches in vasculitis. The team has still a strong desire to develop these translational aspects but dedicated grants were pending.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	**7**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**6**
Total personnels	**13**

EVALUATION

Overall assessment of the team

The overall assessment of the team is excellent.

The team has a very good to excellent output in terms of publication, with some excellent publications over the period. The team was able to secure national funding. The team has excellent international visibility through participation in major congresses and scientific societies and is highly involved in national boards. The participation in education programs and training investment of the team are excellent.

Strengths and possibilities linked to the context

The team includes 4 clinicians supporting development of translational research and access to samples from cohorts of patients.

The PI has a significant reputation, she received the "Woman in Science Award" from the International Association of Inflammation Societies in 2022 and is editorial member of Journal of Innate Immunity and Journal for leucocyte biology. The PI has got the opportunity to expose her research in 19 meetings, 9 in France, 10 abroad and she participated in the organisation of conferences (SFI, World Congress of Inflammation, etc.).

The training investment of the team is excellent with 6 PhD students mentored by the team over the period. Each doctorate had an article as first author and between 2 and 4 publications in total. The team demonstrated aptitudes to attract 3 foreign postdocs over the period.

The team has been active in raising funds mainly through charities or patient association representing a total of 830 k€ over the period. The team appears as partner in 2 national grants, one ANR (25 k€ for the team) and one from the Labex Inflamex program (180 k€). Several grants from charities were obtained, among which the major "labellisation équipe FRM" funding (446 k€) and 1 grant from the Foundation Arthritis (24 k€). The association Vaincre la Mucoviscidose offered 3 "subvention recherche" to the team, for a total amount of 140 k€.

Over the period, the team was able to maintain its publication standard, with a very good to excellent publication output. The team produced 43 publications including 28 original articles including 15 original publications as lead/senior author (5 for the PI) and 15 reviews. Among the publications, 8 were developed in collaboration with a Cochin team and 21 with external collaborators. The highlighted publications of this review period include a publication in Kidney International (2019) that analysed the proteome of neutrophils in granulomatosis with polyangiitis identifying new mechanisms involved in apoptotic cell clearance and pathophysiology of the disease. The second highlighted publication in Journal of Experimental Medicine demonstrating a major role of PCNA in NADPH oxidase assembly and the ROS production by neutrophils. They demonstrated that PCNA inhibitor could represent a promising therapeutic strategy using murine model.

Weaknesses and risks linked to the context

Success in obtaining external funding could be improved. The lack of international funding and participation in European or international research consortia appears contrasting with the recognition of the research performed in the team by the community.

There is a lack of outreach activities towards the general public and innovation. This could be improved.

The recruitment of postdoc and technicians on short-term contracts, together with the absence of permanent engineer staff in the team might hamper the transfer of skills and the long-term development of the projects.

Analysis of the team's trajectory

The team will join the one currently led by Pierre-Régis Burgel and Frédéric Pene (team 12). Both teams have already a sustained collaboration related to cystic fibrosis. More recently, their collaboration uncovered the contribution of neutrophils in acute respiratory distress syndrome in patients with severe SARS-CoV-2. The complementary research expertise of the teams is synergistically integrated in the proposal.

The three axes proposed by the team, after fusion, are based on previous successful work performed independently by the 2 groups, the common trajectory appears then highly attractive and straightforward. The axis 1 relates to the role of PCNA in the control of neutrophil functions, the team proposes to analyse the molecular and structural details of the PCNA-S1008 interaction in neutrophils from COVID-19 patients, to define the PCNA interactome in neutrophils of COVID-19 patients using proteomic and identify potential molecules with therapeutic interest. The team identified NAMPT, involved in N1 to N2 transition in cancer, as a PCNA partner and will study the role of this interaction in murine model and patients with lung cancer in collaboration with colleagues from Germany and Cochin hospital. Axis 2 is related to chronic airway bacterial infection relevant to cystic fibrosis and bronchiectasis (developed in team 12): it will integrate the expertise of team 40 in relevant murine models and clinical activities to characterize the role of neutrophil proteases and the effects of CFTR inhibitors in CF models and patients. Axis 3 will study how sepsis-induced alterations of the intestinal microbiota and gut epithelium could modulate airway epithelium functions and contribute to defective lung defences. The future project associates both basic and translational research with the aim to define new actionable therapeutic strategies.

Based on the present report of team 40, fundings are not secured for the next years. This matter of fact could have represented a risk for the future team. However, during the oral presentation, the team has mentioned a 3-years funding from Vaincre la Mucoviscidose (150 k€).

RECOMMENDATIONS TO THE TEAM

As presented in the team trajectory, the team 40 will merge with team 12. This synergy is encouraged in order to increase the success in fundraising, to increase the workforce, to apply to ambitious translational/clinical research projects federating all basic and translational research and translate the results in clinical applications. The panel recommends that the PI emphasize on senior author papers.

Action for valorisation should be encouraged in the team. The fusion with team 12 and the translational possibilities may represent strong opportunities to develop innovation outputs. Action for dissemination to lay public should be encouraged in the team.

CONDUCT OF THE INTERVIEWS

Dates

Start: 16 octobre 2023 à 08h00

End: 19 octobre 2023 à 18h00

Interview conducted: on-site

INTERVIEW SCHEDULE

Monday, October 16th 2023 Dinner

Tuesday, October 17th 2023

08h00 – 08h15 Welcome. Presentation Hcéres committee

08h15 – 10h00 Unit presentation: achievements and trajectory

10h00 – 10h30 Coffee break

10h30 – 12h45 Parallel sessions. Team presentations
Committee A: Allanore/Batteux; Ingersoll; Helft
Committee B: Niedergang; Ariey; Berlioz/Emiliani
Committee C: Bertherat; Dentin/Alves-Guerra

12h45 – 14h00 Lunch

14h00 – 15h30 Parallel sessions. Team presentations
Committee A: Passaro; Donnadieu; Bercovici/Blondel
Committee B: Bomsel/Ganor; Bourdoulous
Committee C: Peyssonnaux; Lehuen/Beltrand

15h30 – 16h00 Coffee break

16h00 – 17h00 Parallel sessions. Meetings with ITA, Researchers, PhD/postdocs

17h00 – 18h00 Committee debriefing
20h00 Dinner

Wednesday, October 18th 2023

08h30 – 10h00 Parallel sessions. Team presentations
Committee A: Witko/Burgel/Pène; Miotto/Chaumeil
Committee B: Lavazec; Margottin/Pique
Committee C: Marullo; You/Mallone

10h00 – 10h30 Coffee break

10h30 – 12h45 Parallel sessions. Team presentations
Committee A: Aractingi/Fontaine; Romagnolo; Pasmant
Committee B: Matic/Tenaillon; Arrieumerlou/Tazi
Committee C: Jockers/Dam; Vaiman

12h45 – 14h00 Lunch

14h00 – 15h30 Parallel sessions. Team presentations
Committee A: Fontenay/Simoni; Lucas
Committee B: Delon/Pierobon; Chassaing; Hosmalin/Cheynier
Committee C: Postic/Issad; Maire/Viollet

16h00 – 18h00 Coffee break + Committee debriefing
20h00 Dinner

Thrusday, October 19th 2023

09h00 – 10h30 Meeting with supervising bodies

10h30 – 11h00 Committee debriefing
11h00 – 12h30 Meeting with the direction and co-direction of the unit
12h30 – 13h30 Committee debriefing

13h30 – 14h30 Lunch

14h30 – 18h00 Redaction of the report

18h00 End of the visit

GENERAL OBSERVATIONS OF THE SUPERVISORS

Université Paris Cité

Le Président

Paris, le 6 février 2024

HCERES
2 rue Albert Einstein
75013 Paris

Objet : Rapport d'évaluation de l'unité **DER-PUR250024175 - Institut Cochin.**

Madame, Monsieur

L'Université Paris Cité (UPCité) a pris connaissance du rapport d'évaluation de l'Unité de Recherche **Institut Cochin**

Ce rapport a été lu avec attention par la direction de l'unité, de la part de laquelle vous trouverez ci-joint un courrier décrivant des erreurs factuelles à corriger, le vice-doyen Recherche et le doyen de la Faculté de Santé d'UPCité, par la vice-présidente Recherche d'UPCité et par moi-même.

Je souhaite indiquer, avec le Doyen de la Faculté de Santé, que le changement de direction du centre de recherche Institut Cochin, qui a été fait en cours de quinquennat, a été accompagné par l'ensemble des tutelles. Ceci a permis à la nouvelle directrice de piloter le dépôt du dossier de renouvellement et, ainsi, d'insuffler sa marque sur la trajectoire et de donner ainsi une nouvelle dynamique organisationnelle à l'Institut. La politique scientifique portée par la nouvelle direction s'appuie par ailleurs sur l'avis d'un SAB international. Je tiens également à souligner que ce centre de recherche, multidisciplinaire, est la plus importante UMR de la Faculté de Santé et une des plus importantes de l'université, en terme d'effectifs comme de poids dans la stratéie de recherche.

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

Édouard Kaminski

Présidence

Référence
Pr/DGDRIVE/2023

Affaire suivie par
Christine Debydeal - DGDRIVE

Adresse
85 boulevard St-Germain
75006 - Paris

www.u-paris.fr

Annexe 1 – Observations CNRS – Institut Cochin

De : CNRS-Hcéres Evaluation unités <hceres.eval-unites@cnrs.fr>
Envoyé : mercredi 10 janvier 2024 17:55
À : ged.der@hceres.fr; hceres2023@u-paris.fr; Coordinatrice des CIC INSERM <helene.esperou@inserm.fr>; Correspondant INSERM <eval-structures.desp@inserm.fr>; Correspondant 2 INSERM <samia.deghmoun@inserm.fr>
Cc : berengere.iapella@hceres.fr
Objet : RE: Hcéres - demande de retour des observations des tutelles sur le rapport d'évaluation - DER-PUR250024175 - Institut Cochin

Madame, Monsieur,

Je vous remercie de nous avoir transmis de ce pré-rapport et prie de bien vouloir noter que le CNRS n'émettra pas de réponse institutionnelle de type « observations de portée générale ».

Je reste à votre disposition pour tout complément d'information.

Bien à vous,

--

Frédéric FRANCOIS-ENDELMONT

CNRS – DAPP

Direction d'appui aux partenariats publics

3 rue Michel-Ange - 75794 Paris Cedex 16

Secrétariat : 01.44.96.41.10

Ligne directe : 01.44.96.40.56

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