Research evaluation

EVALUATION REPORT OF THE UNIT

IMRB - Institut Mondor de Recherche Biomédicale

DYNAMIC - Dynamique des interactions microbiennes au sein du microbiote

TREPCA - Résistances thérapeutiques du cancer de la prostate

EPIDERME - Épidémiologie en dermatologie et évaluation thérapeutiques

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université Paris-Est Créteil

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

École nationale vétérinaire d'Alfort

Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail - Anses

EVALUATION CAMPAIGN 2024-2025

GROUP E

Report published on March, 27 2025

High Council for evaluation of research and hihter education

In the name of the expert committee:

Julien Diana, chairman of the committee

For the Hcéres:

Stéphane Le Bouler, acting president

In accordance with articles R. 114-15 and R. 114-10 of the Research Code, the evaluation reports drawn up by the expert committees are signed by the chairmen of these committees and countersigned by the president of Hcéres.

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

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

MEMBERS OF THE EXPERT COMMITTEE

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Experts:	Mr Damien Carrel, Université Paris Cité Mr Javier Cubero, Complutense University of Madrid, Spain Mr Jean-Christophe Deschemin, Inserm, Paris (supporting personnel) Ms Christelle Faveeuw, Institut Pasteur de Lille Ms Marion Fusellier, Oniris, Nantes (representative of Cneca) Ms Pascale Gaussem, Université Paris Cité (representative of Inserm CSS) Mr Xavier Loyer, Inserm, Paris Mr Michel Samson, Inserm, Rennes Mr Matthias Titeux, Inserm, Toulouse

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Mr Christophe Degueurce, EnvA
Mr Bassam Haddad, CHI Créteil
Ms Valérie Langlois, UPEC
Ms Hélène Maury, Inserm
Mr Pierre Wolkenstein, UPEC

ADDED NOTE:

Three independent units named DYNAMiC, TREPCA and EPIDERME will join the IMRB as teams 15, 16 and 17 respectively. As such, a global assessment of their activities as independent units for the 2018-2024 period is provided in the beginning of the team evaluation report.

CHARACTERISATION OF THE UNIT

- Name: Institut Mondor de Recherche Biomédicale
- Acronym: IMRB
- Label and number: UMR_S955
- Number of teams: 17
- Composition of the executive team: Director: Mr Jorge Boczkowski

SCIENTIFIC PANELS OF THE UNIT

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

THEMES OF THE UNIT

The Mondor Institute for Biomedical Research (IMRB, Inserm U955, Université Paris Est Créteil (UPEC)) is a multi-thematic biomedical research institute that conducts translational research in four major scientific areas: Translational Psychiatry and Neuroscience (ESPRY Division), Muscle Biology and Physiopathology (ESPRY Division), Vaccinology/Immunology/Infectiology (VIC Division), and Senescence, Metabolism and Chronic Diseases (PHYDES Division). A fifth transversal theme, "Diseases and Environmental Aggressions", has recently emerged. The general objective of the IMRB is to conduct translational research and training in the biomedical field to respond to critical unmet needs such as new diagnostic tools and treatments for psychiatric, genetic muscular diseases, viral infections and obesity. To achieve this goal, IMRB relies on 632 people working in fourteen teams, 22 in shared administrative and technical services and 28 in technological facilities and shared services. The biomedical specificity of IMRB, with 133 physician-scientists for 37 full-time scientists, is rooted in its strong and long-standing partnership with the Créteil hospitals, the French Blood Bank (EFS) and the Veterinary School of Maisons-Alfort (EnvA).

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The IMRB was created in 2007 by merging the pre-existing units of Inserm-Université Paris Est Créteil (UPEC). From this new structure, IMRB has grown from 350 people in eleven teams to 650 people in fourteen teams, making it a well-established biomedical institute. The IMRB occupies 12,000 m², mainly in the UPEC Faculty of Medicine and the Henri Mondor Hospital. In addition to these sites, one team is partially located in the Albert Chenevier Hospital, one team and part of other teams are located in a building of the French Blood Bank (EFS) within the Mondor campus, and part of two teams are located in the Veterinary School in Maisons-Alfort (EnvA).

Therefore, there is an obvious opportunity for exchange between research teams and hospital services and to conduct cutting-edge translational research and to promote the core of science conducted by IMRB in terms of bench to bedside basic and translational research.

The development of IMRB's research activities progressively raised significant issues regarding the available space. To address this problem, UPEC programmed three real estate operations: Restructuring of the School of Health building, construction of a new biomedical research building (BRB), and construction of a new research building (4000 m²) at EnvA in 2020-2022 to house. These operations will increase the IMRB space (from 12,000 to 16,500 m² at the end of 2025), allowing a better installation and development of teams and core facilities, as well as free space to host new teams.

RESEARCH ENVIRONMENT OF THE UNIT

The IMRB is part of a rich medical, biomedical and basic research environment within the Mondor Campus.

The Henri Mondor Hospitals, major university hospitals in the “Grand Paris” area, are a major asset because the location of the IMRB on the university medical campus and the important presence of medical staff in the research teams leads to excellent exchanges between research teams and hospital services, fostering translational research. The presence of the Clinical Investigation Center (CIC), managed by members of the IMRB, perfectly illustrates the strong relationship between the Institute and the Henri Mondor Hospital. Similarly, IMRB

members coordinate nine centers for rare diseases at the Henri Mondor Hospital and 1 national reference center (for viral hepatitis).

The Maisons-Alfort Veterinary School (EnvA) hosts two joint IMRB teams.

The French Blood Bank (EFS) supports and hosts two IMRB investigators and provide materials for cell therapy clinical trials.

Outside the Mondor campus, IMRB also has strong interactions with the École Normale Supérieure de Paris (ENS) and the Commissariat à l'Énergie Atomique et aux Énergies Renouvelables (CEA), with one IMRB team partially hosted by ENS and two IMRB teams using the CEA imaging facility. The IMRB also has close links with the UPEC laboratories: the Laboratoire Inter-universitaire des Systèmes Atmosphériques (LISA) for the development of the Pollurisk platform, the Observatoire des Sciences de l'Univers (EFLUVE) for the management of the Future Investments Program (PIA) Inno-SEnSE project, and the East Paris institute of chemistry and materials (ICMPE) for the development of various projects.

With 47 IMRB members who are teaching scientists and 133 who are physician-scientists at the Université Paris Est Créteil (UPEC), the Institute is naturally very involved in teaching activities. IMRB doctoral students are affiliated to two doctoral schools: École Doctorale Sciences de la Vie et de la Santé, directed by an IMRB member and affiliated with Université Paris Est (UPE) and UPEC, and Ecole Doctorale de Santé Publique, affiliated with Université Paris-Saclay and UPE).

The IMRB is part of high-level scientific networks at local, regional and national levels. It participates in the Scientific Committee of the Domaine d'Intéret Majeur (DIM) QI2 of the Ile-de-France region, and an IMRB member is coordinator of the One Health 2.0 DIM. IMRB teams are involved in the creation and management of structures related to the Future Investments Programme (PIA): labex Vaccine Research Institute (VRI), Graduate School (EUR) Life Trajectories and Vulnerability in Health (LIVE), EUR Frontiers in Cognition (Front-Cog) and Programmes et équipements prioritaires de recherche (PEPR, Propsy).

Members of three IMRB teams have created a start-up related to their research activities.

UNIT WORKFORCE: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	111
Maitres de conférences et assimilés	92
Directeurs de recherche et assimilés	15
Chargés de recherche et assimilés	21
Personnels d'appui à la recherche	248
Sous-total personnels permanents en activité	**487**
Enseignants-chercheurs et chercheurs non permanents et assimilés	26
Personnels d'appui non permanents	27
Post-doctorants	18
Doctorants	141
Sous-total personnels non permanents en activité	**212**
Total personnels	**699**

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons at 31/12/2023. Non-tutorship employers are grouped under the heading "others".

Nom de l'employeur	EC	C	PAR
UPEC	169	0	70
Inserm	0	19	48
EnvA	17	0	8
Autres	17	17	122
Total personnels	**203**	**36**	**248**

GLOBAL ASSESSMENT

During the last mandate, IMRB achieved an impressive scientific output in terms of the quantity and quality of studies published in internationally renowned and peer-reviewed specialist and general journals, the majority of which were signed by IMRB members as first or last authors. The range of publications reflects the multi-thematic scientific scope of the Unit, with research ranging from basic science to translational and applied science, including studies with patient cohorts and work by clinicians in the fields of Psychiatry, Neuroscience, Muscle Biology and Physiopathology, Immunology, Infectiology, Metabolism, Cancer and Senescence. IMRB has an outstanding level of external funding around €100 million, which supports interdisciplinary research. It has an excellent network of collaborations at national and international level.

The recommendations of the last evaluation have been considered and addressed. Efforts have been made to improve internal communication, IMRB management increased the frequency of Codir meetings and launched a weekly newsletter on the life of the Institute. To expand and modernize platforms, IMRB management responded to nine tenders for new equipment. To improve computing resources, the Institute purchased storage and computing servers. To ensure space to accommodate new and existing teams, the UPEC is conducting real estate operations to increase IMRB's space by the end of 2025. To increase international visibility, IMRB is developing three international summer schools, supporting student exchanges and hosting foreign researchers, including a Nobel laureate. In order to improve administrative support for the management of grant applications, IMRB carried out an audit of IMRB's administration and a Grant Office of the IMRB, GO-IMRB is developing since early 2022. Management is excellent in terms of overall governance, including measures of sustainability (GreenLab), gender and equity.

There is some risk that the newly integrated teams will maintain high standards of quality and quantity in their publications. New teams have been recruited from existing IMRB teams, but there is no clear plan to attract new teams from outside to support the Institute's new signature. Indeed, IMRB, like other multi-thematic institutes, lacks international visibility and an identifiable identity. A structured and strategic recruitment and internationalization policy is therefore needed to strengthen the IMRB in general and the new priority areas of environmental aggression in particular.

The new real estate plan for the Mondor campus will provide a unique opportunity to showcase the Institute's new identity, and the trajectory of the IMRB appears very promising.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

IMRB management took several actions to address the recommendations of the previous report. To improve internal communication, IMRB management increased the frequency of Codir meetings and launched a weekly newsletter on the life of the Institute. To expand and modernize platforms, IMRB management responded to nine tenders for new equipment. To improve computing resources, the Institute purchased storage and computing servers. To ensure space to accommodate new and existing teams, the UPEC is conducting real estate operations to increase IMRB's space (from 12,000 to 16,500 m2 by the end of 2025) with the aim of attracting new teams. To increase international visibility, IMRB is developing three international summer schools, supporting student exchanges and hosting foreign researchers, including a Nobel laureate. In order to improve administrative support for the management of grant applications, IMRB carried out an audit of IMRB's administration and a Grant Office of the IMRB, GO-IMRB is developing since early 2022.

B – EVALUATION AREAS

Guidelines for all areas of evaluation (1, 2, 3 and 4): Considering the references defined in the unit's evaluation guidelines, the committee ensures that a distinction is made on the outstanding elements for strengths or weaknesses. Each point is documented by observable facts including the elements from the portfolio. The committee assesses if the unit's results are consistent with its activity profile.

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

Assessment on the scientific objectives of the unit

The scientific objectives of the unit are outstanding, very ambitious and have considerable potential for socio-economic valorisation through the generation of potential medical advances.

Assessment on the unit's resources

The unit has access to all the equipment necessary for the execution of its projects. The financial resources at the unit's disposal are both outstanding and sufficient to support its projects.

Assessment on the functioning of the unit

The functioning of the unit is outstanding in terms of organization, and human resource management.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

IMRB is an academic research institution affiliated with Université Paris-Est Créteil (UPEC) and Inserm, maintaining close partnerships with Créteil hospitals, the French Blood Bank (EFS), and the National Veterinary School of Maisons-Alfort (EnvA).

The IMRB's scientific strategy is closely aligned with the strategic plans of its partner institutions, emphasizing clinical practice, public health policy, cutting-edge research, pressing issues related to the pathologies under its purview, and technological innovation. With a strong presence of clinicians within the IMRB, the unit actively contributes to health research and education, engages in national and international projects, and prioritizes responsible, transparent, and reproducible research practices. Driven by a commitment to collaboration,

excellence, and innovation, the IMRB seeks to expand the boundaries of knowledge by harnessing the diverse expertise of its community.

These projects are not only ambitious but also offer valuable solutions to pressing medical and societal challenges within the relevant research fields.

Weaknesses and risks linked to the context

It remains unclear whether the 19 clinical research programs funded by the Assistance Publique – Hôpitaux de Paris (APHP), totaling 5 M€, also contribute to the Institute's basic and translational research efforts.

Teams tend to be unevenly funded.

Given the challenges posed by an aging workforce, with the upcoming retirement of several Inserm and UPEC researchers and PAR, it is crucial to ensure that new scientists are encouraged to apply for recruitment through Inserm.

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

Over the period 2018-2023, the IMRB institute has enabled teams to lead or participate in numerous large-scale projects (around 500 projects acquired) at both the national and European levels, securing significant funding in the process (more than 100 M€).

This exceptional ability to secure funding is truly noteworthy.

Weaknesses and risks linked to the context

The continuation or transformation of structures such as labex, DFU or FHU, from which the IMRB benefits.

The proposal for three departments remains an open question regarding the added value of structuring the organization into departments with the risk of creating silos that may hinder the development of interdisciplinary and innovative projects, which are essential for breaking away from traditional disciplinary boundaries.

The close partnership with the École Vétérinaire de Maisons-Alfort (EnvA) presents a valuable opportunity to develop innovative projects in the field of 'One Health,' an area that is not yet sufficiently emphasized in our scientific strategy.

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

IMRB has established a governance structure well-suited to the modern and efficient management of a research center. This includes a steering committee (Codir), an Institute Management Board (Institute Council), a General Assembly, a Scientific Advisory Board (SAB), and a research support team that serves as the unit's administrative secretariat.

IMRB follows human resources management principles in accordance with directives from its supervisory authorities.

Staff benefit from training and career development opportunities through workshops organized by Inserm, UPEC, and IMRB itself.

Ensuring staff safety is a priority, overseen by the director with support from designated prevention officers. Data management practices comply with IT security standards and GDPR regulations, with staff receiving appropriate training. Additionally, the unit conducts environmental risk assessments and integrates sustainable development practices in alignment with institutional strategies.

Weaknesses and risks linked to the context

Currently, 54% of IMRB members are women. However, for the next mandate, the proposed leadership structure includes only six women among the 17 researchers in team-leader positions (35%), which falls short of the goal of gender parity.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractivity of IRBM is excellent to outstanding. Connections between clinical research and fundamental studies are strong and successful. Seven platforms implement high level and innovative technologies carried by high-profile engineers. Links with private companies, patient associations, international collaborations are proofs of excellence. A high number of PhD and postdoctoral fellows were welcomed. Research and development are guaranteed by competitive international and national grants. Excellence of the members is recognize by their participation to diversified scientific organizations.

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

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

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

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

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

The Unit is attractive in terms of its scientific influence and is part of the European research area:
Members of the IMRB participates to international and European congresses. They organize important events as: EMBO muscle meeting, Global hepatitis summit, Journées neurosiences Psychiatrie et Neurologie, franco-japanese meeting, international symposium in haemolytic Transfusion reaction in sickle cell disease, AIDS Vaccine, different international workshops, Liver Cancer Summit, Conference on stem cells, Eur summer school and summer school in the institute. Members of the unit participate to international conferences to present their works, including PhD students and post-docs. Members of the unit are engaged in editoriall responsabilities in journals (Front. in pharmacology, Int. J. Mol. Science, American Journal of Hematology, Scientific Reports, PlosOne, Revue Neurologique, Circulation…). Members are involved in steering bodies or as scientific experts at internal and national level (workpackage leaders in different Horizon2020 projects, clinical trials, founds obtained from ANR, FRM, ANRS, expert for French government and national assembly…). They have responsibilities in scientific institutions and learned societies (UPEC, hospitals, EnvA, FRM scientific committee, European society of cardiology, Inserm committee and scientific council, ARC foundation, Anses, INRS, AFD…). Their excellence is recognized by numerous scientific or non-academic prizes and distinctions (Grand Prix de l'Inserm, Prize from Institut de France, Grand Prix de la Recherche Infirmière, Légion d'Honneur, Palmes académiques, numerous prizes for thesis, poster presentation…).

The unit is attractive for the quality of its staff support policy:
The unit welcome numerous national and international PhD students and post-docs invited researchers and new scientists, physicians and teaching scientists. All new members are invited to a welcome half-journey to discover IMRB organization. New researchers are invited to present their works to the community, can benefit a financial welcome package. PhD students, post-docs, engineers and technicians benefit to a regular career meeting. Members are invited to present scientific seminars and participate to biannual retreat. Various committees are implemented to support integration and development (human resources and financial support, Communication, Health and safety, Comité d'animation scientifique, grant office, sectorial committees, psycho-social risk committee…).

The unit is attractive thanks to its success in competitive calls for projects:
Members of the unit compete to international and national funds. They highly succeed and obtained 495 grants for a total amount of 102 million euros. As principal investigator (74%) or partners (26%) they collect 21.1 million from European grants (several H2020), 32.8 million from national grants (ANR, ANRS, INCA, DIM…), 5.7 million from Programme d'Investissement d'Avenir. To these ones, funds from foundations (FRM, AFM…) and local grants

expose the high level of attractiveness of IMRB. Moreover, founds are obtained by core facilities thanks to service delivery (Biomarkers core facility).

The unit is attractive for the quality of its equipment and technical skills:
The unit uses seven high technology core facilities (Imaging, Cytometry and cell sorting, Genomics, Bioinformatics, Experimental physiological, Biomarkers, Pollurisk) which are all certified ISO 9001. All of them are equipped with state-of-the-art apparatus (thermostatic time lapse microscope, life cell imaging system, cells sorters, Illumina systems shared with the hospital, equipments for physiological investigations, Luminex and Simoa…). High-profile engineers and technicians manage these core facilities, are in charge of maintenance and increasing innovative technical approaches. Two million of funding were invested in the renewal of oldest equipment or acquiring innovative ones.

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

Two weaknesses were identified.

The first one concerns core facilities. Despite innovative and high technologic tools, some core facilities suffered from a lack of staff.

The second one concerns the heterogeneous success to obtain highly competitive international grants among the IMRB teams.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The IMRB's scientific output is outstanding, with 3,400 peer-reviewed articles, many published in leading journals, contributing to its outstanding international visibility. Team members play a key role in driving research impact, with 38% of articles authored by them as first, last, or corresponding authors. A strong commitment to open science, scientific integrity, and interdisciplinary collaboration ensures the unit's continued advancement of knowledge and its meaningful societal impact.

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

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

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

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

The unit's scientific production is outstanding, comprising approximately 3,400 original peer-reviewed articles, with 38% featuring team members as first, last, or corresponding authors. Additionally, the unit has published 542 letters and reviews. Of the original articles, 203 rank in the top 10% most cited globally, with 15.6% of these highlighting the team as first, last, or corresponding authors.

The original articles demonstrate exceptional international visibility.

The unit's output includes publications in leading international journals, such as *The New England Journal of Medicine*, *The Lancet*, *Nature*, *Science*, *Cell*, *The Lancet Respiratory Medicine*, *The Lancet Gastroenterology*, *JAMA*, *Cell Metabolism*, *Cell Stem Cell*, *Nature Medicine*, *Nature Genetics*, *Nature Communications*, *Nature Immunology*, and *Immunity*, among others.

The unit's governance demonstrates a strong commitment to fostering inter-team collaboration, reflected in the fact that nearly 36% of its publications result from collaborations between IMRB teams, a significant increase from 19% in the previous term.

The unit places a strong emphasis on robust theoretical and methodological foundations as its members manage various patient cohorts, research platforms, rare disease centers, and a national reference center, generating high-quality data that have significantly advanced our understanding of health determinants across different life stages and a range of pathologies.

The unit maintains a balanced scientific output aligned with its research potential, prioritizing the advancement of knowledge over the quantity of publications. It has implemented robust initiatives to uphold scientific integrity and rigor, including protocol registration, comprehensive data management plans, and open access to research data and software.

To ensure ethical and regulatory compliance, particularly with GDPR and human research regulations, the unit has appointed dedicated Ethics and Scientific Integrity referents. It adheres to guidelines set by the EU and French regulatory bodies and actively participates in the Inserm LORIER program, which promotes ethical and responsible research practices.

The unit also engages in collaborative efforts and national and international initiatives, demonstrating its commitment to research quality and transparency. Regular training sessions for members further reinforce its dedication to fostering a culture of integrity and trustworthiness in research.

The unit fosters a collaborative approach, valuing the contributions of all its members, including full-time researchers, university hospital clinicians, hospital clinicians, doctoral and postdoctoral researchers, and research support staff. Each role plays a vital part in advancing the unit's scientific mission, whether through publishing in peer-reviewed journals, developing tools and software, or managing research platforms.

This collaborative spirit has yielded exceptional results, exemplified by numerous publications co-authored by members from multiple teams. The unit is also committed to the principles of open science, with the majority of its research published in open-access formats. Additionally, efforts are made to encourage the use of HAL for disseminating publications, further enhancing accessibility and visibility.

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

It is important to distinguish the evaluation of IMRB as a mixed research unit, focused on both fundamental and translational research, from that of the Clinical Investigation Center (CIC 1430) at Henri Mondor Hospital, which is independently assessed by Hcéres. There is a potential risk of overlapping or confusion between the presentation of publications from the CIC and those attributed to the IMRB, which should be carefully clarified during evaluations.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The contribution of the IMRB to society is excellent. Members are involved in international and national advisory bodies. Interaction with patient association and general public shine their own studies. Members develop education courses and share knowledge using all media. Partnership with industries are dynamic and successful.

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

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

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

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

Members of the unit are largely engaged in interactions with the non-academic world. Members valorized research by creating spin off and start-up (Orixha, Innovhem, Tricares, Brightflow, Linking Vax). Discoveries and tools developed by team members were valorized by 44 patents and 9 licenses. They developed research projects with industries in 81 collaborations (Novaris, Roche, GSK, Jansen, Astellas…). Partnerships with socio-

economic world made it possible to obtain 38.6 million euros. Some contracts with industries allow Cifre grants for PhD students. They developed the Inno-SenSe core facility for companies engaged in global health and environment studies.

Members are implicated in various course trainings in many domains and at different levels. They developed continuing trainings and summer schools and also innovative learning transfer as MOOC. They are engaged with patient's associations to transfer knowledge (workshop with patients by the French Federation of cardiology, days and meetings with Huntington Disease patients, PCD association patients…) and offered public restitution of clinical trials and studies. They organized a day for generous donors (Journée des donateurs). They are also recognized experts by health authorities and learned societies and can participate to establish guidelines and recommendations.

Members participates to events for general public to share scientific values and discoveries. They are engaged in Fête de la Science (global public), Apprentis Chercheurs (high school students), Cordée de la Réussite and the Déclic program to sustain and help school students. Members are present in media (TV: France2/3…, Radio: France Culture, RCJ…, Journals: Le Monde, Ouest France…, Internet : Youtube, LinkedIn…). They also developed innovative and artistic events to mix scientific talks and poetry (Le souffle de l'eau) or make scientists affordable (Les causeries d'Emma le clown).

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

Some teams or groups are not engaged in social meeting to share scientific knowledge.

It appears a problem of visibility for some non-principal investigators. Each one should be engaged in nonacademic interaction.

ANALYSIS OF THE UNIT'S TRAJECTORY

Since its creation, the IMRB has experienced strong growth and today faces a number of challenges (space, attractiveness, identity, cohesion, aging, international visibility). Many of these challenges have been partially addressed during the last mandate, but the IMRB must continue to evolve while maintaining the level of excellence in biomedical research that has been built during previous mandates.

As outlined in this report, IMRB has multiple strengths to overcome these hurdles: multidisciplinary expertise, state-of-the-art core facilities, excellent scientific production, excellent level of funding acquisition, and an ongoing real estate master plan for the Mondor campus.

In order to carry out this new mandate, a new director from outside the IMRB has been selected following an international call for applications by the 2020-2025 Executive Committee, with the aim of consolidating the IMRB as the leading biomedical research institute in the Paris region. The new IRMB direction defines four main objectives for the next five years: To promote research excellence by recruiting talented scientists, fostering interactions between the different teams, and facilitating links with clinic to improve translational research; To develop national and international visibility by defining the identity of the institute; To increase attractiveness by continuing to develop core technological facilities, by taking advantage of the UPEC real estate master plan, and by improving administrative support; To increase links with society, by developing relationships with various players in the society.

The proposed new scientific organization aims to break the "silo" effect generated by the three strong departments that have constituted IMRB since its beginning. The new scientific organization around three main transversal research axes (Environmental aggressions, infections and health; Vulnerabilities, aging, and mental health; Biotherapies, health tools, and prevention strategies) is ambitious but very promising by meeting critical health challenges. Compared to the previous mandate, the number of teams will increase. Out of the 17 teams proposed, nearly a third of the teams are being assessed for the first time. This team restructuring is the result of a continuous effort by the current direction to capitalize on IMRB's scientific strengths while preserving the core expertise and infusing fresh leadership into the teams. The recent appeal of the center has resulted in a substantial influx of researchers notably from Inserm, who have joined during the preparation phase or at the beginning of the mandate. However, there should be a clear strategy for recruiting junior scientist with the goal of building new teams within the new scientific perimeter of the IMRB.

Three independent units named DYNAMiC, TREPCA and EPIDERME will join the IMRB as independent team (EPIDERME) or as part of pre-existing IMRB teams. There is no doubt that the EPIDERME team adds a valuable string to the IMRB's bow, but the integration of the two other two teams needs to be carefully monitored. The proposed new governance of the Institute will be aligned with the new scientific organization based on a Management Team, a Steering Committee and an Executive Committee. This organization will be supported by various committees (Scientific Animation Committee, International Relations Unit, Internal Grant Office, Greenlab, (Sciences Avec et Pour la Société, and ALUMNI IMRB) that will promote the visibility and attractiveness of the Institute. Overall, the new governance appears to be excellent and will ensure the continuation of the very high level of management.

One of the key objectives of the new unit head will be to create a clear signature for the IMRB, which is a complex task for an institute with a multi-topic focus. Four key words emerge from the new scientific organization that define IMRB: environmental aggression and vulnerability on the one hand, and disease prevention and treatment on the other. The new director will need to translate these concepts into a defined IMRB identity and communicate this new identity widely. The new real estate plan for the Mondor campus, currently under development, will provide a unique opportunity to showcase the Institute's new identity.

In conclusion, the trajectory of the IMRB appears to be very promising.

RECOMMENDATIONS TO THE UNIT

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

Strengthen communication by enhancing the existing newsletter, making it more comprehensive and detailed. Increase awareness and provide targeted training for team managers to support career development of postdocs, PhD students, ITAs and BIATSS staff.

Recommendations regarding the Evaluation Area 2: Attractiveness

In light of core facilities, increasing number of technicians and engineers could improve innovation, better service for IMRB's teams and service provision for companies.
About high competitive international grants, collaboration between the new grant office, the direction, senior PI and young applicants could be a key of success.

Recommendations regarding Evaluation Area 3: Scientific Production

While IMRB's scientific output is outstanding, the new management should ensure that the newly integrated teams maintain high standards of both quality and quantity in their publications.

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

To share scientific knowledge with the general public, PhD students, post-doc and ITA's could be promoted leaders in this field.
Promotion of media training, and more delegation of representation, could help young PI to increase their visibility and develop links and benefits with the cultural, economic and social worlds.

TEAM-BY-TEAM ASSESSMENT

Team 1: Transfusion and pathologies of the red blood cells

Name of the supervisor: Ms France Pirenne

THEMES OF THE TEAM

The team is studying the pathophysiological mechanisms of red cell disorders and transfusion complications, especially in Sickle Cell Disease (SCD) patients. During the 2020-2025 period, the structure of the team consisted of four groups:

Group 1: Genetic and transfusion immunology that investigates the risk of allo-immunization secondary to red blood cell (RBC) transfusion in SCD patients and the development of alloantibodies that cause life-threatening delayed hemolytic reactions (DHTR).

Group 2: Sickle Cell Disease and hemolysis with the aim to gain a better understanding of the pathophysiology of chronic manifestations of SCD and of vaso-occlusive crises, organ damage and hemolysis.

Group 3: a-hemoglobin pool and hemoglobinopathies with the main objective to find new biomarkers of Hb disorders, such as sickle cell disease.

Group 4: Autoimmune Cytopenia investigates the immunological basis and the role of B cells in autoimmune cytopenia, with an emphasis on innovative therapies for autoimmune hemolytic anemia and immune thrombocytopenia.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report already highlighted the high quality research of this team and suggested to put more effort into original research articles rather than reviews. As recommended, the team has focused on publishing original articles in top international journals as first, second, last or penultimate author in Nature medicine, Nature communication, Science translational, PNAS, Blood, Immunity and Cell.

The previous evaluation committee had recommended securing long-term funding and obtaining European funding. An effort was undeniably made with the coordination of three projects that have obtained European funding HORIZON-HLTH-2022 and H2020-SC1-FA-DTS-2018-2020 (RADEEP, GENOMED4ALL, SYNTHEMA).

Concerning team's organization and life, possibilities to provide tenure track positions to young talented scientists or medical doctors seem not to exist and are recommended. Efforts to attract more international scientists might be taken into account. As recommended, the team has helped to attract three young medical researchers who are about to defend their HDRs and should be promoted as University Professors – Hospital Practitioners in the next three years. The Mayotte reference center recently expressed its desire to join the unit. The RED has been able to secure 80 k€ in funding for a local branch at the Mayotte hospital.

Recommendations on scientific strategy and projects. Given the risk that the research questions are widening, the focus on SCD and the access to SCD patient cohorts, which is the major strength of the team should be maintained. As recommended, the team has refocused on SCD, with different aspects all related to the management of the patients, in conjunction with the coordinating reference center at the hospital. The transfusion aspect, which has always been a major component of the unit, has been strengthened around sickle cell disease, with the study of transfusion accidents and their treatment and transfusion issues related to blood group mismatches specific to this population.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	6
Maitres de conférences et assimilés	4
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	5
Personnels d'appui à la recherche	18
Sous-total personnels permanents en activité	**34**

Enseignants-chercheurs et chercheurs non permanents et assimilés	3
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**7**
Total personnels	**41**

EVALUATION

Overall assessment of the team

The team is outstanding given the quality and high levels of publications, the quality and originality of research projects, the balance of academic/industrial collaborations, the collaborations at the international level (participation to two European contracts), the translational research (from clinic to bench and vice versa) with cohorts of patients as PI, participation to clinical trials, high levels of funding in terms of R&D contracts, numerous grants from DIM and French foundations, two Cifre PhD contracts, however only few from ANR (three with one as PI).

The team has filled seven patents, three of them being licensed to the INNOVHEM start-up in 2019. The team has built up a unique erythrocyte expertise platform.

Strengths and possibilities linked to the context

The team has a clear international visibility and strong connection with international learned societies, is part of the GRex labex (labex – Biogénèse et Pathologies du Globule Rouge) and was part of the DIM gene therapy. This has led to the development of new gene therapy strategies and a high level academic consortium. This consortium was recently funded by the AFM Telethon as part of an ambitious project ranging from in vitro to a basic clinical editing studies in sickle cell disease in children (Necker) and adults (Mondor). The team co-coordinates the National Multidisciplinary Concertation on Rare RBC Pathologies, created in 2020 the "Réseau Erythrocyte et Drépanocytose du grand Paris (RED – GRAND PARIS)". The center represents Europe's largest cohort of patients with sickle cell disease. It coordinates the work of 17 constituent referral centers and 38 competence centers in mainland France and Indian Ocean. The center is also accredited by EuroBlooNet, an ERN (European Reference Network) for rare hematological diseases.

The laboratory is one of the few in the world to participate in American and European space programs to characterize anemia in space (SpaceX Polaris and European Space Agency [ESA] Spin) and has established new expertise and collaborations in acquired hemolysis related to extracorporeal circulation (with Henri Mondor ICU units).

During the 2018-2023 period, the team published 292 articles, of which 174 are scientific and 118 medical articles (as a whole 37% FLC); 65 scientific articles have one unit member as last author, 43 scientific articles have one unit member as first author and 84 scientific articles have two unit's members as first and last authors. During the same period, the team published 35 review articles (fourteen as FLC). Most members of the team published in high-profile journals of the specialties and generalist journals, however some full-time researchers published few articles in FLC position during the past contract.

The team has raised 1,938 K€ (23 grants, including as PI five DIM thérapie génique, one ANRS, various foundations, associations such as telethon, Force Hémato, ASH), with 705 K€ as industrial collaborations for sickle cell disease, RBC storage for transfusion, and autoimmune cytopenia (GSK, Novartis). The team is partner of two grants H2020 (HLTH-2022-IND-13 and SC1-FA-DTS 2018-20).

All the members of the team work in a single laboratory and organize a lab meeting every week. The unit has built up a unique erythrocyte expertise platform, a flow cytometry platform and are now developing a 3D printing fluidic model by combining analyses of the container (platelets and whole blood) and the vessel wall (to be patented).

Interactions with industry are frequent, and framed by collaboration contracts (Roche, Pfizer, Vertex, Novartis, GSK, Emmaus, Hemanext etc.) These links with industry have enabled to fund two Cifre scholarships over the past three years, as well as several research programs (EMMAUS, GSK, NOVARTIS, ROCHE, HEMANEXT). Team has created a start-up company, INNOVHEM, in 2019.

Team members are actively involved in university teaching, with three Interuniversity Diploma coordination (two international with Africa), a University Diploma and a University Capacity.

Team members have international visibility, as evidenced by invitations to American society of hematology (ASH), annual scientific conference on sickle cell and thalassemia (ASCAT), European midwives' association (EMA), French society of hematology (SFH), French society of transfusion (SFTS), French society of internal medicine (SNFMI), French society of medical resuscitation (SRLF), New York Blood Center, Université de Chicago (UIC), NIH etc. Team awarded ASH and SFTS prizes.

Team members are associated editor of the American Journal of Hematology and Haematology, Transfusion Clinique et Biologique, Editorial Board of Hemoglobin and are members of steering committee: Novartis, Roche, Addmedica, Pfizer. Team members have been guest editor: Quarterly Medical Review, presse médicale, la revue du praticien, Journal of Clinical Medicine.

The unit has many interactions with civil society on a regular basis, through its participation in scientific presentations dedicated to the public, coordination of a magazine for the general public, "le Globinoscope", its participation in meetings with various patient associations, it regularly interacts with the Ministry of Health to guide health policy in their respective fields.

The unit uses media such as television programs, radio programs and mainstream journals in France, Africa and West Indies, takes an active part in World Sickle Cell Day and launched the "course du globule rouge", a virtual race around the world to raise awareness.

Team coordinates the MCGRE website, accessible to the general public and is in charge of the MCGRE research working group, with a dedicated section on the MCGRE website. Team is actively involved in France's blood donation awareness day.

Weaknesses and risks linked to the context

During the 2018-2023 period, the team has trained 20 Masters students but only seven PhD students (five students defended their PhDs and two students are still in progress).

Most of the grants were raised by the team leader. The team has obtained only few ANR grants (three with one as PI).

There are no senior scientists (DR) in the team.

Although most members of the team published in highly recognized journals of the specialties and generalist journals, however some full-time researchers published few articles in FLC position during the past contract (less than one per year).

Analysis of the team's trajectory

The team will be headed until 2026 by Pr Pirenne (UPEC and EFS), and will be continued by Pr. Bartolucci from 2026. Pr. Bartolucci is responsible for the Red Cell Disorders Unit (UMGGR - Internal Medicine Department), which is the coordinating referral center for sickle cell syndromes, thalassemias, and other rare red blood cells (RBC) and dyserythropoietic's pathologies.

The DREAMS team will consist of 5 groups:

1. Mechanisms and Vascular Impacts group. The role of erythrocyte particles in complement activation and endothelial damage, as well as studying acute vaso-occlusive vasculopathy will be studied.

2. Modulator Genes and Molecules. Project will use cohorts of several hundred patients over a period of more than 10 years, with an associated DNA and biological collection (GENMOD), to analyze phenotype-genotype relationships during SCD. Team is part of a European cohort project (GENOMED4ALL). Goal is to build predictive models.

3. Intercellular Cross Talk, Signaling, and Organ Impact specialized in the Pathophysiology of Glomerular Diseases, will join the team Bartolucci as part of DREAMS to study the organ impact of vascular damage related to hemolysis and SCD (cellular cross-talk). The group proposes AHSP as a new biomarker in SCD and develop a

future test intended for routine use in hospitals through two patent applications filed (WO2023285690 and EP23305063.2).

4. Transfusion and Blood groups. Using genotyping, conventional immunohematology tests and innovative 3D protein modelling, the group will continue to investigate the relationship between blood group polymorphisms, alloimmunization and hemolytic reactions. The group secured funding with Force Hémato and ASH Global Research Award to conduct a transversal project investigating how the polymorphisms of complement proteins (blood group or other)

5. Antibodies and Blood Cells group. The hypotheses developed on the mechanism of alloimmunization against RBC, the impact of hemolysis on endothelial cells from SCD patients, the involvement of complement developed by the team will be tested on patient samples and prospective studies to validate these hypotheses and to test new drugs.

The 5 groups are balanced, with the addition of a new group with expertise in red blood cell membranes. Indeed, the arrival of a professor will bring a new expertise in lipidomics and the effect of oxidative stress on RBC membranes. The projects are excellent, in line with the existing work but with the development of innovative aspects such as phenotype-genotype relationships during SCD. The team combines the expertise of different specialists in RBC disorders and especially during SCD (from clinical to fundamental aspects), in order to progress in the pathogenesis understanding, to develop and evaluate new therapeutic approaches and to improve the safety of actual treatments (including transfusion and gene therapy)

RECOMMENDATIONS TO THE TEAM

The team should recruit permanent basic scientists, since tenured researchers are aging and are missing in the trajectory and new group leaders should apply to more academic funding (such as ANR) as PI.

The team should welcome more PhD students.

Team 2: Clinical Epidemiology and aging

Name of the supervisors: Ms Sylvie Bastuji-Garin & Ms Florence Canoui-Poitrine

THEMES OF THE TEAM

The CEpiA team is a research team of clinical epidemiology and public health applied to aging, frailty and multi-morbidity and joined the IMRB in 2020. The team addresses challenges tied to global demographic shifts toward an aging population. This trend leads to increased chronic diseases and disability, while clinical trials often exclude older patients, complicating the application of new treatments. Their objectives include: 1) characterizing the diverse manifestations of aging and identifying health risk factors in older adults across hospital and primary care settings, and 2) developing and evaluating tailored care strategies for this population through a better comprehension of the heterogeneity of older people and their health-determinants.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations were:

1) To develop international relationships and respond to international grants as PI

2) To improve communication via social networks

3) To improve administrative support, to increase space for the upcoming incorporation of new members of the team and to improve the number of PhD students

4) To develop independent projects

The team has clearly met the expectations outlined during the last evaluation. It has established numerous national and international collaborations, both within Europe and beyond, and successfully responded to two international grants as WPL. The team has also enhanced its presence on social media thanks to its own Twitter, LinkedIn accounts and a website.

Additionally, a medico-administrative assistant joined the team and new staff can now be accommodated thanks to the creation of new workspace and the expansion of remote working options.

The number of PhD students has significantly increased, rising from six in January 2018 to twelve in January 2024, enabling the supervision of 20 PhD candidates during this period, eight of whom have successfully defended their thesis. Finally, improved communication between the CEpiA team and IMRB management has fostered the development of collaborative research projects with IMRB teams on topics aligned with CEpiA's research focus.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	7
Maitres de conférences et assimilés	7
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	11
Sous-total personnels permanents en activité	**25**
Enseignants-chercheurs et chercheurs non permanents et assimilés	5
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	6
Sous-total personnels non permanents en activité	**12**
Total personnels	**37**

EVALUATION

Overall assessment of the team

This outstanding team has grown significantly over the period. Its multi-disciplinary allows the establishment of a strong link between care and social sciences. The team produced a large number of publications in high-quality journals and actively involves young researchers in scientific activities. It developed numerous national and international collaborations, with members actively participating in various scientific societies. The team plays also a major role in education (e.g. "Campus des Métiers et Qualifications").

Strengths and possibilities linked to the context

The CEpiA team focuses on the critical area of ageing, combining clinical epidemiology with social and data sciences. Its research agenda spans over both hospital and primary care settings. The team has grown significantly from 19 members in 2015 to 36 in 2023, incorporating a broad range of expertise, including clinicians, social scientists, allied health professionals, biostatisticians, data scientists, clinical research technicians, and data managers. The supervision of PhD students has increased notably, with students actively involved in writing scientific articles and contributing to the team's scientific strategy and activities.

The team fosters a collaborative scientific environment, with regular meetings encouraging the emergence of new projects and enhancing collaboration (e.g. scientific meetings, reading clubs, English-language discussions, and dedicated sessions for Master's and PhD candidates to exchange ideas).

CEpiA has achieved international recognition, securing €9M in funding during the term (PREPS, INCa, PHRC, ANSM, Ligue contre le cancer, RESP-IR…), including two international grants as WPL (IMI2, H2020). The team has developed sustainable collaborations at local, regional, and national levels, participating in several scientific groups, which has boosted its visibility. The team is committed to innovative methods, such as decision-curve analysis and artificial intelligence, and has created large multicenter cohorts and trials, including data from over 20,000 patients in hospital and primary care settings.

Since 2018, the team has published 523 original articles in peer-reviewed journals, with 404 based on its own research. CEpiA members have served as first, last, or corresponding authors for 166 of these (41%), and the team has produced 55 review articles and achieved four publications in major international specialist journals, including two led by CEpiA PhD students.

CEpiA's members are also deeply involved in teaching and clinical practice. Four researchers lead clinical research structures at Henri-Mondor Teaching Hospital, linking hospital-based research with CEpiA. Two other members run an Ambulatory Healthcare Center and a multi-professional healthcare office, ensuring continuity between outpatient care and research. They also teach epidemiology, clinical research, ageing, and chronic disease management at all academic levels, from bachelor to PhD, and lead specialized clinical training programs aligned with their research.

The team's socio-economic impact is substantial. It addresses medical challenges related to patient care and broader socio-economic issues like elderly care, home automation, and professional training. CEpiA created the "Campus des Métiers et Qualifications," dedicated to training and innovation in healthcare for aging populations, personal assistance, and gerontechnology. The team has assessed the cost-effectiveness of geriatric assessments for frailty detection and chemotherapy toxicity prevention and contributed to health monitoring during the Covid-19 pandemic in nursing homes. CEpiA is also actively engaged with civil society through publications, associations, participation in health policy authorities, and involvement in various learned societies.

Weaknesses and risks linked to the context

Weaknesses Identified:

1. Lack of a Full-Time Tenured Researcher: this will be solved with the application of a researcher for an Inserm tenured research position.

2. No European project led as principal investigator: despite participating in multiple European projects as work package leader, the team has not yet secured leadership of a European project.

3. Need for Expanded International Development: While the team is making strides in international collaboration, as evidenced by increasing involvement in European projects and expert groups, further growth is required to achieve leadership status in global initiatives.

Analysis of the team's trajectory

Since 2020, the leadership of the CEpiA's team has been gradually transitioning, with final approval by the Executive Group in 2022. Previously a single research entity, the growing size of the team and its projects has prompted a restructuring into three scientific axes. These axes are not distinct groups but are designed as collaborative spaces for dialogue and knowledge-sharing in key areas. Regular seminars featuring team members, IMRB collaborators, and external experts will promote collective dynamics and the development of new projects.

During the 2023 annual general assembly, the three axes and their objectives were approved, along with designated leaders:

1. Multimorbidity, Frailty, and Dependence
Extending the team's historical focus, this axis explores the variability of aging and the risk factors for adverse outcomes in frail or multimorbid older patients. The research will delve into quality of life, loss of autonomy, and treatment toxicities, leveraging existing clinical cohorts and population data to identify pre-event risk factors. Biomarkers of aging and their prognostic value will also be investigated.

2. Health and Illness Trajectories and Care Pathways
This new axis aims to document care trajectories and patient experiences while identifying factors contributing to suboptimal care. Research will use medico-administrative databases, matched clinical cohorts, and ethnographic approaches. The framework will combine qualitative and quantitative methods, supported by collaborations with data scientists, pharmaco-epidemiology teams, and social science specialists.

3. Tailoring Diagnostic and Therapeutic Approaches
Building on another historical focus, this axis seeks to refine diagnostic and therapeutic strategies for older, frail, or multimorbid patients. The team will expand its work on bridging the gap between clinical trial settings and real-life application through implementation studies, focusing on transferability, fidelity, and cost-effectiveness. A European project is also in preparation to improve older cancer patients' access to innovative treatments.

RECOMMENDATIONS TO THE TEAM

The multidisciplinary approach of the projects has allowed the team international recognition and must be maintained across the proposed research axes. The involvement of early-career researchers should also continue, along with the team's active scientific engagement. Emphasis should be placed on securing funding by taking leadership roles in international projects.

Team 3: Immunoregulation and Biotherapy

Name of the supervisor: Mr José Cohen

THEMES OF THE TEAM

The Immune Regulation and Biotherapy (I-Biot) team, formed in 2020, focuses on modulating immune responses in the settings of organ and hematopoietic stem cell transplantation, as well as in solid and blood cancers. The team's research builds on significant discoveries related to immune regulation, including insights into Foxp3+ regulatory T cell subsets and the immunosuppressive enzyme Interleukin-4-induced-1, which remain active areas of investigation.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has made real efforts to address the recommendations from the last evaluation, particularly by implementing student co-supervision to strengthen interactions between the different subgroups. Students now sign publications as first authors. The team's organization has been reviewed.

The team has integrated international networks in Argentina and the USA (New York). The director is a co-founder and co-president of the Franco-Argentinian Immunology Congress. However, the team should continue its efforts to integrate European networks, as this has not yet been achieved.

Efforts were made to recruit permanent full-time researchers which remain a weakness of the team however no CRCN nor DR Inserm or CNRS were recruited. In the next mandate, a full-time researcher will join I-Biot demonstrating the efforts to recruit permanent researchers.

The team initiated two collaborations inside IRMB which was a strong recommendation from previous review.

Concerning the interactions between groups the team obtained several fundings and shared PhD supervisions between the different groups. It should be noticed that five new HDR are expected for the next mandate.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	8
Maitres de conférences et assimilés	8
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	8
Sous-total personnels permanents en activité	**24**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**4**
Total personnels	**28**

EVALUATION

Overall assessment of the team

The overall assessment of the team is excellent to outstanding. I-Biot's research theme aligns perfectly with Inserm's objectives by promoting excellence, integrating scientific advancements with patient care and public health, and fostering technology transfer with industry. I-Biot's project serves a dual purpose: advancing fundamental knowledge of immune regulatory mechanisms and testing potential new therapeutic targets for diverse immune-related conditions. However, the very low number of full-time researchers and the lack of researchers leading international projects remain a weakness.

Strengths and possibilities linked to the context

The team I-biot (23 permanents and 11 non-permanent staff) is essentially composed by hospital/university staff. The scientific output is excellent, with 350 papers including 40 reviews, primarily featured in clinical journals. However, several articles in which students signed as first authors have been published in high-profile journals such as Science Translational Medicine, Nature Communications, The Lancet, The Lancet Hematology, eLife, and Blood Advances. Notably the team filled five patents and several partnerships with industry were initiated with international Strat-ups of pharmaceutical companies.

The team works across distinct scientific fields, which highlights its broad expertise (GVHD, cancer, immunology) and diverse research interests. Despite the disciplinary differences, the team has made concerted efforts to foster collaboration, particularly through inter-group projects and the co-supervision of PhD students. To address this, Axis 4 has been designed as a unifying framework, bringing these areas together by focusing on immuno-interventions in transplantation and cancer. In addition to advancing various individual research projects, the PIs of I-Biot have focused on developing transversal projects that allow all members to benefit from the collective expertise.

The team also recruited three postdocs during the mandate and one obtained an assistant position at PSL. These initiatives have not only strengthened internal synergy but also enhanced the team's collective output. Furthermore, several graduates chose to continue working within the team, a testament to the supportive and stimulating research environment the team provides.

The attractiveness is high due to the elevated number (29, 21 as coordinator, 72%) and the diversity of the grants (academic, valorization, industry) obtained during the mandate including academic grants: ANR (three, one as coordinator), ANR PRCE (one), Ligue contre le Cancer (two as coordinators), Inca (one), Cancéropôle (two), Inserm Plan Cancer (one), UPEC (one as coordinator), ARC (one), FHU (one); subventions from associations and foundations (eight, all as coordinators); maturation and valorization contracts: BPI, Erganéo ; industrial contracts: Bristol Myers, HIFIBIO, Egle Tx, Bioinvent, Calithera Biosciences.

The team holds a strong internal reputation, particularly in allo-HSCT, having identified the critical role of Tregs in this context. Notably, they were the first to conduct a clinical trial of Treg-based therapy, paving the way for industry collaborations – a significant strength of the team. Partnerships have been established with start-ups in Sweden and the pharmaceutical company Bristol.

Additionally, the team was the first to identify the role of the immunosuppressive enzyme IL4I1 in regulating the immune response across various pathophysiological conditions. This latest discovery led to publications in high-profile scientific journals.

Weaknesses and risks linked to the context

The team currently lacks a sufficient number of full-time researchers who could bolster the research axes and improve the quality of scientific publications. This may partly explain the relatively low number of publications in high-profile scientific journals. While the large number of grants obtained is commendable, it should be noted that no European or international grants were secured. Additionally, several of the grants are short-term, which may pose challenges to sustaining long-term project development.

The contribution of the research activities to society is valuable, but it does not fully involve enough researchers from the team.

Analysis of the team's trajectory

The project for the next mandate is consistent and fully aligned with previous work, with the same director remaining in charge. However, there is an additional intention to strengthen successful areas and to refocus certain aspects.

One group (pre-clamps) will leave the team.

One team led by a permanent researcher form EFS will join I-Biot. This recruitment will address the shortage of permanent researchers and may encourage other groups to recruit CRCNs or DRs. This is a step in the right direction, and efforts to recruit permanent staff should continue in the next term.

The main axes renamed groups will continue their development: (group 1) immune regulation basic and therapeutic aspects (IL4I1, Allo-HSCT), (group 2) oncology and therapeutic aspects exploring therapeutic impact of combined immunosuppressive (TNFR2, IL4I1) and oncogenic factors (CDLN2A, nucleonic), (group 3, new group) alloreactivity and therapeutic aspects (GVHD, NK cells, CD4+ T cells and Tregs, and EV immunomodulation). All of which converge to group 4: center for clinical evaluation in biotherapy.

The proposed project is coherent and based on previous axis with the addition of a new team.

RECOMMENDATIONS TO THE TEAM

To further enhance the impact and visibility of the team, it is crucial to reinforce the basic science aspect of the research. This can be achieved by recruiting permanent, full-time researchers who can focus on expanding the foundational scientific work. A stronger emphasis on basic research will also contribute to increasing the quality and number of publications in top journals, which is essential for the team's recognition in the global scientific community.

In addition to strengthening basic science, it is equally important to maintain the involvement of early-career researchers. Their continued engagement will not only support the development of innovative ideas but also help sustain the team's momentum in scientific progress. Moreover, securing additional funding should be a key objective, with a particular focus on taking leadership roles in international projects.

To maximize this societal impact, it is essential to dedicate more effort to communication and public outreach.

In summary, strengthening basic science, recruiting permanent researchers, fostering early-career involvement, and increasing international visibility should be central to the team's strategic goals. At the same time, enhancing communication efforts will ensure that the societal benefits of their research are fully realized and appreciated.

Team 4: Senescence, Metabolism and Cardiovascular diseases

Name of the supervisor: Ms Geneviève Derumeaux

THEMES OF THE TEAM

The research focus of Team SENCODE headed by G Derumeaux is the study of cellular senescence and its implications in aged related diseases especially in the inter-organ communication such as liver-heart and skeletal muscle-heart axis. SENCODE team aims to decipher and understand mechanisms involving cellular senescence in various physiopathological's contexts, in order to develop novel diagnostic and therapeutic strategies. The SENCODE team involves scientists, clinician physiologists, bioinformaticians leading to cutting edge translational and clinical research.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has made real efforts to address the recommendations from the last evaluation. Recommendations were:

1-to continue publishing in top journals and promoting young PIs as leaders,

2 – to encourage interactions between scientists and clinicians,

3-to favor different PIs to interact as much as possible.

The team has clearly met all the expectations outlined during the last Hcéres evaluation.

First, they succeeded in promoting a Young PI as leader and successfully recruited an Inserm's Junior Professor Chair. Additionally, they keep publishing at high levels in high standard international journals especially in specialized journals such as Circulation, European Resp Journal or JACC.

Second, they integrated new researchers in various specialties (senescence, pneumology, nephrology) allowing the development and maintenance of collaborations between basic researchers and clinicians. Additionally, a new focus on biostatistics and bioinformatics is currently being developed within the team, further promoting exchanges between clinicians and scientists.

Finally, the previous committee recommended greater interaction between the different PIs. The team has implemented weekly meetings to foster these interactions.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	15
Maitres de conférences et assimilés	5
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	20
Sous-total personnels permanents en activité	**42**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	2
Post-doctorants	2
Doctorants	20
Sous-total personnels non permanents en activité	**25**
Total personnels	**67**

EVALUATION

Overall assessment of the team

The overall assessment of SENCODE team is outstanding given the quality and high levels of publications, the originality of research projects and the interactions between different groups.

SENCODE team produced a large number of publications in specialized high-quality journals (668 articles including 93 original basic sciences (60% as first or corresponding author), 391 clinical research papers, 35 reviews, 69 editorials or letters). SENCODE team developed numerous national and international collaborations, with members actively participating in various scientific societies. During the past period, the team has significantly grown, indicating major activity (one Inserm's Research Fellow, one CNRS Director, two Associate Professors, three Full Professors, and one Junior Chair Professor). The SENCODE team has also made significant efforts in valorization through the filing of four patents. Furthermore, the team obtained a large number of contracts (> € 20M), both at the national level (five ANR grants, five FRM, five INCA) and internationally (H2020 CARDIATEAM, NIH), indicating a positive dynamic within the team. Finally, the team has demonstrated its ability to structure collaborative networks, having been awarded competitive grants such as the Investment for the Future, RHU CARMMA, and EUR LIVE. The SENCODE team is also highly involved in multicenter randomized clinical trials (PHRC).

Strengths and possibilities linked to the context

The SENCODE team focuses on the role of cellular senescence and its implications in age-related diseases. Over the past period, the team has grown significantly by recruiting several principal investigators (PIs), thereby incorporating a broad range of expertise. This includes basic researchers, clinicians from various specialties, and biostatisticians/bioinformaticians. The team fosters a highly collaborative scientific environment, with regular meetings among PIs and clinicians that encourage the emergence of new projects and enhance collaboration.

The SENCODE team enjoys strong national and international recognition. During the last term, the team secured over €20 million in funding, including major international grants such as the H2020 IMI CARDIATEAM and NIH projects, both as coordinator and partner (e.g. INTERCEPT-T2D). It has also established sustainable collaborations locally (within IMRB) and nationally, participating in several scientific groups that have boosted its attractiveness and visibility.

Since 2018, the team has published 668 original articles in high-profile journals (e.g. *Genomics* 2023, *Circulation* 2018 and 2021, *Aging Cell* 2023, *JCI* 2023). These include 93 articles focused on basic science and 391 on clinical research. Impressively, 30% of these articles feature SENCODE team members as either first or last authors. Furthermore, nearly 30% of publications are co-authored by at least two of the research theme leaders, reflecting a high level of internal collaboration. Additionally, the team has produced 35 review articles and filed three patents during the 2018–2023 period. SENCODE team contributed also in the founding of two start-ups, indicating their strong involvement with the industrial partners.

SENCODE members are deeply involved in teaching (e.g. through the EUR Live graduate school and IUF) and mentoring students. The team has supervised 21 PhD students, thirteen of whom defended their theses before the end of 2023, with all associated publications listing the students as first authors. SENCODE has also developed an interesting approach to collaboration by inviting visiting professors annually. Notably, the team hosted a Nobel Laureate in 2019, leading to ongoing scientific collaborations until 2023. To date, five visiting professors have been invited.

Career development is a clear priority for the SENCODE team. Between 2018 and 2023, four promotions were secured (one PR, one DR, one IR1, and one IR), underscoring the team's commitment to effective human resource management.

The team is actively participating in social media (e.g.: French radio).

Weaknesses and risks linked to the context

Despite the recognition of the team's work through patent filings, there are only few collaborations with industrial partners.

Analysis of the team's trajectory

The team's trajectory for the next term appears very clear and seems to have been well managed. The multidisciplinary approach of the projects has allowed the team international recognition and must be maintained across the proposed research axes. Integration of new research groups (Kidney aging and skin aging) will bring new expertise and facilitates new collaboration within the SENCODE team but also within IRMB. SENCODE team will broaden its multidisciplinary expertise by developing its own bioinformatics facility that will help both basic science and clinical research.

RECOMMENDATIONS TO THE TEAM

The recommendation would be to maintain the team's current level of excellence in terms of funding and publications. To achieve this, it will be necessary to encourage the recruitment of researchers to act as the interface between PIs and students/post-docs especially in the groups of Kidney aging and skin aging (smaller than the historic ones), either through competitive recruitment, or through mobility within the university system or Inserm.

Efforts to develop industrial collaborations are recommended.

Moreover, the committee recommends to further participate in non-academic activities, that will certainly add more visibility to the team.

Team 5: Pharmacology and Technologies for cardiovascular diseases

Name of the supervisor: Mr Bijan Ghaleh

THEMES OF THE TEAM

The Protect team is dedicated to the development of pharmacological strategies and technologies aimed at combating cardiovascular diseases and their consequences, such as myocardial infarction. This multidisciplinary team, encompassing expertise in basic science, preclinical, and clinical research, possesses unique capabilities (ex. large animal surgery, ECMO).

The team brings together fundamental researchers and clinicians, enabling the study of fundamental processes at both clinical and preclinical levels. This is made possible through the involvement of clinical staff from Henri Mondor Hospital, including resources such as the CIC (Clinical Investigation Center) and the biobank.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The PROTECT team has made significant efforts to address the recommendations from the last evaluation. The recommendations were:

1. To increase the number of publications in high-profile journals as first and/or last authors and secure highly competitive international grants.
2. To achieve a higher level of excellence by fostering strong collaboration between subgroups.
3. To encourage subgroups to collaborate closely to maximize efficiency and achieve key milestones swiftly and effectively.

The PROTECT team has clearly met all the expectations outlined during the last Hcéres evaluation.

First, the PROTECT team has significantly improved its number of publications in major high-profile journals, with first and/or last authorship in journals such as *JACC*, *Nature Communications*, and *Circulation*, among others.

Secondly, to emphasize and promote collaboration between subgroups, the PROTECT team developed a project investigating the role of heme during myocardial infarction by securing funding from FRM Equipe and FFC grants. Furthermore, in response to the aging of the PIs, the PROTECT team recruited two Assistant Professors, one MCF, and one MCU-PH during the last period and was highly involved in promoting PIs (PUPH, PU EnvA, PR UPEC).

Additionally, the PROTECT team developed a transversal project on the consequences of ECMO on the pharmacokinetics of drugs used in intensive care, which was recently published in *J Antimicrob Agents* in 2023. This demonstrates that the PROTECT team has taken the previous Hcéres committee recommendations into account.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	10
Maitres de conférences et assimilés	7
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	8
Sous-total personnels permanents en activité	**28**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	1
Post-doctorants	2
Doctorants	6
Sous-total personnels non permanents en activité	**10**
Total personnels	**38**

EVALUATION

Overall assessment of the team

The overall assessment of the PROTECT team is excellent to outstanding given the quality and high levels of publications, the originality of research projects and the interactions between different groups.

The PROTECT team has produced a large number of publications in specialized, high-quality journals (254 publications, with 80 as first or corresponding author, and 31% FLC). The team has developed numerous national and international collaborations, with members actively participating in various scientific societies. During the past period, the team has grown significantly, reflecting major activity. The PROTECT team has also made highly significant efforts in valorization, filing four patents, one license agreement, and creating one spin-off. Furthermore, the team's strong fundraising success, primarily at the national level (six ANR grants, two FRM), and several industrial partnerships (nine grants), is noteworthy. Finally, the team has participated in international collaborative networks, including TRANSCEND and IMPACT.

Strengths and possibilities linked to the context

The PROTECT team is a multidisciplinary group, including Inserm/CNRS scientists, veterinarians, and clinicians. This complementary expertise allows access to diverse resources, as many team members are also actively involved in the Clinical Investigation Center (CIC) and the biobank at Henri Mondor Hospital.

The PROTECT team raised more than 5M€ during the last period. Interestingly, a significant portion of the funding comes from industry.

The PROTECT team enjoys strong national and international recognition. During the last term, the team secured over 5M€ in funding, including industrial partner grants (ANR, FRM, Fondation de France, PHRC, industry, Federation Francaise de Cardiologie) It has also established sustainable collaborations locally (within IMRB) and nationally, participating in several scientific groups that have enhanced its attractiveness and visibility.

The PROTECT team is also highly involved in clinical research. They were able to coordinate the PHRC (PROVERB), highlighting their strong recognition in the field.

PROTECT members (MCF, MCU-PH, PR) are deeply involved in teaching, such as the Master 2 Biocoeur program directed by B. Ghaleh, and in mentoring students.

A major new achievement for the team is leading the establishment of a new mass spectrometry platform at Henri Mondor Hospital, with half of its activity dedicated to preclinical research.

As a significant marker of its attractiveness, the creation of a spin-off derived from the PROTECT team's work has led to the acquisition of two grants (BPI I-Lab and BPI-INOV), supporting a pioneering clinical study on total liquid ventilation at the global level. Furthermore, the PROTECT team is participating in an ERC Starting Grant program (in collaboration with U1273).

The PROTECT team has a strong scientific output, publishing in high-standard journals. Over the last period, the PROTECT team published 311 papers, with 30% originating from the team. The team has published in prestigious journals such as *eBioScience* (2020), *JAHA* (2020), *JACC* (2018), *Nature Communications* (2021), and *JCI* (2018), demonstrating the high quality of their research. The scientific production of the PROTECT team involves all members, including students and technicians.

The PROTECT team has strong activity in socio-economic valorization. It also filed four patents and one license agreement. Furthermore, the PROTECT team created a spin-off (Orixha). Indeed, this spin-off will soon launch the first clinical trial using total liquid ventilation technology. Additionally, the PROTECT team has filed several patents involving new strategies for the treatment of cardiovascular diseases (e.g. Sonic Hedgehog, ANGPTL4). The team is also highly involved in student communication programs (Apprentis Chercheurs, Déclic).

Weaknesses and risks linked to the context

Despite participating in multiple international projects as Work Package Leader, the team has not yet secured leadership of a European project.

The PROTECT team's expertise in pathophysiology is strong, but molecular and cellular approaches need to be further developed.

The team's expertise in its international recognition are driven by PAR, but this staff is limited and aging.

Analysis of the team's trajectory

The project for the upcoming mandate is well described and managed. One group (HO-1/CO group) will be leaving, while a new group from Collège de France will be joining the PROTECT team. This new group will bring expertise in molecular and cellular biology, as well as additional human resources and funding. The joining group has already been collaborating with the PROTECT team for over 10 years, co-authoring several papers and securing joint funding, which will facilitate their smooth integration into the team.

The PROTECT team's research program will focus on the development and evaluation of new pharmacological strategies and technologies to treat heart and circulatory failure in various pathological contexts. Each group will benefit from the expertise of the others, and they will work together on ambitious projects:

1. Preventing left ventricular remodeling and dysfunction after myocardial infarction by studying the role of angiopoietin-like 4 (ANGPTL4) in large animal models.
2. Evaluating organ damage following cardiac arrest.
3. Developing strategies to support and treat organ dysfunction.
4.

Notably, the development of AI-based technologies by the newly joined group will also benefit the other teams.

RECOMMENDATIONS TO THE TEAM

The PROTECT team should continue on its path of valuable scientific achievements, with high-quality publications and successful funding. The arrival of the new group will introduce a dynamic shift, fostering closer collaboration with the two existing groups.

Team 6: From Pathophysiology towards Immune-based interventions in HIV

Name of the supervisor: Mr Yves Lévy

THEMES OF THE TEAM

The team's work centers on understanding infectious diseases and developing effective vaccines, especially for emerging and re-emerging infections. Their approach combines extensive expertise in advanced technologies, enabling a thorough analysis of immune responses both during natural infections and following vaccination.

Research activities cover a broad spectrum, including genomics, proteomics, ex vivo imaging, and immunogenetics, which inform vaccine design, preclinical modeling, and clinical trials from phases 1 to 3. Among these innovations, the team has developed a platform that targets vaccine antigens directly to antigen-presenting cells (APCs), currently progressing through phase 1/2 clinical trials. This targeted APC platform has recently been adapted to address virus-related cancers, demonstrating the team's commitment to versatile vaccine strategies.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The main recommendations from the previous Hcéres review were addressed by conducting two trials with CD40-targeting vaccines, creating a start-up, strengthening collaborations with private industry, and making a significant effort to communicate scientific findings through television and national press. The team expanded its number of principal investigators and non-permanent staff, reaching a total of 50 members.

However, there was no recruitment of young PIs, such as CRCN Inserm or CNRS researchers, and only one MCU was added. Additionally, the number of PhD students (six) and postdocs (two) remains low, given the size of the team.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	24
Sous-total personnels permanents en activité	**32**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	7
Sous-total personnels non permanents en activité	**7**
Total personnels	**39**

EVALUATION

Overall assessment of the team

The overall assessment of the team is outstanding. Among various innovations, the team has developed a platform that targets vaccine antigens directly to antigen-presenting cells, currently progressing through phase 1/2 clinical trials. The number of publications and grants (national, European) is very high, making the team very attractive. To test and produce vaccines a start-up was created (Inserm, UPEK and Linkivax). This greatly enhances the societal impact of the team.

Strengths and possibilities linked to the context

The team Accelerates relies on internationally recognized PI and is composed by 50 members, including four PUPH (UPEC-APHP), one DR Inserm, two PU (UPEC), one MCU (UPEC), two researchers based in Texas, three MDs (APHP, VRI). The team receives strong support from both UPEC and Inserm with thirteen permanent support staff, and 16 non-permanent staff. The team also includes six PhD students and two postdoctoral researchers. The team benefits from internationally recognized leaders.

The publication output is substantial, with 218 total publications, 43 of which (20%) list team members as first, last, or corresponding authors. Most publications stem from collaborations (80%) and are featured in clinical journals. In addition, the team published 28 letters and 14 reviews. The publications are of high quality, with several appearing in high-profile journals such as NEJM (1), Cell (1), Science (1), Nat Immunology (1), Nat Com (3), Immunity (1), JCI (1), J Exp Med (1), Plos Pathogens (3), Blood (2).

The strengths of the team are rooted in strong scientific collaborations, both nationally and internationally, with renowned research teams at institutions such as the Institut Pasteur, Institut Curie, the CEA, and various institutions in the United States. Additionally, the team has demonstrated a remarkable capacity to attract significant funding, having secured numerous national and European grants where they often serve as project coordinators. This dynamic approach has led to the successful acquisition of over 16 million euros in funding during the mandate, an impressive achievement that highlights the team's effectiveness. Importantly, the team is associated with the labex VRI, which has been renewed twice since 2011 and will continue until 2027.

The team has discovered and developed a vaccine strategy based on the activation of antigen-presenting cells (APCs), specifically dendritic cells, through membrane receptors. One of these vaccines utilizes an antibody targeting CD40, combined with pathogen antigen sequences. This approach appears to be a promising method for generating a robust B and T cell immune response. The low injection doses required further enhance the appeal of this strategy, as it suggests a more efficient vaccination method with reduced side effects. The use of CD40-targeting antibodies in the vaccine design represents a novel immunotherapeutic approach, as CD40 plays a critical role in the activation and coordination of immune responses. Several preclinical studies and clinical trials had been performed on HIV, SARS-Cov2, Ebola (with creation of laboratories in Africa) and pneumoccocal/influenza/pertussis. This demonstrates the capacity of the team to rapidly react to emergence or reemergence of pathogens.

The social impact of the team, particularly through the clinical trials and the creation of a start-up that is strongly funded by BPI (Banque Publique d'Investissement), is remarkable. This start-up focuses on the development and production of vaccines, marking a significant step in the team's mission to translate innovative scientific research into real-world applications. By securing substantial financial support from BPI, the team has been able to scale up its efforts, translating their discoveries into market-ready product. This initiative has the potential to greatly improve public health outcomes.

Weaknesses and risks linked to the context

As highlighted in the document, the team's projects are highly dependent on the global policy framework for vaccine development, which sets the overarching priorities and strategies guiding their progress. Additionally, these projects are particularly influenced by international competition, as advancements in vaccine technologies continually reshape the landscape. In this context, it is essential to evaluate how CD40-targeted vaccines position themselves relative to mRNA vaccines. This includes assessing their advantages, limitations, and unique contributions to immune response activation, durability, and specificity. Understanding this comparison could help determine the competitive edge of CD40-targeted vaccines in an increasingly innovation-driven market.

The team is supported by internationally recognized principal investigators (PIs), but the current team structure offers limited opportunities for young PIs, postdocs and PhD students. An effort was made with the recruitment of a MCU and a young PU; however, no young CRCN has been hired. The attractiveness for young researchers is low, which raises concerns about the medium-term future of the team. Given the significant investment in the team, ACCELERATES should establish a medium – and long-term vision.

The research topics of the PhD students and postdocs are not clearly defined in the document. Almost all the publication from the lab were signed as first authors by PIs and not by PhD students or postdocs. The team explains this by citing the long-term nature of patient immunomonitoring studies, which, they say, cannot involve PhD students or postdocs. This reasoning, however, is unsatisfactory to the committee.

Analysis of the team's trajectory

The team's trajectory for the next term is in line with and perfectly aligned with the previous project. The leadership will change with the appointment of Véronique Godot as the new team director, and the team will build on the success of the CD40-targeting vaccines, expanding the CD40-targeting platform.

The team will broaden its multidisciplinary expertise by incorporating immunocompetent organoids and multiplexed tissue imaging, recruiting a cancer immunotherapy expert with expertise in related mouse models, an immunogenetics specialist in infectious diseases, and adding a DR Inserm expert in cell and gene therapy (head of ART-TG). These initiatives will strengthen the team's capacity to deliver integrated, translational research programs focused on developing innovative vaccines for (re)-emerging infectious diseases, as well as immunotherapies and combined cell and gene therapies for HIV/AIDS and virus-related cancers.

RECOMMENDATIONS TO THE TEAM

The team must make real efforts to attract young principal investigators (PIs), researchers, and students. This is essential for a long- and medium-term strategy to ensure the sustainability of the team after the PIs retirement. Compared to the previous term, efforts have been made, but they remain insufficient. PhD students and postdoctoral researchers should be the first authors on publications. A strong focus on this point is more than necessary.

Team 7: Translational Neuropsychiatry

Name of the supervisor: Ms Marion Leboyer

THEMES OF THE TEAM

The team aims to unravel the pathophysiological processes of major neurologic and psychiatric disorders. With access to several large cohorts, they characterize patients with clinical, cognitive, genomic, immunology, brain imaging assessments, and recordings of environmental risk factors to which they have been exposed. The team develops cellular, brain organoids and mouse models reproducing the context in which the disease is triggered and proposes innovative approaches to treat patients. They gather psychiatrists, psychologists, and neurologists, as well as specialists in epidemiology, genetics, immunology, brain imaging, and biotherapy, working in five complementary research groups, with the aim to develop therapeutic strategies tailored to patients and precision medicine in psychiatry.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Following the previous evaluation, the recommendations to the team were (i) to continue with outstanding scientific production and activities, (ii) to be co-located in the same place whenever possible, and (iii) to provide further preliminary or supporting evidence on the efficacy of mesenchymal stem cells in autism.

In line with these recommendations, the team pursued its scientific production and expanded its activity with the registration of several patents and the development of clinical trials. Moreover, even though the team is not based in a single location, efforts have been made to consolidate its activities. They are now located on two scientific campuses: the wet lab and biological experiments are conducted at Créteil (IMRB, UPEC-Inserm, Créteil), where patient assessment and epidemiological studies are performed through the University affiliated departments of psychiatry and neurosurgery at Mondor University Hospitals (University Paris Est Créteil and APHP, Créteil). Brain imaging exploration and preclinical models are carried out at the CEA Saclay Campus (Neurospin and NeuroPsi) to conduct experiments in parallel in patients. Finally, the project that raised concerned during the previous evaluation seems to have been set aside and does not seem to have been an issue for the team.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	20
Sous-total personnels permanents en activité	**30**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	6
Post-doctorants	1
Doctorants	12
Sous-total personnels non permanents en activité	**21**
Total personnels	**51**

EVALUATION

Overall assessment of the team

This is an outstanding team, internationally recognized for its work on the characterization of neuropsychiatric disorders and the development of innovative therapeutic strategies. The team is well funded and coordinates high-profile national projects. It is very attractive (multiple awards, organization of congresses, recruitment of many PhD students and post-docs). In addition, the team's scientific output is prolific and of high quality and it is effectively included in society (interactions with the private sector, four patents, regular contributions to the information of the public).

Strengths and possibilities linked to the context

The team draws on multidisciplinary and complementary approaches to better understand, diagnose and treat heterogeneous and overlapping psychiatric and neurological disorders. It has been successful in raising financial support from national and international sources (e.g. ERA Net NEURON, Horizon 2020, ANR, PHRC-I, PREPS, Fondation de France, Fondation FondaMental) to develop their projects (10.5M€ since 2018). The team promotes career development of its members, respecting gender equality in this process (five promotions or full-track positions were obtained, three for women and two for men).

In addition, the team presents a very high attractiveness on different aspects. Several members of the team have been recipient of international or national awards and have organized international or national congresses. The team leader, Marion Leboyer, is highly renowned both in France and internationally. In particular, she was awarded the "Grand Prix Inserm de la Recherche" in 2021, was promoted to the rank of Officer of the Legion of Honor in 2022, and was invited to give several keynote lectures in international and national congresses. Furthermore, the team recruited 23 PhD students during the evaluated period, 5 post-doctoral fellows (two of whom were recruited as Inserm researchers), and hosted two invited professors from England and Canada for one year. The team is actively involved in the management of national programs. Marion Leboyer has been granted the management of two new national investment programs, i.e., the PROPSY exploratory PEPR (80M€, 2022-2027) and in 2023 the Brain & Mind Biocluster (100M€) within France 2030. The team also built a platform for high throughput genotyping or methylome analyses that resulted in their involvement in a European project (REMEDIA).

The team has a highly prolific scientific production that led to a better characterization of neuropsychiatric disorders and to propose innovative therapeutic strategies. During the evaluation period, they published 489 original articles and 50 reviews, including 103 signed as first author and 122 signed as last author (41.74%). A significant amount of first- and/or last -authors publications was in top-tier journals (eg. Molecular Psychiatry (2), Biological Psychiatry (2), Lancet Psychiatry, Brain, Journal of the American Chemical Society, Neuropsychopharmacology (2), or Brain, Behavior, and Immunity (3)).

Finally, the team displays an active inclusion in society. They have a significant interaction with the private sector, both by obtaining grants from private companies and by developing partnerships with companies, including startups. They registered four patents and created a startup (Beams Cie) to develop surgical beta emitting detection and resection tool for tumors, which was winner of the i-Lab 2023 competition. In addition, all team members regularly make presentations for general audiences, in interaction with patient associations, give interviews for the press, and interact with school students (Apprentis Chercheurs).

Weaknesses and risks linked to the context

The research of the team remains undertaken in two different scientific campuses: IMRB in Créteil and the CEA Saclay Campus. This can be an issue in terms of team interaction, particularly when it comes to organizing team-wide meetings or setting up collaborative projects between certain research groups of the team.

In addition, among the seven group leaders or co-leaders of the team, there is only one woman.

Finally, the team has not coordinated any European grant, although they actively contribute to several international programs.

Analysis of the team's trajectory

The team's success over the evaluation period in terms of scientific output, impact within the biomedical community, and acquisition of funding clearly indicates that they will continue to excel in these areas in the coming years. The team's proposed trajectory is compelling and clearly builds on the scientific and clinical achievements from the previous years.

For the next five years, the team will follow its goals of stratifying patients by the identification of genetic, immunological or brain imaging biomarkers associated with clinical dimensions or environmental risk factors, by understanding pathophysiological mechanisms of neuropsychiatric disorders, and by developing targeted therapeutic strategies. The team will continue to be structured into five research groups, working with each other towards the common goal of developing precision medicine in psychiatry. For this, they will benefit from the PEPR PROPSY (PI: M. Leboyer), which will recruit a longitudinal cohort of deeply phenotyped patients (N=3,000) with overlapping neuropsychiatric disorders. In parallel, the causes and consequences of risk factors for neuropsychiatric diseases will be studied in preclinical models useful for biomarker identification, pathophysiological models deciphering, and therapeutic strategy development.

Stéphane Jamain, who led the team with Marion Leboyer during the last five years, and was promoted to Inserm DR2 position during the previous mandate, has been designated by team members to lead it for the next contract. The general organization of the team will remain stable, with the current principal investigators continuing to lead their research groups. Two additional professors will be recruited during the contract.

The team will keep the same localization either on Creteil University hospitals (UPEC, AP-HP) or on Saclay (CEA, Université Paris Saclay). Epidemiological and clinical explorations of patients, as well as the innovative therapeutic strategies will be carried out within the University hospital Mondor-Chenevier. Genomic and immunopsychiatry will be carried out at IMRB, to facilitate access to genomic and immunology platforms. Brain imaging will continue at NeuroSpin at CEA Paris-Saclay, where the team has been based for 10 years. Part of the team is installed in the recently created Paris-Saclay Institute of Neuroscience (NeuroPsi) to develop, study and conduct brain imaging studies on them at NeuroSpin. Partnership agreements are currently being signed between all involved institutions (CEA, Inserm, UPEC, CNRS and University Paris-Saclay).

RECOMMENDATIONS TO THE TEAM

Overall, the team should continue with outstanding scientific production and activities.

The team should pursue its effort to be located in the same location, wherever possible.

The team should improve parity among its group leaders.

Team 8: Genetic and environmental interactions in COPD, Cystic Fibrosis and other (rare) respiratory diseases

Name of the supervisor: Ms Sophie Lanone

THEMES OF THE TEAM

The team results from the merging in 2020 of two former IMRB teams with a long-time expertise in lung diseases: one focusing on the molecular and genetic bases of cystic fibrosis and surfactant metabolism dysfunction, and the other aiming to study the respiratory consequences of environmental aggressions, including the development of chronic obstructive pulmonary disease. The scientific objective is to gain a deeper understanding of the complex relationships between genetic and environmental factors in the development of lung pathologies throughout the lifespan, from childhood to adulthood. The team is multidisciplinary, comprising physicians and scientists enabling the development of a comprehensive approach, ranging from *in vitro* experimental work to preclinical models and patient cohorts.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Most of the recommendations made during the previous report were implemented. Regarding international collaborations and highly selective grants, S. Lanone is the coordinator of the H2020 REMEDIA project dedicated to understanding the impact of exposome on the course of lung diseases. The project gathers thirteen partners from eight European countries. As coordinator of REMEDIA, the team is part of the European Human Exposome Network, studying the impact of exposome on human health. It brings together nine research projects (including REMEDIA) from Horizon 2020. Finally, they are also partner of the International Human Exposome Network (IHEN) gathering twelve partners from eight countries. The team maintained the number of research engineers with a permanent position (two from UPEC), but failed to obtain more permanent positions. Currently, in addition to two research engineers with permanent positions, four non-permanent engineers are part of the team. The newly recruited full-time researcher should introduce novel biological approaches to decipher the complex mechanisms of genetic surfactant disorders at the cellular level. Indeed, the team has developed an iPS-derived cell model recapitulating two levels of the lung airway tree. This model is useful to identify potential drug candidates and therapeutic targets and the development of translational approaches has been initiated.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	6
Maitres de conférences et assimilés	8
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	**24**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	4
Post-doctorants	2
Doctorants	5
Sous-total personnels non permanents en activité	**12**
Total personnels	**36**

EVALUATION

Overall assessment of the team

The overall assessment of the team is excellent to outstanding. The team has published 226 original articles and filled four patents since 2018. The team has recruited two new assistant professors. The team is internationally recognized as a leading group in the research field of lung diseases and environmental aggressions. The team has secured more than 7.3 M€ euros since 2018 through continuous financial support from several European and national agencies and patient associations. The team has developed the PolluRisk core facility which is also used by six other IMRB teams.

Strengths and possibilities linked to the context

The reputation as a leading group in the research field of lung diseases and environmental aggressions is internationally recognized internationally. S. Lanone is coordinator of a large EU-funded projects (H2020, REMEDIA and RCA, IHEN), gathering thirteen partners from eight European countries.

The team has a strong expertise in complementary fields (pulmonary & occupational medicine, biology, immunology, molecular genetics, and functional genomics) and has a close partnership with clinicians and patient associations. The team has demonstrated a remarkable capacity to attract funding, having secured numerous national and European grants where they often serve as project coordinators. This dynamic approach has led to the successful acquisition of over 7.3 M€ in funding since 2018 through continuous financial support from several agencies (EU, ANR, Anses) and patient associations (VLM, Fondation du souffle, Ligue contre le cancer).

The team is involved in PIA programs (labex Serenade, Equipex NanoID, EUR live, PEPR Exposome, CPER 2021-2027).

All research groups have secured funding that will last after the end of the term. The team demonstrated a good dynamic of recruitment with two assistant professors newly recruited.

The team has an excellent publication record with a mean annual publication rate of five papers per permanent staff, despite a limited number of publications in generalist journals. The team has published 226 original articles, some in high-profile journals including Am. J Resp Crit Care Med, PNAS, Thorax, and Am J Hum Genet, 26 letters and 27 reviews published since 2018. In terms of valorization, the team has also filled four patents.

The team is well integrated within the IRMB research unit and has published numerous papers in collaborations with other IMRB team. Together with the LISA laboratory (CNRS UMR7583), the team has developed the PolluRisk core facility, a unique experimental tool to study the impacts of environmental exposures on health, which is also used by six other IMRB teams. One team member is part of the CIS of IMRB.

Weaknesses and risks linked to the context

The team lacks support staff, in particular engineers. The team is composed of 24 permanent staff and only twelve non-permanent staff. In addition, two permanent research engineers will retire during the next mandate, and it is important to maintain enough workforce to initiate and maintain projects and to secure specific know-how and knowledge. There is also a lack of post-doctoral fellow's recruitment, which should also help to maintain a good dynamic and help to foster new projects.

One clinician of the team is PI in two clinical trials, but despite the close interactions with clinicians and clinical departments of the Créteil hospital, translational approaches are not enough developed, in particular considering the number of clinicians in the team (six PU-PH, three MCU-PH and five PH).

Analysis of the team's trajectory

The team's trajectory for the next term is consistent and in line with the previous project, aiming to strengthen the link between basic and clinical research. One strength is the close partnership with clinicians and patient's associations, which should help this goal.

For the next five years, the same director will remain in charge and the team will be composed of three groups:
1- Molecular and genetic bases of chronic alveolar and bronchial diseases
The decision has been made to merge the "Genetic and cellular bases of CF and surfactant disorders" axis together with the "Molecular bases of cigarette smoke-induced COPD" axis in order to consolidate these groups and help foster identification of potential drug candidates and therapeutic targets both for CF and surfactant disorders and COPD.

2- Resolution of inflammation in lung diseases
Work we will be pursued on the molecular and cellular bases of persistent inflammation that characterize chronic respiratory diseases.

3- Environmental aggressions and course of lung diseases
The previous work on deciphering the consequences of environmental aggressions on respiratory health will be pursued following three main axes:
- Occupational exposures and respiratory health
- Early determinants of chronic lung diseases
- Role of exposome in the course of lung diseases

The three groups are unbalanced, (eight permanent researchers in group 1, three permanent researchers in group 2 and five permanent researchers in group 3), but the team is more balanced than in the previous mandate.

RECOMMENDATIONS TO THE TEAM

The recommendation would be to maintain the team's current level of excellence in terms of funding and publication record, and to make an effort towards publishing more in generalist journals.

The team is composed of 24 permanent staff and only twelve non-permanent staff, with a lack of technical support staff. This is an important consideration, as two permanent engineers will retire during next term.

This could further help to develop experimental and translational research, including the iPS cell-derived lung epithelium model.

Also, while most of the permanent staff are PIs on obtained grants that will last after the end of this term, there is a great imbalance in funding among the research groups with 70% of the total amount being obtained by the head of the team.

Team 9: Biomechanics and Respiratory Apparatus

Name of the supervisor: Mr Bruno Louis & Mr Marcel Filoche

THEMES OF THE TEAM

¨Biomechanics and Respiratory Apparatus¨ which addresses mechanical ventilation and biomechanics of the airways. This team is a continuation of the Cellular and Respiratory Biomechanics team. The tools include patient's cohorts as well as in silico and in vitro models.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team satisfactorily addressed the comments of the previous report. In terms of funding, the team raised approximately 900 k€ during the previous period. Regarding recruitment of basic scientists, the team allocates more attractiveness to the private sector. New recruitments of full professors are helping the team to introduce new lines of research, including the nasal respiratory epithelium as a new route of administration of therapeutics and the local anchorage in the field of mechanical ventilation. Finally, the team has initiated three collaborative projects within IMRB.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maitres de conférences et assimilés	2
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	11
Sous-total personnels permanents en activité	**19**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**4**
Total personnels	**23**

EVALUATION

Overall assessment of the team

The overall assessment of the team is excellent. The team has an attractive scientific reputation for its involvement of non-invasive ventilation (NIV) and positive pressure inspiratory support (AI), alongside a long-standing experience on the modelling of flow and transport in the airways. The team has a great number of tenured track positions. The team worked hardly during Covid19 developing methods of mechanical ventilation. The team members have obtained 900K€ in public and private research grants. The team exhibits strong relations with industry partners.

A major outcome of the team´s research is the significant clinical impact.

Strengths and possibilities linked to the context

The team is internationally recognized for its involvement in non-invasive ventilation (NIV) and positive pressure inspiratory support (AI), alongside a long-standing experience on the modelling of flow and transport in the airways. The scientific project is solid, mostly in the continuity of the work done during the previous contract and will rely on an interdisciplinary approach based on the confrontation between patient data and modeling. The team benefits from the experience of the clinical teams and the access to serval networks of patients with pathophysiological problems.

The running internal collaborations between basic scientists and clinicians from Créteil Hospital clinical departments are of pivotal importance for the success of the project and are a strength of the project.

Overall, in the last period, the scientific production is of high quality (45 articles in high-profile journals), consists of 368 papers (131 scientific articles, 19 reviews, and 21 letters and others). Importantly, 173 publications have at least a team member as first or last author, which is impressive. Some of these publications are part of the five items included as team´s portfolio, which includes publications in Neonatology, PLoS Comput Biol, Int. Forum Allergy Rhinol., J. Med. Gen. and Int. J. Mol. Sc. These studies illustrate the optimization of mechanical ventilation axis, its modelling, the impact of surgical masks during Covid19, a tool to measure the efficiency of cilia, and finally, the possibility to use the nasal respiratory epithelium as a new route of administration of therapeutic agents. The team presents a mean ratio of fifteen publications per member and meets the requirements of the doctoral school for PhDs candidates.

The team by the end of the last contract was composed by three researchers (two and one emeritus), seven teaching researchers (six full professors and one emeritus), seven hospital practitioners (six and one emeritus), one laboratory technician and one postdoc, benefits from a large number of tenured positions but shows a limitation in postdoctoral positions.

The team was able to raise 900 k€ during the last contract. The team has obtained three grants from inter-team IMRB projects, one grant from the Fondation de la Recherche Médicale, one grant from ANR and benefits from several support grants from ENT young doctor from the French Society of ENT.

The scientific interactions with other IMRB teams appear to be interesting with two different groups, and the team contributes with their expertise in primary culture model of human nasal epithelial cells and cilia.

Supervised students have at least a meeting including junior and senior researchers in basic science and clinicians is held once a week. The team regularly welcomes researchers from other French or foreign institutions such as the University of Navarra and Michigan). This shows that the team has a large collaboration network which includes Paris, Poitiers, Tours, Michigan and several companies.

The team has been involved in non-academic interactions including the translation of scientific works, the hosting of young students of 13-14 years of age. Dissemination is also performed by the team in interviews or in articles in the press.

Weaknesses and risks linked to the context

Whilst the amount of found from French funds is acceptable, the project does not include any plans of applying for European and/or international funding at least for the next contract period, even though the committee recognizes that still the project might be in early stages of development. The number of postdocs in the team appears to be limited, even though the team envisages several physician researchers by 2026, the team would benefit from more postdoc positions that will bring expertise in culture/in vivo modeling. Perhaps, implementing industrial partnerships would help to get funding for these positions.

The women-to-men ratio of the current team versus the one expected by 2026 is not clear in all levels from the report.

Scientific exchanges between basic scientists and intensive care specialists should be encouraged in order to understand specific mechanisms of disease.

Analysis of the team's trajectory

So far, the team focused on understanding the physiological and pathophysiological mechanisms of chronic and acute respiratory distress, as well as improving patient management. For the next contract period, the team will focus more on critical illness: AXIS-1-acute respiratory failure (ARDS) and AXIS-2-acute circulatory failure (shock). One axis of research will focus on optimization of mechanical ventilation in adults which is already a strength of the team, but this research will be focused on the development of new modes and new tools to

diagnose respiratory failures and optimize mechanical ventilation. Research will concern adults but also children and newborns. Thus, the focus on the pediatric population is exciting to understand mechanisms of airways in premature infants.

The second axis will focus on biomechanics of the airways. It will characterize interactions between the airway wall (the organ) and airflow using physical and mechanical studies. A special focus will be made on deciphering the interaction between the cellular function and types of aggression (mechanical, inflammatory or virulent). Obviously, the last step is to perform translational research in relation with patient cohorts present on the site (for instance patients with primary ciliary dyskinesia) that will certainly lead to innovative discoveries improving patient clinical management. This focus is coherent with the existing literature on the topic, and the hypothesis that the crosstalk of signaling (mechanical and biological) between epithelium and endothelium membranes of the pulmonary alveoli is a key driver for respiratory and hemodynamic failure is sound. The objective of the scientific project will follow a multi-scale and interdisciplinary approach. The research is innovative since it will explore physiology across ages, bringing novelty to the project. For both axes, the team will employ different scales that encompass modeling, cell mechanics, and bedside clinical physiology. Interestingly, for AXIS-2, the team will also use cadavers.

The team aims at maintaining a high national and international visibility thanks to their high scientific production, their expertise, their patent activity and their dissemination activities. It is envisaged that by 2026, the team will be composed of 21 members who will be permanent staff and 14 non-permanent. The later will include five physician-researchers and nine PhD (two of them from industry).

RECOMMENDATIONS TO THE TEAM

The high scientific quality of the team should prompt the researchers to apply in the future for competitive European or international research grants that will undoubtedly have a positive impact on the team´s attractiveness.

It is recommended to re-inforce the interactions between basic scientists and clinicians in order to favor integrated approaches of scientific issues and to promote grant applications. Understanding disease-specific mechanisms will promote further the team´s excellence (e.g.: Organoids, lung-on-a-chip).

To strengthen industrial partnership could help recruiting new postdocs that further develop experimental and translational research.

Team 10: Neurofibromatosis and Lymphoma oncogenesis

Name of the supervisor: Mr Philippe Gaulard & Mr Nicolas Ortonne

THEMES OF THE TEAM

The NFL team project focused on two distinct cancer models: lymphomas and neurofibromas in NF1 patients. The primary objectives of the team are to (i) uncover molecular alterations involved in the transformation of cancer cell progenitors, (ii) assess their diagnostic and/or prognostic relevance, and (iii) identify new actionable targets for future therapies.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Some recommendations made during the previous term were implemented. The main suggestion that was fully implemented focused on highlighting the co-director expertise as a team leader (mid-term evaluation in 2021). Additional suggestions concerning publications (in terms of quality and team members as first/last authors), PhD recruitment, strategies to foster team cohesion and efforts to improve outreach activities have been partially addressed, with some aspects remaining challenging to achieve, particularly the issue of team cohesion.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	8
Maitres de conférences et assimilés	3
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	12
Sous-total personnels permanents en activité	**23**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	10
Sous-total personnels non permanents en activité	**13**
Total personnels	**36**

EVALUATION

Overall assessment of the team

The overall assessment of the team is excellent. The team focuses on highly relevant pathologies to human health. Over the past five years, the team has produced valuable data, increased their visibility, attractiveness and has secured external funding from various sources. Team members are deeply involved in teaching and PhD supervision. Nevertheless, the interaction between the two axes remains rather unclear. The visibility, attractiveness and valorization strategy can still be improved for the members of Axis 1.

Strengths and possibilities linked to the context

By the end of 2023, the team comprised 37 members with 25 permanent members, among whom are PUPH, MCUPH, MCF, IR, IE and technicians. The team currently focuses on two research areas: (i) lymphomas and (ii) neurofibromas from patients with NF1. Members of Axis 2 joined the lymphoma team in 2020. The leader of Axis

2 initially held a position as a full researcher (DR Inserm) and obtained a PU-PH position in 2020. The arrival of this group has undoubtedly strengthened the molecular expertise of the lymphoma team.

The team evolves in a very good local environment and has numerous collaborations with other IMRB teams such as Cohen or TrepCa teams. Similarly, thanks to pathologists in the team, they engage frequently with other IMRB teams, although this expertise was lost with the retirement of the IR. The team is well organized. The executive team comprises team members of both axes (mainly IR). The executive team contains one HAL and health/safety referent and one GreenLab referent. The team leader is aware of the well-being of his team members. Moreover, despite the intensive hospital responsibilities of a significant number of the team members, weekly formal team meetings are organized, including meetings with external speakers. In addition, weekly informal meetings are planned for each axis (Lymphoma and NF1). The team complies with safety, ethics, and intellectual property guidelines established by local (IMRB), national (e.g. Inserm), and international institutions. Additionally, they uphold the principles and standards of scientific integrity. Regarding resources, the team members have secured external funding from various sources during the last five years (2,165 M€ and 3,940 M€ for axis 1 and 2, respectively). They secured funds from national associations and foundations (FRM, ARC, SFD, CTF) (>1M€). They are also PI in international grants such as NTAP (Axis 2)(1,11 M€ total) or national grants like INCa or ITMO Cancer. They are also partners of ANR (DIAL, RHU SPRINT, CureNF1, Peristem). Additional fundings were also obtained from pharma compagnies such as Bohringer Ingelheim, Pierre Fabre or Sanofi. Visibility of PIs is reflected by numerous invitations to give lectures in national and international conferences in the field (European Congress of Pathology, Hematopathology Research Meeting, Lymphoma Forum in San Francisco, the Global Neurofibromatosis Conference…) and participation to committees (SAB (Children Tumor foundation), Scientific councils (Inst. Carnot CALMYN), executive boards (LYSA)…), conference organizations (ELI, Development of therapeutics targeting RASopathies meeting, Global Neurofibromatosis Conference…) and coordination of competitive grants (INCa, FRM…) grants. Moreover, the team leader of axis 2 is coordinator of international grants in the field of Neurofibromatosis. Team members established multiple industrial/pharmaceutical contacts.

The former director, remains actively involved in PhD teaching, securing funding for axis 1 (FRM 360k€, BMS BioRoCHOP 150k€) and maintaining the team's visibility by serving on the LYSA and CALYM boards and being part of the European network TRANSCAN2.

Among past PhD students, the majority (three out of four) authored two to three first-author publications. Team members have ongoing local, national and international collaborations.

The scientific objectives of the team are highly relevant in the context of human health.

To carry out the project, the team brings together scientists (primarily engineers and MCF) and medical professionals with complementary expertise in clinics, in haemato-, dermato- and NF1 tumors pathologies and also genetic and molecular approaches. Some team members also have strong expertise in in vitro and in vivo functional approaches (e.g. in PTCLs).

The team leveraged its medical staff and clinical environment (e.g. Henri Mondor Hospital or other medical partners in France and internationally) to conduct numerous translational studies, sample cohorts to clinical trials.

Relevant data have been published over the past five years, relevant. Regarding Axis 1, clinical samples, the team (i) identified recurrent mutations targeting epigenetic modifiers in and JAK – STAT pathway in BI-ALCL (ii) developed a gene expression assay for the classification of peripheral T-cell lymphomas and (iii) proposed 2 novel therapeutic targets, KIR3DL2 and CCR8, in aggressive PTCL and CTCL respectively. Of note, KIR3DL2 was the basis for the new KILT multicentric clinical trial involving the team's Director. The team also published the results of the phase 2 clinical trial ALYCANTE (CAR-T therapy targeting human CD19). For myeloid neoplasms, a longitudinal study was conducted to identify reliable predictors of MDS progression to "overt" CMML.

Thanks to collaborations, other molecules of interest have been identified in the context of lymphomas including CD81, PD1, ICOSL. The team is also highly involved in the diagnostic, prognostic and predictive biomarkers in B- and T-cell lymphomas.

For Axis 2, the team developed highly relevant models to investigate the cellular and molecular mechanisms underlying the development of NF1-associated neurofibromas and to establish in vitro and in vivo assays for exploring new therapeutic strategies. In this context, they identified a three-stage process driving cNF development and highlighted the significant role of the tumor microenvironment (TME), particularly innervation, in this process. For pNF, a transient dysplastic stage (dNF) has been identified in mouse and human with a potential role for T cells (PD1+ in humans) and/or M2 macrophages. Genetic events have also been identified in dNF and GMT.
Over the past five years, the team published 56 original articles with team leader as first or last author (20.5%) in good to very good journals and some in high-profile journals (Nat Med, Cancer Discovery, Gut, Blood, J Haematologica…).

The team offers a variety of experimental approaches, ranging from human cell lines. It also has access to large cohorts of patient tissues with PTCL and NF1-type tumors. The team also developed tools widely used for drug discovery, drug validation, and the investigation of genetic, epigenetic, and transcriptomic mechanisms driving tumor development. One team member developed an asymmetric capture sequencing strategy which was licensed by APHP to Agilent Technologies. He also co-developed software designed to detect and quantify fusion genes. The team members have been active in protecting their intellectual properties and have deposited 3 patents (under process). Some team's members are active in outreach activities: welcome of a college students for intership observation, participation to the annual sporting event "marche Calipsso" where they share their knowledge with the public.

Weaknesses and risks linked to the context

Despite efforts over the past five years to enhance interaction between the two axes, concrete outcomes remain limited, such as a lack of joint publications, PhD students/post-docs or shared grants.

Although highly proficient at raising funds, members of axis 1 who are significantly more numerous than members of axes 2, should strengthen/develop national/international collaborations to apply for national and European grants as team leaders. Moreover, as mentioned in the previous term, the team has secured a high number of industrial contracts, but this is not supported by a clear valorization strategy, as evidenced by the low or absent number of licensed patents and Cifre contracts.

The percentage of original research articles with team members as last-authors is low for international standards (20%) in comparison to the one published as partners.

Team members appear to have limited involvement in peer reviewing, editorial roles, or scientific project evaluations, likely due to their extensive hospital responsibilities.

Outreach activities could be significantly improved and should involve a greater number of team members.

The team likely faces challenges due to the absence of permanent full-time researchers.

Analysis of the team's trajectory

For the next term, the director will lead a new team focused on lymphomas, named MOON-LYT. The leader and members of Axis 2 will integrate one Professor..

MOON-LYT will consist of 15 permanent members, including a full-time researcher, several PU-PH and other hospital and technical personnel (IE, IR).

The future plans for the MOON-LYT team represent a logical progression of ongoing projects focused on PTCL (TFH-PTCL and non-TFH-PTCL) oncogenesis, diagnosis, and treatment. From a fundamental research perspective, the team will continue the molecular, cellular, and functional characterization of these lymphomas. For innovative treatment strategies, they will target novel candidates identified during the current term, such as ICOS/ICOSL, PD1/PDL1, and CD81, with an emphasis on achieving in vivo proof of concept in the next term.

As in the current term, the team will conduct extensive translational studies, ranging from research on PDX and on cell lines to cohort-based studies (e.g., biopsies) and clinical trials (ORACLE, KILT). The diverse expertise of team members is a key strength, enabling a multidisciplinary approach.

Additionally, the team benefits from strong collaborations with industry partners (e.g. Sanofi, Innate Pharma), the Carnot Institute CALYM, and national networks such as LYSA. They will also leverage access to large national sample cohorts, which are being established by team members, to further advance their research.

Some fundings are secured until 2028 with national grants, *i.e.* ANR DIAL and RHU SPRINT, in which team members are partners.

RECOMMENDATIONS TO THE TEAM

The numerous projects and the hospital responsibilities of most team members could pose a challenge to achieve all project goals. To address this, it will be crucial to recruit full-time young researchers, i.e. PhDs and Post-docs to provide dedicated support and ensure the successful completion of all projects.

A concern also lies in the decrease in the number of permanent members holding an HDR during the next term. This highlights the importance of attracting permanent full-time researchers.

The team should continue enhancing their national and international collaborations to secure additional grants for advancing their ambitious project.

The team should establish a clear valorization strategy for the next term.

Team 11: Virus, hepatology, cancer

Name of the supervisor: Mr Jean-Michel Pawlotsky

THEMES OF THE TEAM

The main research themes of the unit are ¨Viral infections¨ and ¨Liver Diseases¨.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

“No major weaknesses” were identified in the previous Hcéres' report, which highlighted the outstanding national and international reputation in the area of HCV virology, drug development and resistance, and liver pathogenesis. However, the number of postdoctoral fellows was highlighted and in the last period the unit has recruited six postdocs. Moreover, international funding including EU was further recommended in the previous report. However, the team has been successful in obtaining French grants in the last five years for more than 7.5 million euros.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	7
Maitres de conférences et assimilés	9
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	16
Sous-total personnels permanents en activité	**34**
Enseignants-chercheurs et chercheurs non permanents et assimilés	3
Personnels d'appui non permanents	4
Post-doctorants	1
Doctorants	14
Sous-total personnels non permanents en activité	**22**
Total personnels	**56**

EVALUATION

Overall assessment of the team

The overall assessment is outstanding. The team has an outstanding national and international reputation in the area of HCV virology, drug development and resistance, and liver pathogenesis. The scientific strategy of the team is in line with the missions of the Inserm, the French National Institute for Medical Research, the IMRB, the Henri Mondor University Hospital and the Faculty of Health of Créteil. The international scientific expertise and recognition of the team is reflected in its production, and in the scientific collaborations with national and international research groups. The team organization is excellent in terms of leadership, management and team member participation in final decisions. The unit´s attractiveness for its capacity to host staff is outstanding. The team benefits from fully equipped facilities and technical skills which guarantee the success of research programs. The team has shown great innovation, adaptability and dynamism to research needs. The team guarantees scientific integrity using electronic lab notebooks. The team has an impressive commitment in expertise activities including consulting for industry.

Strengths and possibilities linked to the context

The scientific goals are based on shared tools and expertise which include patient cohorts and clinical trials (national and international), large human specimen and tissue collections, large databases, serological and molecular virological tools, original NGS-based molecular biomarkers (-OMICS) for diagnosis, epidemiology, surveillance and monitoring, and pathophysiological studies, assessment of antiviral efficiency, in vitro models, bioinformatics and biostatistics tools and artificial models.

The team presents seven items in its portfolio which reflect the quality of their scientific production, including five original papers (including publications in excellent journals such as PLOS Pathogens, Gastroenterology or Lancet Oncology), one international meeting organization and one patent.

The team has a strong publication record of original scientific articles: 664 scientific articles (over 27% as first, last or corresponding author), 57 reviews and editorials. Whereas the Team Director is a world-renowned leader in the field of viral Hepatitis and Hepatology, the members of the research team have collectively delivered 231 invited lectures, most of them at international meetings. A Team´s strength is the fact that they participate in editorial boards of international journals and/or in national and international scientific committees, in scientific advisors, juries and monitoring committees, and are active members of important scientific societies.

In the last period, the team has continued with its work on viral hepatitis, performing phase I-III, clinical trials and cohort's studies in patients with HCV, HBV and HDV. A team´s uniqueness is the next generation sequencing platform specialized in infectious diseases which is unique to phenotype HCV genotypes and reporting HCV unusual subtypes. Moreover, the team´s studies on clinical virology and epidemiology have led to a great number of publications in international peer-reviewed journals and is a partner of the French National Agency to conduct national surveys in populations at risk. The team has also benefited from the recruitment of an experienced scientist in mechanisms of occult HBV infection and the assemblance of a collection of over 4,500 HDV strains from all over the world. Their activity during the SARS-CoV-2 pandemic has been pivotal since they established collaborations with 45 hospital virology laboratories and 45 medical intensive care units in France and as a result several papers have been published including mechanisms of cellular entry of respiratory viruses alongside the development of several – omics techniques.

A competitive scientific strategy is the basis for the prevention and treatment of primary liver cancer and includes the development of a learning model capable of predicting response to drug treatment for liver cancer and understanding intra-tumor heterogeneity as well as the role of autophagy in macrophages to induce tumor evasion. Moreover, the use of the previously discovered family of new cyclophilin inhibitors as a new tool for organ protection in the context of ischemia-reperfusion injury is a research priority.

The team has an excellent internal management procedure. On the one hand, newcomers are required to attend an orientation program. On the other hand, junior researchers are paired with senior mentors. Scientific integrity is assured by an Ethics Committee and all team members are strongly discouraged from publishing in predatory journals but encouraged to publish in open science. The team´s excellence in success for competitive calls is the result of a strategy that targets results via the critical discussion of all team members.

As a result of this strategy, and since 2018, the team has been able to raise over 7.5 M€ obtained by applying to calls from Inserm and the University as well as to other sources of private funding including Bayer, Gilead, Grifols Diagnostic LTD, Moderna, Fondation Bristol Myers, etc. Of note, the financial management of the team involves partial pooling of resources to cover common expenses such as materials and supplies commonly used in the lab, as well as the use of research facilities.

The team has a reasonable internal dissemination strategy via scientific meetings and ad hoc meetings ensuring the productivity of the team. Communication with the general public has been done regularly involving national and international media and websites.

The team´s capacity for transferring knowledge is impressive with recent patents filed and the formation of a new company to exploit the metagenomics patent.

The team has been very dedicated to society providing a fast and integrative response to emerging viruses such as SARS-CoV-2 pandemics and the outbreak of other respiratory viruses as well as the increased incidence of primary liver cancer. Dissemination with the public has been organized via educational activities, conferences and testing in the general public for hepatitis virus.

Weaknesses and risks linked to the context

No major weaknesses were identified. The team organization suffers from the different location of the lab space in the campus. However, it seems that the new building will solve the problem. The team is reasonably balanced women/men, even though, still the ratio men (33) to women (20) is higher. It seems that it will be balanced with the new team joining for the new research topic ¨Viral Pathogens¨ in the next contract period.

Analysis of the team's trajectory

The "Viruses, Hepatology, Cancers" research team is a translational, multidisciplinary research group that, following the historical legacy of its creation in the context of hepatitis C virus (HCV) research, its diagnosis, pathophysiology, antiviral treatment success and failure, and drug development. Since 2015, the team has expanded its research focused in Virology to include other hepatitis and respiratory viruses. Later the team has also expanding its research to primary liver tumors (hepatocellular carcinoma, cholangiocarcinoma, mixed tumors) and opened its research to other emerging liver diseases including toxic, metabolic, alcohol-related, etc. This organization will be maintained for the next mandate (2026-2030). In fact, the research team is a translational, multidisciplinary research group that includes permanent scientists, virologists, hepatologists, intensive care and infectious disease specialists, pathologists, radiologists, liver surgeons, engineers, and technicians, as well as post-doctoral and predoctoral students with a scientific, medical or pharmaceutical background. This research team is open to the arrival of new researchers and new themes related to its historical themes. Clinical, translational and basic studies will be conducted with a focus on elucidating pathophysiological mechanisms and discovering and applying innovative approaches to diagnosis, prognosis, monitoring and treatment of viral and liver diseases.

Importantly, the team will benefit from its relocation within the main hospital building and in close connection with the future Biology and Pathology platform in the beginning of 2025. Also, the next contract will be the last for the current founder and director.

The scientific objectives of the team for the next contract are related to clinical and translational hepatology research, viral hepatitis research, respiratory virus research, new antiviral drug research and liver diseases and cancer research. In addition, two new groups dedicated to the study of non-viral pathogens will be added during 2026-2030: Bacteriology and Bacterial-fungal interactions.

RECOMMENDATIONS TO THE TEAM

The main recommendation here is to maintain excellent productivity, publication record, including clinical guidelines.

The team is further recommended to apply to EU and other international calls (e.g.: EU Cost Action, MSCA) for funding if possible.

The inconvenience of having physical separation needs to be tackled if not solved.

The virology team is recommended to continue using the cyclophilin inhibitors as a step earlier to bedside. Regarding the Liver Disease team, the topics chosen are state-of-the-art, but the etiology of liver tumorigenesis in HCC versus CCA is different (although a great number of liver cancer is mixed HCC/CCA), the team should include different experimental models that trigger each of these cancers in order to exactly reproduce what happens in the patient (e.g.: MASLD/MASH/ALD…)

The team demonstrated an excellent public engagement but the educational output in terms of books, book chapters and involvement of postgraduate programs should be included.

The team is recommended to keep working on industrial collaborations and support young scientists, providing them with a clear structured career path. Women are less represented in the team (PIs) and need to be further supported.

The significant risk in the trajectory is the integration of the DYNAMYC team, whose themes are far from the current projects of the team. Close attention must be given to the integration of this team.

Team 12: Interventional Neuropsychology

Name of the supervisor: Ms Anne Cathérine Bachoud-Levi

THEMES OF THE TEAM

The "Interventional Neuropsychology" team was established based on the hypothesis that cognitive functions can be studied not only through their decline in brain-lesioned patients but also through their restoration following therapeutic interventions. This approach stemmed from a pilot study on intra-striatal cell transplants in Huntington's disease (HD) patients. Since becoming a full Inserm team in 2007, the group has expanded its research to include: innovative digital assessments, brain imaging follow-up and exploration of new affection.

The team's research has identified early deficits in language and other cognitive domains in HD and developed innovative cognitive assessment tools capable of longitudinal evaluation. These tools demonstrate potential for assessing therapy efficacy and, when combined with clinical and biomarker data using machine learning, could predict the progression of neurodegenerative research. Recently, the team has applied these concepts to Parkinson's disease and initiated new tasks for stroke research.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous evaluation raised two points: a question regarding the expansion of the team's focus to other neurological diseases and the relative dependence on biotherapy trials.

Regarding the first point, the team continued to develop research topics centered on the function of the striatum beyond Huntington's disease (e.g. Parkinson's disease and stroke) and secured funding for these projects.

For the second point, the team developed alternative approaches, such as original cognitive batteries to assess patients with neurodegenerative diseases, enabling evaluations in larger cohorts, as well as simplified tablet-based tests for remote patient monitoring at home.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

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

EVALUATION

Overall assessment of the team

The overall quality of the team is excellent. The team demonstrates a high level of publications, is well funded, and contributed to the development of innovative tools. It is extremely attractive for the quality of its staff hosting policy. Despite being spread across multiple sites, the team's coordination seems to ensure strong cohesion. The originality of the data acquisition makes the team unique for their technological skills. The team has an excellent policy for data management and storage.

Strengths and possibilities linked to the context

The team is small but multidisciplinary and benefits from a joint affiliation with the École Normale Supérieure, the Department of Cognitive Studies, and Henri Mondor Hospital. Weekly meetings bring together the project director and all principal investigators for strategic committee sessions, as well as the entire team for scientific discussions. Additionally, more informal gatherings are organized to strengthen team-building. Since the last evaluation, the team has expanded with the tenure of a university lecturer, a speech therapist, a neuropsychologist, two project managers, and the promotion of two senior researchers. The team also enjoys high levels of funding.

The researchers are involved in multiple national and international networks and are frequently invited to or organize national and international meetings. Additionally, members of the team are or were Editorial Boards members and reviewers of prestigious journals as well as French national evaluating committees. During this term, the team has developed an innovative approach to creating new cognitive assessment tools for measuring cognitive deficits. These tools are used to track the progression of conditions in the natural course of diseases or to assess clinical improvements during therapeutic trials. The team's expertise has expanded from language to other cognitive domains related to neurodegenerative diseases and strokes. Altogether, these procedures are highly relevant in the study of neurological disorders.

The team's research is supported by large cohorts managed by tenured scientists, enabling long-term follow-up studies. The development of cognitive assessment tools by the team has positioned them as leaders in evaluating motor, cognitive, and functional scores of patients, allowing them to monitor the natural progression of neurodegenerative diseases and assess the potential effectiveness of treatments. The close collaboration with Henri Mondor Hospital gives the team access to advanced brain imaging and electrophysiology tools.

Since 2018, team members have published 94 original articles in peer-reviewed journals (Cortex, Eur J Neurol, Alzheimers Res Ther, J Neurol), 52 of which (55%) list team members as first, last, or corresponding authors, alongside nine review articles and four letters. A patent has also been filed (CALAP patent FR1654259-100034703). The researchers coordinate fifteen clinical trials or cohort studies sponsored by pharmaceutical companies, including two as lead coordinators and thirteen as partner. The team has solid funding, with 2018-2023 funding amounting to 10,842 k€ from diverse sources (PIA2-Investments for the Future, CHDI Foundation, ANR, Ministry of Health, etc.).

The team is actively engaged in educational initiatives, working with schools and colleges, and shares scientific knowledge through national scientific events. The team communicates with the general public via traditional media (books, newspapers, TV) and modern platforms (YouTube, websites). Strong relationships have been established with patient associations for Huntington's and Parkinson's diseases, with team members involved in unique initiatives aimed at public outreach.

A team´s strength is its expansion since it was created fifteen years ago based on successful grant application (e.g: ANR, FP7, H2020, Roche). Not only that, but the unit has also raised an impressive number of doctoral and postdoctoral contracts and the team is involved in multiple multicenter programs sponsored by the academia or the industry. The team is also working in close collaboration with associations of patients with HD and PD.

There is parity of opportunity for women, with near equal representation at each level of seniority, which is still unusual, and impressive. Indeed, the team is composed of sixteen women and fourteen men.

The team benefits from an excellent team-building approach that maintains a great scientific environment. Scientific integrity is ensured by double or triple checking data and the promotion of open science.

The strategy of the team to become ecological and more sustainable is a strength since they are committed to reducing the carbon footprint.

Weaknesses and risks linked to the context

The multiplicity of affiliations makes it challenging to clearly identify each member's contributions within the team. Moreover, the research is undertaken in different locations, includes different institutions and at different levels of specialization and complexity.

The number of publications appears adequate given the number of researchers in the team and the disciplines involved. However, the quality of the journals could be improved, as it currently appears heterogeneous.

While the team's overall funding seems secure, most of it relies on a small number of tenured scientists. Broader involvement from the team would be necessary to stabilize funding over the long term. Additionally, partnerships with private entities are weak and not very visible, limiting their potential to support funding beyond doctoral and postdoctoral contracts.

The strategy of the team to become ecological and more sustainable is unlikely to align with the needs of the multiple meetings and networks they participate in, as many researchers continue to favor in-person meetings.

Analysis of the team's trajectory

For the upcoming term, the team will maintain a focused scope and will be organized around a "strategic committee," involving the senior lead researchers, and a "methodological committee." The team leader and the project director will belong to both committees (strategic and methodological) to ensure a smooth flow of information. Weekly strategic and scientific meetings will be maintained.

The projected scientific strategy appears to follow the path developed during the previous term, focusing on the development and enhancement of cognitive tools and studies of large patient cohorts, facilitated by the integration within Henri Mondor Hospital. These innovative tools will be extended to other brain disorders (e.g. Parkinson's Disease, Dementia with Lewy Bodies, stroke), and the team will also rely on multimodal biomarkers (clinical, biological, and functional imaging markers) to assess patient trajectories. A combined structural and functional imaging platform (MRI, fMRI, PET, EEG) will be established to study disruptions in brain networks during aging and neurodegenerative diseases.

The team will also conduct studies aimed at developing tools to predict cognitive decline, both in clinical cohorts (e.g. Alzheimer's Disease, Parkinson's Disease) and in the general population, with the long-term goal of considering prevention strategies for at-risk individuals and strategies for modifying cognitive trajectories (eCALAP®, the rehabilitative version of SelfCog, and prism adaptation therapy). The TRACeR team will also participate in therapeutic trials aimed at altering the clinical and cognitive trajectories of these diseases.

RECOMMENDATIONS TO THE TEAM

While the scientific strategy for the new team is well-defined, several uncertainties remain regarding key aspects of its future development. Clarification is needed on the strategy for securing new funding and on the evolution of the partnership with private structures, including specific plans to foster collaboration with private industry.

The approach to human resources requires attention, particularly in terms of attracting young researchers through recruitment strategies, mentoring programs, and career development opportunities. Additionally, strengthening communication and collaboration among researchers located at different sites will be crucial. Exploring the polluted environment as an etiological factor for neurological disorders could also represent a valuable future direction for the team's work.

Team 13: Biology of neuromuscular system

Name of the supervisor: Mr Frédéric Relaix

THEMES OF THE TEAM

The team draws on its complementary expertise in fundamental muscle biology, translational, preclinical, and clinical research to develop innovative therapies based on preclinical tests for transfer to the clinic. The team focuses on musculo-skeletal disorders and myopathies, encompassing rare Neuromuscular Disorders and, in some cases, common disorders like metabolic syndromes. It uses transversal approaches, combining clinical work at Henri Mondor and Necker hospitals, tissue engineering at the Etablissement Français du Sang, and at the Faculty of Medicine, molecular regulation, cellular interactions of muscle stem cells and bone progenitors, as well as the study and manipulation of repair mechanisms.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team received many outstanding comments on the previous report, regarding their productivity, activities, organization, and life. No major recommendation was made.

However, the committee did make some minor recommendations, which the team has taken on board in a very satisfactory manner.

The committee pointed out that the team should consider strengthening their links with industry to facilitate their translational program. Since the last report, the team created new partnerships with the private sector, they developed in preclinical and proof-of concept studies. These partnerships include contracts with Audentes/Astellas for gene therapy evaluations, Cytokinetics, Pliant and Peptris for pharmacological approaches, NTrans for targeted CrispR/Cas9 strategies.

In addition, due to the large and increasing size of the team, the committee suggested to increase support staff and to delegate specific tasks to other members of the team to facilitate management and maintain focus, especially in light of clinical translation of some gene therapy/editing projects. The team recruited additional personnel through grant funding, while no additional institutional support has been obtained, and displays a clear distribution of responsibilities among group leaders and among permanent researchers in each group.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	11
Maitres de conférences et assimilés	16
Directeurs de recherche et assimilés	4
Chargés de recherche et assimilés	5
Personnels d'appui à la recherche	25
Sous-total personnels permanents en activité	**61**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	1
Post-doctorants	6
Doctorants	26
Sous-total personnels non permanents en activité	**34**
Total personnels	**95**

EVALUATION

Overall assessment of the team

The overall assessment of the team is outstanding. The team is recognized internationally for its proficient contribution to the understanding of the neuromuscular system, from disease characterization to understanding and treatment. The team is well funded and actively involved in high-profile national and international networks. It is very attractive (organization of international meetings, recognized preclinical modeling platform). Moreover, the team has a prolific and high-quality scientific output, and its activities contribute to society (public-private collaboration, public outreach in particular linked to AFM).

Strengths and possibilities linked to the context

This translational research team brings together various specialties and expertise related to the neuromuscular system, encompassing disease characterization, understanding, and treatment. It has been highly successful in raising financial support from national and international sources (e.g. AFM, Horizon 2020, ANR, FRM, ANRS, US Dept of Defense, NIH-NIAMS) to develop their projects (19.5M€ since 2018).

The team is very attractive on several levels. It has a strong involvement in numerous national (e.g. Filnemus neuromuscular disease network) and international (e.g. RENOIR, MAGIC, ORTHOUNION, and MAXIBONE European consortiums) networks. The team has also organized major meetings in the field (e.g. EMBO muscle meeting, Paris, 2022), as well as a series of French-Japanese and French-Hong Kong meetings. In addition, the team has developed an advanced organization to provide best possible welcome for collaborators for short or long stays, including colleagues from international Universities (1-5 days), students and post-docs for collaborations or training (1-16 weeks). This includes in particular assistance with their settling in France, and, for those joining for experiments, with training and guidance during their stay in the laboratory. Finally, the team has access to recognized unique structures and technological skills. In particular, at Alfort National Veterinary School, the team has actively contributed to develop a unique preclinical modeling for Duchenne muscular dystrophy. This facility gives the team visibility for its neuromuscular expertise, enabling the development of an expanding network and collaborations with private partners wishing to test innovative treatments in these unique models.

The team has a highly prolific scientific production that led to decipher multiple mechanisms underlying neuromuscular and musculo-skeletal specification, development, growth, maintenance and function in physiological or pathogenic conditions, from molecular to systemic levels. During the evaluation period, they had 556 publications including 350 original articles. Among these publications, ~50% were signed as FLC. A significant amount of the latter was in high-profile journals (e.g. Nature, Science Translational Medicine, Cell Metablism, Cell Stem Cell (2), Nature Communications (3), Science Advances, Brain, eLife (3)).

Finally, the team shows an active inclusion in society. The team has established or is finalizing public-private collaboration contracts with several French (Encefa) or international (Audentes/Astellas, NTrans, Cytokinetics, and Pliant Therapeutics) companies. They are also involved in information to the public, through participation to a website and a video on bone augmentation repair enabling implant replacement, and regular commitment in the AFM's annual family and patient day, as well as in the "1000 chercheurs" initiatives, during which researchers talk to young people in secondary schools.

Weaknesses and risks linked to the context

The localization of the team on four different sites, although all either on the same campus (H Mondor hospital, Faculty of Medicine, and Etablissement Français du Sang) or at 15 min Metro distance (Alfort National Veterinarian School), is challenging for its management.

The self-assessment report of the team highlighted the need for more supporting staff, administrative support, and working space for such a large team. In particular, the lack of space induces a very dense use of lab space creating difficulties of organization and generating internal tensions with space sharing.

Analysis of the team's trajectory

The team's success over the evaluation period in terms of scientific output, impact within the biomedical community and funding clearly indicates that it will continue to excel in these areas over the coming years. The team's proposed trajectory is convincing and coherent.

The team has significantly grown since its establishment in 2015, going from 70 members to more than 100, and after extensive internal discussions, they have collectively made the decision to reorganize the team into four distinct groups (one will leave in 2025). The team MUSE (directed by Frederic Relaix), MUSKETHER, and StemRepairNF will undergo evaluation for independent establishment by 2026. In addition, a group will relocate in another Institute to start an independent research team. This restructuring is meant to improve several aspects. While conserving a huge size, smaller teams should face less administrative difficulties and have more possibilities of research funding as some grant providers limit the number of projects funded per team. In addition, this reorganization should provide a better consideration of its specific needs and contributions from the institutions for each individual team.

The team MUSE proposes to be structured into six groups, three of them emerging from the current group led by the team leader, two of them already existing, and one joining from another team (team Ghaleh). Some of the groups will be led by young and promising researchers who will assume key responsibilities. This reorganization will also contribute to a well-balanced distribution of responsibilities in terms of gender equity (four men and five women will be group leaders or co-leaders).

The team MUSE will develop three main research axis (Fundamental research in muscle biology and stem cells, Preclinical modelling and innovative therapies) in interaction with each other. A first axis in fundamental research in muscle biology and stem cells will explore the heterogeneity of skeletal muscle stem cells, focusing on molecular and epigenetic regulation at the single-cell level. The second axis focused on preclinical modelling will be developed to characterize and manipulate trajectories of muscle diseases. The third axis will establish and validate innovative therapies, including cell, gene, and pharmacotherapy, by combining the knowledge generated in the team with basic investigations of muscle stem cells and repair through public-private partnerships.

RECOMMENDATIONS TO THE TEAM

Overall, the team should continue with outstanding production and activities.

Following the reorganization of the team, the Committee recommends that strong links and collaboration should be maintained between the four teams emerging from the current Relaix team to continue to benefit from their strong complementary expertise in the field of the neuromuscular system.

Team 14: Pathophysiology of glomerular diseases

Name of the supervisor: Mr Dil Sahali

THEMES OF THE TEAM

The main focus of the team is the study of human glomerular diseases, one of the leading causes of chronic kidney disease and end stage renal disease in the world. There are two main axes around idiopathic nephrotic syndrome (axis 1) and nephro-oncology, a new area of clinical, translational, and fundamental research, as well as educational training in close collaboration with the Oncology Departments (axis 2). Axis 1 focused on the immunopathological mechanisms of glomerular diseases, for example the Cmaf inducing protein (CMIP), a major adaptor of signaling pathways involved in Idiopathic Nephrotic Syndrome (INS) pathogenesis, which is induced both in lymphocytes and podocytes of INS patients). The team is also exploring the immuno-pathogenic link between environmental stress (infection, pollution) and relapses of INS, encompassing the role of T and B cells, as well as the search for diagnostic and predictive biomarkers of INS relapses in blood plasma, with a particular focus on proteomics and lipidomics. Axis 2 aims to understand the pathogenic mechanisms underlying glomerular diseases induced by oncology targeted therapies, at the cellular and molecular level, including, but not limited to, thrombotic microangiopathy induced by Gemcitabine and VEGF/VEGFR inhibitors.

Within Axis 1, the team coordinates the National Reference Centre for Idiopathic Nephrotic Syndrome and has access to the associated cohorts of patients and biobanks, and received a label extension (2023-2028) from the French Ministry of Health. Within Axis 2, the team has been labelled as a new rare research discipline by the French Ministry of Education, Research and Innovation (2022).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report highlighted the high quality translational research of this team. As recommended, the team has developed and made an effort to improve the preclinical production, allowing more "non-clinical" publications with basic-translational research publications in high-profile journals (J Autoimmunity, Cellular and Molecular Immunology, Kidney International, Clinical and Translational Medicine). The added value of young recruits was developed. Unfortunately, a PI in the NephroOncology research program, who had led to several important publications, left the team for personal reasons.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	4
Maitres de conférences et assimilés	4
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**13**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	3
Sous-total personnels non permanents en activité	**5**
Total personnels	**18**

EVALUATION

Overall assessment of the team

The team is excellent with respect to the quality of its scientific production, despite a limited number of publications in generalist journals, its international visibility as a leading group in the field of glomerular diseases and translational studies. A strength of the team is the close partnership with clinicians and development/access of/to several biobanks. The team developed an innovative program on nephro-oncology. The team coordinates the National Reference Center for Rare Disease Idiopathic Nephrotic Syndrome and has been labelled as a new rare research discipline. The team has secured more than 2M euros since 2018 through continuous financial support from several agencies in addition to recurrent funds associated with the National Reference Center and the host institutions, and the SATT erganeo. Two patents have been filled.

Strengths and possibilities linked to the context

A main strength is the expertise in glomerular diseases with several important outputs in term of candidate gene identification/validation and novel therapeutic targeting approaches, as well as the coordination of the National Reference Center for Rare Disease Idiopathic Nephrotic Syndrome, that includes five French nephrology departments.

Grants raised as PI (1600 K€) are mostly provided by the PHRC RIFIREINS (750 K€), then by foundations, network activities, regional calls.

A second major achievement is innovative development regarding nephro-oncology with i) the de novo research group in the team focused on the cellular and molecular mechanisms underlying these renal complications, ii) educational teaching activities with creation of a university degree since 2020 with 30% of trained nephrologists from foreign countries, iii) establishment of specific care for these patients (dedicated consultations, creation of multidisciplinary NephroOncology meetings). The team is well integrated in national and international networks facilitating research collaborations.

Thirteen PhD students have been trained (ending or starting during the evaluation period) (seven women and six men).

The team members have strong commitment with patients and clinical duties as well as strong commitment with patients and major academic responsibilities.

Team members have published 100 original articles (51% in major positions) and 68 reviews.

Publications as PI are most often in specialized journals: (J Autoimmunity, Cellular and Molecular Immunology, Kidney International, Clinical and Translational Medicine, Am J Kidney disease, Am J Transplant, J Am Soc Nephrol) although not limited to kidney disease: Br J Haematol, J Cachexia Sarcopenia Muscle.

Two patents have been filled during the past contract. One is related to innovative therapeutic approaches based on targeted nano-interference using nanocapsules carrying miRNA-coding DNA, in collaboration with the Institut de Chimie des Matériaux Paris Est (CNRS/UPEC, Thiais).

Team members contribute to the coordination of the "Association de Malades atteints de syndrome néphrotique", to a network of the "Fondation Maladies Rares".

One member has a Youtube channel and one other member coordinates the program “apprentis chercheurs” of the UPEC.

Weaknesses and risks linked to the context

Funding for preclinical studies were limited. No ANR/PIA/European supports have been obtained. This limited the recruitment of postdocs and the increase in manpower dedicated to basic/translational research.

Scientific production covered basic, translational and clinical works but publications in generalist journals are lacking.

There is no implication of team members in 1) administrative and collective duties, 2) European or international consortia. Only few participations in scientific organizations (European Rare Kidney disease network (ERKNet), member immune glomerulopathies working group committee since 2016; ERA-EDTA scientific committee since 2012), 4) few meeting' organization (French rare disease network).

A risk for the next contract period is the inability to pursue immunological studies in the new team they will integrate (Sickle Cell Diseases and Hemolysis), which was a previous expertise of the team.

Analysis of the team's trajectory

Not relevant, as the current team did not propose a new project. The team will merge with another PI´s team and will focus on Sickle cell Diseases & Hemolysis with the goal to understand mechanisms of renal toxicity.

RECOMMENDATIONS TO THE TEAM

In order to integrate in a new team, the team is recommended to further explore mechanisms of increased oxidative stress and mitochondrial dysfunction triggering autophagy. Moreover, the role of the immune system in renal toxicity should not be omitted.

The unit Dynamic

Team 15:	Dynamics of microbial interactions within microbiota: its consequences on colonization, infection, therapeutics and resistance to anti-infective drugs in humans and animals
Name of the supervisor:	Ms Françoise Botterel

Team 15 is formed from the merging of the unit Dynamic (UPEC).

THEMES OF THE TEAM

The main objective of the team is to study microbial interactions within the microbiota of humans and animals, and their consequences on colonization, infections, treatments, and the development of drug resistance. The team addresses issues related to infectious agents that emerge in both medical and veterinary environments.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The Dynamyc team took seriously the previous recommendations. Efforts were made to reinforce the PI expertise as editor in specialized journals. In terms of teaching, team members have been highly involved since 2021 (Licence 2, 3 Sciences pour la Vie). In 2023, the team launched a new One Health Master's program (directed by F. Botterel). In term of PhD supervision and national collaborations, significant efforts were also made. For instance, F. Botterel was awarded an ANR grant as PI, collaborating with three other national teams.

The team attractiveness was improved with the recruitment of foreign post-doc/researcher.

Regarding the research project, substantial efforts have been made in fundamental research. Concerning studies on microbiota (WP1), the team generated substantial amounts of data that nevertheless remained quite descriptive. For the epidemiology section of azole resistance, the team has considered the feedback from the previous term, notably by including (1) a study on azole-resistant A. fumigatus isolated in France (WP1) and a research activity on spontaneous models of diseases in wildlife, i.e. aspergillosis in captive birds (WP4).

One of the weaknesses of the team remains its international visibility (limited international collaborations). As already suggested in the previous term, organizing seminars with international speakers could be a way to foster collaborations.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maitres de conférences et assimilés	8
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	8
Sous-total personnels permanents en activité	**19**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	7
Sous-total personnels non permanents en activité	**11**
Total personnels	**30**

Global Assessment of the unit Dynamic

DYNAMYC is a small unit (30 people) headed by Françoise Botterel and under the supervision of UPEC. The unit focuses its research on the study of microbial interactions within the human and animal microbiota, their consequences on colonisation, infections, treatments and the development of drug resistance. The team addresses issues related to infectious agents emerging in the medical and veterinary environment, particularly in the context of fungal infections.

The DYNAMYC unit has produced excellent scientific output over the period, with 117 publications as principal investigator in very good specialist journals (Emerg Microbes infect, J Antimicrob Agents, Clin Microb Infect, Nat Comm, etc.).

The unit has demonstrated an excellent ability to raise funds, totalling €3.5M over the period evaluated, from national (DGOS, PHRC-N, several ANR, ANRS, etc.) and regional (MVT Regional Centre) sources. The team has also been awarded a DIM1Helath Chair of Excellence in 2020.

The unit's members are recognised by their peers, in particular through awards such as the Palmes Académiques and the Légion d'Honneur.

DYNAMYC's research activities are well integrated into society, with collaborations with a number of industrial companies such as MSD, Pfizer, Astellas and Elanco. Members of the unit are involved in drafting national and international recommendations in bacteriology, mycology and infectious diseases. One patent was registered during the period.

Members of the unit are involved in disseminating their research to the public through their activities on social networks, meeting patients and their families (Vaincre la mucoviscidose) and promoting their profession among young people. They also take part in interviews on national television (France 2 and France 3), on the radio and in the press (Le Monde, l'express).

EVALUATION

Overall assessment of the team

The overall assessment of the team is excellent. Dynamyc sets relevant objectives in both the clinical and veterinary fields. The team offers a continuum from preclinical and clinical research to fundamental research. Team members are actively involved in teaching and PhD supervision. The team also increased its attractiveness and visibility. The Director of the team played a key role in these efforts. The main issue lies in the lack of cohesion between the research projects, particularly the microbiology section.

Strengths and possibilities linked to the context

The “Equipe d’Accueil” Dynamyc is a university team (UPEC), officially recognized in 2015 and renewed in 2020. The team is led by Pr Françoise Botterel.

The scientific objectives of the team are relevant in the context of fungi infections and anti-microbial resistance. To conduct the project, the team encompassed veterinary and human mycologists, as well as hygienists, bacteriologists, and infectiologists from hospitals, specialized in human infectious diseases. They use original and innovative multidisciplinary approaches. The team evolves in an excellent regional environment. Due to the diverse expertise of team members, the team has multiple regional connexions/collaborations: CHIC, CHIV, Reference Center for tick-borne diseases Nord/Paris, Parc zoologique de Paris, Ménagerie du jardin des plantes, iEES… Additionally, they have access to different core facilities/equipments: NGS (GenoBioMics), imaging, genomic, mass spectrometry…

The team is well organized and managed. The director is assisted by two deputy directors. The executive team is also composed of HAL and webmasters’ referents. The team has a laboratory council composed of all researchers, the research engineer and a representative of each staff category (students and PH). The laboratory council assisted the Director to make final decisions (finance, recruitment, project progress…). The scientific policy of Dynamyc is discussed during these meetings (four/year). A general assembly is also held once a year. Moreover, despite the intensive hospital responsibilities of a significant number of the team members, weekly meetings for students and senior staff are organized.

The team is also highly dedicated to support the well-being and working conditions of its employees and places a strong emphasis on health, safety, and the prevention of psychosocial risks (one health/safety referent). *The team also adhere* to the principles and standards of *scientific integrity*.

Regarding resources, apart from the recurring fundings (UPEC, EnvA, Anses), the team members have secured external funding from various sources during the last five years (3.5 M€ in total): (1) PI of national grants DGOS, PHRC-N, ANR (GASP), SPILF or VLM or partners of ANR (CO-PROTEC), ANRS, SPILF or VLM grants. (2) PI and co-PI in regional grants, *e.g.* Centre regional MVT. The team also obtained one Chaire d'Excellence DIM1Health in 2020. Additional fundings were also obtained from pharma compagnies such as MSD or Pfizer.

Over the past five years, the team expanded with the arrival of one MCF and one MCUPH in 2023 and several PH, AHU and non-permanent staff. The team was strongly involved in training through research and hosted twelve PhDs (seven still ongoing) and 17 Master students. According to the report, the team also recruited six post-docs and thanks to funding, the team also recruited one non-permanent IR and five technicians. The team also hosted a guest researcher with Chair of excellence (One Health DIM).

Regarding teaching, the team provides very good training to post-graduate students. Team members have in charge a DIU since 2019 and more recently (2023/2024), a One Health Master degree (UPEC/EnvA). The originality of this master's program lies in its extensive focus on human and social sciences, a feature not found in any other program in France.

Over the past five years, the team has boosted its national/international visibility by for example developing a "French multicenter research into the diagnostic and therapeutic management of filamentous fungal infections" or being invited or participated (as speakers) to national/international conferences. National visibility has also improved, particularly with the acquisition of national funding such as ANR (*e.g.* ANR GASP).

The scientific objectives of the team are relevant. The team focused on bacteria and filamentous fungi. In this context, the major pathogens studied were *Aspergillus fumigatus* and *Stenotrophomonas maltophilia*. Dynamic has three major aims: (1) – Understanding the place of these microbes in respiratory and intestinal microbiota, (2) – Dissecting the interactions between the pathogens (in biofilms) and also with host cells, mainly respiratory epithelial cells, at a molecular and cellular level and (3) – Evaluating the emergence of resistance. This work is part of the "Urban One Health" approach. Studying antibiotic/antifungal resistance through the interaction between *A. fumigatus* and *S. maltophilia* in the biofilm phase, is highly relevant in the natural niche of these two organisms in the respiratory system.

Over the last five years, substantial data were obtained in each WP. Some of them have been published and others are in the process of submission or review (WP1).

Significant progress was made in WP2 concerning both microbial interaction and their interaction *in vitro* with airway epithelial cells, with a particular interest in the role of GAG. In WP3, the team continued its research on azole-resistant *Aspergillus* species, a global health problem, developing an in vivo model of infection using *Galleria mellonella* larvae. They also evaluate the risk of exposure to *Aspergillus* species (including resistant strains) in a Humboldt penguin colony (WP4).

The vast majority of their publications are related to their hospital activities. Nevertheless, key results were published as original articles in very good peer-reviewed journals (117 original articles as first or last author), mainly specialized journals such as *Emerg Microbes Infect., J. Antimicrob Agents, J Antimicrob Chemother., Antimicrob Agents Chemother., Clin Microb Infect., J Clin Med., Clin Infect Dis* and some in more general ones: *Frontiers in -Microbiol, –Immunol or - Cell Infect Microbiol, Plos One* or *Nat Comm*. Team members have also published in other formats (reviews, guidelines…) (42 other types). PhD students contribute to 75 publications, with 28 as first/last authors. Each PhD student had at least one publication by the time of their defense.

Team members participate as invited speakers, to national and international conferences (total of 94).

Thanks to their participation in scientific committees (*SFMM, ISHAM, CPIAS, SF2H…*), some team members are highly involved in the organization of scientific days in France (*Lyon, Rouen, Lille*) or abroad (*ISHAM in Amsterdam and Delhi*).

Although team members do not seem to engage significantly in peer reviewing or scientific project evaluation, they are actively involved as editors.

The national visibility of the team leader and one of the co-leaders has also been recognized through the awarding of distinctions (palmes académiques/légion d'honneur).

Dynamyc has a long-lasting collaboration with pharmaceutical companies (MSD, Astellas, Elanco…) and could secure funding. Members also published many book chapters for French physicians and veterinarians and play an active role in writing national/international recommendations in bacteriology, mycology and infectious diseases.

Team members are highly involved in disseminating their research with the general public: they are active on social media, attend conferences where they meet patients and their families (e.g. Vaincre la mucoviscidose) and promote their professions to younger audiences. They participate in TV programs (*e.g.* France 2 et 3), radio broadcasts and are featured in the press (*e.g.* le Monde, l'express).

Weaknesses and risks linked to the context

Few international collaborations.

Regarding the scientific project, the link between the three objectives in WP1 – (i) bacteria/*Aspergillus* sp., (ii) Ec-BLSE and (iii) *Enterococcus faecalis*, remains somewhat unclear. More generally, it is difficult to establish a connection between the studies on fungi (+/– bacteria) and those on other bacterial agents.

The proportion of original research articles with team members as last authors is quite low (23%) compared to those published in partnership. Additionally, there is room for improvement in publishing in high-profile journals.

Despite their strong collaboration with pharmaceutical companies, the number of Cifre program is very limited. The team has also the potential to improve their consulting/expertise activities.

The team likely faces challenges due to the absence of permanent full-time researchers.

Analysis of the team's trajectory

For the next term, the Dynamic' team will join Pr Pawlotsky's team. The mycologists and hygienists will form a new group called RESTART, while the bacteriologists will create a group called DREAM. The veterinarians will join a team at Alfort Veterinary school.

The RESTART group will continue their research on Aspergillus fumigatus and Stenotrophomonas maltophilia. This is a logical progression of ongoing projects. Their main objective will be to gain a better understanding of the pathophysiological mechanisms involved in colonization and infection by these opportunistic pathogens in the respiratory tract to identify innovative therapeutic or preventive approaches.

The DREAM group will pursue their work on bacterial diversity, microevolution and antimicrobial resistance. In line with the current mandate, the team will focus on ESBL-C. *Coli* (WP1: bacterial resistance), Nocardia spp. and *Staphylococcus aureus* (WP2: bacterial evolution) and infective endocarditis (WP3: bacterial micro-diversity).

The split of the Dynamyc team into two groups, RESTART and DREAM, makes perfect sense given the research projects undertaken by each group. Each group has the expertise and the tools to carry out their respective projects.

RECOMMENDATIONS TO THE TEAM

A major risk in the trajectory is the integration of the DYNAMYC team, whose focus areas differ significantly from the "Virus, hepatology, cancer" team's current projects. There is little information regarding future plans to build cohesion in the new team.

Efforts should be sustained to (i) promote international collaborations to create opportunities for securing European and/or international funding and (ii) enhance their attractiveness.

Regarding the DREAM group, the low number of leaders with an HDR raises concerns about the attractiveness for young researchers. The team, whose leaders are only men, also appear to lack technical support for the next mandate. These observations raise questions about the group's organization and the future plans to continue their research activities.

The Unit TREPCA

Team 16: Therapeutic resistance in prostate cancer

Name of the supervisor: Mr Francis Vacherot

Team 16 is formed from the merging of the unit TREPCA (UPEC).

THEMES OF THE TEAM

The TRePCa research unit is an emerging research entity established on 2020. TRePCa conducts translational research on prostate cancer through a collaborative effort involving urologists, oncologists, and basic researchers. The primary focus of the unit is to identify biomarkers of prostate cancer aggressiveness, aiming to uncover factors associated with treatment response and resistance. Ultimately, their goal is to discover new therapeutic targets.

In this context, the team has identified biological markers for aggressive cancer groups and subgroups. They have also demonstrated that the secretome of different prostate cancer cell populations can enable tumor cells to evade immune surveillance and drive tumor heterogeneity and therapeutic resistance. Consequently, the unit has concentrated its research on the role of extracellular vesicles (EVs) in tumor progression and their potential as a source of biomarkers.

Since the Covid-19 pandemic, a new research direction has emerged to explore the role of EVs in SARS-CoV-2. TMPRSS2 is known to play a key role in tumor progression. Both TMPRSS2 and the androgen receptor (AR) are expressed in lung cell lines, and studies have shown that SARS-CoV-2 infection rates decrease when the AR pathway is previously blocked. These findings suggest an active role for AR in regulating TMPRSS2 expression and SARS-CoV-2 infection in lung cells. The team demonstrated the role of extracellular vesicles in SARS-CoV-2 infection. Recent studies indicate that prostate cancer patients are particularly vulnerable to SARS-CoV-2 infection, with a significantly higher risk of developing severe forms of Covid-19 and higher mortality rates compared to patients of the same age group with other cancer types. The ongoing work will enable further investigation into the relationship between prostate cancer and Covid-19.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The TRePCa research unit was established in January 2020 following the non-renewal of Team 7 IMRB – Inserm U955 during the 2018-2019 evaluation campaign.

The Hcéres committee highlighted the quality and expertise of the team in prostate cancer research and recommended refocusing research themes to enhance the visibility of publications while maintaining a translational approach as a key strength of the team.

As a result, the TRePCa team was formed on January 1, 2020, by members wishing to continue translational research on prostate cancer. It was established as an Emerging Research Unit at UPEC, focused on the study of therapeutic resistance in prostate cancer and, more specifically, on the involvement of extracellular vesicles in these processes.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

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

Post-doctorants	1
Doctorants	2
Sous-total personnels non permanents en activité	**4**
Total personnels	**11**

Global Assessment of the unit TREPCA

TREPCA is a small unit under the supervision of UPEC and created in 2020 following the non-renewal of IMRB team 7 during the previous evaluation. It is based at the UPEC Faculty of Health and was directed by Francis Vacherot. The unit conducts translational research on prostate cancer with a view to identifying markers of the aggressiveness of these cancers, as well as factors associated with response to and resistance to treatment. In particular, they are focusing on the role of extracellular vesicles in tumour progression and their use as biomarkers.

The unit is recognised nationally and internationally for its expertise in prostate cancer research. During the period under evaluation, the unit's scientific output was very good, with 38 publications in high-quality journals (Eur Urol, Br J Cancer, J Extracell Vesicles, etc.). However, the number of articles in which members of the unit are main contributors remains low (5). The unit has obtained total funding of €435k from national funding (INCa) and foundations (Ligue contre le cancer). However, there has been no larger-scale funding of the ANR or European type.

TREPCA's research activities are well integrated into society, in particular through several collaborations with pharmaceutical companies (Janssen, Astellas, Imutec) totalling €153k. There were no patents during the period. The members of the unit are committed to disseminating their results to the public, in particular through initiatives such as the Apprentis chercheurs, patient information through the Ligue contre le Cancer and Les Entreprises contre le cancer.

EVALUATION

Overall assessment of the team

The overall quality of the team is very good. Although small in size, the team is well-recognized and adequately funded. The team's scientific activities foster significant involvement from all members in training and scientific publications, including the youngest researchers. Everyone benefits from the team's collective funding, which helps to develop new research topics. However, the number of publications as primary contributors needs improvement, as does the team's societal engagement (interactions with the private sector, patents, and contributions to the general public).

Strengths and possibilities linked to the context

Prostate cancer (PCa) remains a significant cause of cancer-related deaths in men worldwide. Trepca team is uniquely positioned due to its focus on extracellular vesicles and therapeutic resistance in PCa, with limited competition from major institutes like Institut Curie and Gustave Roussy.

The team consists of seven permanent members, two PhD students, and a post-doctoral researcher. While small in size by design to encourage collaboration, the team has allowed PhD students to engage in impactful research and publish as first authors. It supports staff training in specialized areas, regularly attending national and international conferences and workshops.

Regular team meetings every two weeks ensure smooth project management, while quarterly board meetings address strategic planning, including financial, recruitment, and publication goals. Doctoral student supervision has been strengthened through dedicated training for mentors, improving thesis management and student support.

The development of prospective cohorts of patient in collaboration with clinicians and pathologists at Henri Mondor Hospital enable the identification of new biomarkers for disease progression and therapeutic resistance.

The team is well-equipped for cell culture, tissue analysis, molecular studies, isolation and characterization of EVs and benefits from access to platforms of IMRB.

During the period, the team successfully secured over 435k€ in funding from institutional and industrial sources (INCa, Cancer League, Jansen, Astellas...) demonstrating its capability to secure financial support. Funding is pooled to support the team's collaborative approach, enabling exploration of new hypotheses, preliminary experiments, and grant applications. This approach led to significant discoveries, such as the role of extracellular vesicles in SARS-CoV-2 infection, which originated from unfunded exploratory work.

TrepCa team is nationally and internationally recognized for its expertise in prostate cancer research. The team benefits from the extensive experience of key members and collaborates with numerous prestigious institutions, both nationally and internationally. Members are actively involved in scientific committees, grant evaluations, editorial boards, and professional associations. During the period, the team published 38 peer-reviewed articles in high quality journals (Eur Urol, Br J Cancer, J Extracell Vesicles), demonstrating a solid output relative to its size. All PhD students have contributed to publications, with two recently graduated PhD students publishing as first authors. Current students are already co-authors on team papers.

Over the past three years, the team has developed several collaborations with pharmaceutical companies (153k€ from Janssen, Astellas, Imutec).

The unit is committed to sharing its results with social, economic, and cultural actors. Team's members are active in disseminating' knowledge about prostate cancer (Apprentis Chercheurs, Ligue contre le cancer, Les entreprises contre le cancer).

Weaknesses and risks linked to the context

The team is small, and most researchers also have teaching and clinical responsibilities, which limits the time dedicated to research and creates the need to strengthen the team with full-time researchers.

The publication activity is reasonable considering the size of the team. However, the number of articles signed by team members as primary contributors (first authors, last authors, or corresponding authors) remains relatively low compared to the total number of publications (5/38).

The level of funding is limited and would need to be expanded, particularly through national and European funding calls such as ANR, INCA, and Horizon 2020.

Furthermore, while the team has developed several collaborations with pharmaceutical companies over the past three years, interactions with the socio-economic world and the general public remain limited. Additionally, discoveries have not yet been transferred to patents.

Analysis of the team's trajectory

A new team (STORM-MI team) will be built to gather the Trepca's team, the former CHIPI team of A. Boissonnas from the CIMI unit who will join the IMRB for the next mandate with expertise in the study of the dynamic of the myeloid system in health and disease and the Molecular Onco-Hematology Laboratory with expertise in myeloid malignancies.

Environmental aggressions (air pollution, chemical perturbators and infectious diseases) lead to increased inflammatory diseases, neoplastic transformation and infections and are strengthened by an unavoidable aging of the body.

The new team gathers different scientific backgrounds with high complementarity to investigate different aspects of the macrophage system.

1. The spatio-temporal dynamic of the MP response to environmental perturbations
2. The genetic and epigenetic alterations and regulation affecting the myeloid compartment
3. The secretome involved in cell communication and activation.

Three main axes will be developed:
1) Understanding basic biology of the MP dynamic in response to environmental perturbations with focus on the dynamic behavior of monocytes and macrophages in cancer, inflammatory, and infectious contexts. The connection with leading clinicians and external medical services (e.g. Gustave Roussy and Pitié Salpêtrière) will provide access to high-quality patient samples and facilitate the application of findings from in vivo models to human biology. Collaborative efforts will focus on how cancer-derived EVs influence macrophage activation, particularly in prostate and lung cancers, as well as their role in SARS-CoV-2 infections.

2) Molecular genomic and epigenetic characterization for the identification of specific biomarkers. The team will focus on deciphering the biological mechanisms underlying myeloid responses in various pathological contexts and their potential as biomarkers for disease prognosis and severity. The team's expertise in myeloid biology, genomic technologies, and translational research positions them to advance the understanding of myeloid responses in both liquid and solid malignancies, infectious diseases, and inflammatory conditions. This work lays the groundwork for identifying robust biomarkers and therapeutic targets.
3) Therapeutic intervention through the immunomodulation of the MPs. The final ambition of this research program is to propose a therapeutic solution based on the immunomodulation of the MPs.

RECOMMENDATIONS TO THE TEAM

The projects designed for the STORM-MI team are extremely ambitious. This new multidisciplinary team will benefit from additional expertise and foster the emergence of new research themes. It is important for members of the former TRePCa team to showcase their skills and develop their own projects within this larger group. Additionally, it is crucial to finalize ongoing projects and leverage the results.

Furthermore, the effective human resource management observed within the TRePCa's team, which appears to be of high quality, should serve as an inspiration for the new team. This is particularly important to ensure that younger researchers and PhD students can highlight their work, actively participate in scientific activities, and thrive in an environment that promotes genuine professional growth.

The Unit
EPIDERME

Team 17: Epidemiology in Dermatology and Evaluation of therapeutics

Name of the supervisor: Ms Emilie Sbidian

Team 17 is formed from the merging of the unit Epiderme (UPEC).

THEMES OF THE TEAM

The team focuses on assessing drug efficacy and detection of adverse events, using the power of worldwide clinical databases of patients suffering from immune-mediated inflammatory disorders (IMIDs). Targeted drugs have been developed for these diseases but concerns remain about safety. Randomized controlled trials are crucial for assessing drug efficacy and safety, but due to limited follow-ups and populations they should be complemented by real-world data from large databases capturing broader patient spectra. The team aims to optimize therapeutic strategies for IMIDs by integrating big data from administrative databases, clinical cohorts, and published studies, to provide evidence-based guidance and improve treatment outcomes.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

All recommendations made during the previous term were implemented.

- Since the previous evaluation, the team has recruited four post-doc students, one Prof Junior in biostatistics discharged from teaching, an associate professor in epidemiology and an associate professor in rehabilitation sciences. The team has also recruited a permanent PhD research engineer and four non-permanent engineers.
- The team has created, developed and licensed a decision-making tool (Décitox) dedicated to drug-related skin adverse event and imputability which helps clinicians in their daily practice.
- Since 2018, eleven PhD were defended, including two international co-supervision. Currently, nine PhD are members of the team (three in the previous contract), with two out of nine international co-supervision (Lebanon) and three out of nine extra foreign students (Lebanon and Vietnam).
- The achievements of the team and the coherence of its research program with the IMRB highlighted by the several collaborations motivated the team to candidate to integrate the IMRB.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	7
Maitres de conférences et assimilés	3
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	9
Sous-total personnels permanents en activité	**19**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	9
Sous-total personnels non permanents en activité	**12**
Total personnels	**31**

Global Assessment of the unit EPIDERME

EPIDERME is a small unit (30 people) headed by Emilie Sbidian and under the supervision of UPEC. The unit focuses its research on evaluating the efficacy of drug molecules and their adverse effects, using international clinical databases of patients suffering from inflammatory autoimmune diseases. Its aim is to optimise therapeutic strategies for these diseases by integrating 'big data' from administrative databases, clinical cohorts and published studies, in order to provide evidence-based advice and improve treatment outcomes. During the evaluation period, the unit increased in size from 9 to 22 members.

The originality of the research program and methodological approaches, as well as access to large cohorts, considerable expertise in the analysis of big data and strong collaboration between clinicians and epidemiologists, are key assets for the development of the unit's research program. Overall, during the period under evaluation, EPIDERME's scientific output was excellent to exceptional, with over 300 articles in prestigious journals (NEJM, Lancet Public Health, JAMA, Dermatol, etc.).

The unit's members are nationally and internationally recognised as experts in the fields of epidemiology and dermatology, making them highly attractive to students and researchers. The unit has been highly successful in competitive calls for projects totaling €3.2M. This funding comes from national academic agencies (PHRC-N, PHRC-K, ANR, Health Data Hub, Inserm) for a total of €1.5M, national agencies (ANSM, €558k), local authorities (Erganeo, €43k) and foundations (SFD, SFR, FIMARAD; €386k).

The integration of EPIDERME's research activities into society is quite excellent, with collaborations with several companies such as Pleas'Com, with whom the unit has developed the 'Decitox' medical application for identifying toxidermia to be reported to pharmacovigilance. This tool has been registered with the French agency for the protection of programs. They have also set up a collaboration with the start-up Scientalab to identify patients suffering from an inflammatory autoimmune disease at the AP-HP. No patents were filed during the period, but the Decitox application was filed with the program protection agency.

The unit has benefited from high national visibility, notably through interviews in leading national media (Le Figaro, Femme actuelle, Ouest France, TF1, etc.).

EVALUATION

Overall assessment of the team

The overall assessment of the team is excellent to outstanding. The team has published more than 300 papers since 2018, including publications in high-profile journals (NEJM, Lancet Public Health…). The team has successfully obtained grants from national agencies, local authorities, and partnership with industry. In total, the team has obtained 3.2 M€ since 2018. The team size has increased since 2018 from nine to 22 members and has trained eleven PhD students. Team members have gained a great national visibility as demonstrated by regular public interviews in large audience media.

Strengths and possibilities linked to the context

The team has an excellent publication record with more than 300 papers published since 2018, including publications in high ranked journals such as NEJM, Lancet Public Health, Lancet Regional Health-Europe, JAMA Dermatol, JAAD, BJD, JID…

The team size has substantially increased since 2018 from nine to 22 members. It includes one full-time researcher, eleven teaching researchers (MCF/MCU-PH/PU-PH/Pr) among which five with the habilitation to conduct research, one engineer (PhD, 1 APHP), two hospital physicians, four biostatisticians and two post-docs.

The team presents with very good interdisciplinary skills. Out of the fifteen permanent members, six are dermatologists (40%), three pharmacologists, two rheumatologists and four epidemiologists.

The originality of the research program and the methodological approaches as well as the access to large cohorts, the strong expertise in massive data analyses, and the strong collaboration between clinicians and epidemiologists are key assets for the development of the research program.

The team has successfully obtained grants to develop the scientific objectives from national academic contracts (PHRC-N, PHRC-K, ANR, Health Data Hub, Inserm; 1,552 k€), and from national agencies (ANSM; 558k€),

local authorities (Erganeo; 43 k€) and national societies (SFD, SFR, FIMARAD; 386 k€). The team has also developed partnership with industry to support a national cohort of patients with vitiligo (Pfizer; 250 k€, Incyte 420 k€). In total, the team has obtained 3,249 k€ since 2018. The team as developed fruitful collaborations with SMEs: In collaboration with Please'Com, they have developed a medical application called 'Decitox' and the team as collaborated with a startup called Scientalab (French deeptech company) for the MAIIA project aiming to identify IMID patients within the AP-HP's warehouse.

The team has developed and use massive data of complementary sources, mostly already available data, covering the wide spectrum of patients with IMIDS, such as medico-administrative insurance database as well as already published data or national cohort. These databases can be used to set up new projects.

The team has successfully trained eleven PhD students from 2018 to 2023, and nine PhD students are currently enrolled in the team.

The team and its members are nationally and international recognized experts in the fields of epidemiology and dermatology leading to a strong attractiveness for students and researchers. The team has gained a great national visibility as demonstrated by regular public interviews of its members in large audience media such as 'Le Figaro', 'Femme actuelle', 'Ouest France', 'Doctissimo', 'France Inter', 'Europe 1', 'France culture' and 'TF1'.

Weaknesses and risks linked to the context

The team location outside of the Health Faculty of Paris-Est Creteil University is a weakness. Joining IMRB for the next mandate will help foster interactions with other teams of the IMRB.

The difficulty to recruit and retain data scientist positions over the long term due to the competition with the private sector is an issue. The team failed to obtain European grants as PI so far, and efforts should be made in that direction. Collaborations with industries could be reinforced as well as patient association involvement in the team research projects.

Analysis of the team's trajectory

The research team is focusing on improving treatment strategies for IMIDs. They've observed that drug persistence decreases over time due to inefficacy or side effects, and the prevalence of IMIDs is continuously rising. Their primary goal is to shift from an empirical approach to a data-driven, personalized treatment model. This involves:

- Analyzing predictive factors for drug efficacy and safety
- Tracking the growing number of targeted therapies
- Involving patients in the research process to leverage their experiential knowledge
-

The team has recently strengthened its research capacity by recruiting a research engineer specializing in meta-analyses and by bringing on a junior professor focused on statistical methods for determining causal effects.

The team is planning to hire another research engineer for pharmaco-epidemiological projects.

For the upcoming mandate, they will rename their team to focus on epidemiology and evaluation of therapeutics in IMID and structure their research around three key axes:

- Axis 1: Drug efficacy and therapeutic strategies
- Axis 2: Detecting adverse drug events and risk factors
- Axis 3: Identifying design and reporting issues in primary research and evidence synthesis.

The research team is closely aligned with the three main axes of the IMRB:

1. Environmental Stresses and Infections (Axis I):
- The team will initiate a project examining air pollution's impact on IMID severity in collaboration with the Lanone team
2. Vulnerabilities, Aging, and Mental Health (Axis II), collaboration with the Canoui-Poitrine team
- Working on therapy access for specific populations (elderly, women, those with comorbidities) in IMIDs and cancer
- Studying the prevalence of psychotic disorders n IMID patients to explore potential immune system connections
3. Biotherapies, Health Tools, and Prevention (Axis III) in collaboration with the Cohen team.

RECOMMENDATIONS TO THE TEAM

The main recommendation would be to maintain the team's current level of excellence in terms of funding and publications. The multidisciplinary approach of the projects has allowed the team international recognition and must be maintained across the proposed research axes. The high scientific quality of the team should prompt the researchers to apply for competitive European research calls.

To help develop the research program, the team should strengthen the link with patient's associations.

Finally, joining IMRB should foster collaborative opportunities and help bridge basic and clinical epidemiological research.

CONDUCT OF THE INTERVIEWS

Dates

Start: 04 December 2024 at 09:00

End: 06 December 2024 at 16:30

Interview conducted: on-site

INTERVIEW SCHEDULE

Day before the interview: 3rd of December 2024

18h00 **Arrival of the committee at the hotel**
19h30 **Work dinner with all members of the committee**

Interview day 1: 4th of December 2024
8h50 at the IMRB gate, 8 rue du général Sarrail, 94000 Créteil

9h00 – 9h10 **Hcéres committee welcome**
Room: amphitheater A2

9h10 – 9h30 **Hcéres committee meeting**
Room: amphitheater A2
Closed-door meeting

9h35 – 9h40 **Hcéres rules and procedures by J. Dutrieux**
Room: amphitheater A2
Public session (all unit members)

9h40 – 10h40 **Administrative and scientific presentation of the unit's achievements and future by J. Boczkowski and C. Combadière**
40min presentation
20min discussion
Room: amphitheater A2
Public session (all unit members)

10h40 – 11h00 **Committee debriefing and coffee break**
Room: amphitheater A2
Closed-door meeting

Teams audition #1 *Public session (15min presentation + 15 min discussion)*			
Time	**Room**	**Team Number**	**Presentation by**
11h00 – 11h30	amphitheater A2	**SENCODE**	**G. Derumeaux**
11h35 – 12h05	amphitheater A2	**TREPCA**	**F. Vacherot**
12h10 – 12h40	amphitheater A2	**STORM-MI**	**A. Boissonas**
12h45 – 13h15	amphitheater A2	**I-Biot**	**J. Cohen**

13h15 – 14h25 **Lunch break and committee debriefing**
Room: 314 (3rd floor)
Closed-door meeting

Teams audition #2 *Public session (15min presentation + 15 min discussion)*			
Time	**Room**	**Team Number**	**Presentation by**
14h30 – 15h00	amphitheater A2	**CEpiA**	**F. Canouï-Poitrine**
15h05 – 15h35	amphitheater A2	**BIOCRIT**	**A.Mekontso Dessap**
15h40 – 16h10	amphitheater A2	**TRACER**	**P. Remy**
16h15 – 16h45	amphitheater A2	**Accelerates**	**V. Godot**

16h45 – 17h15 **Committee debriefing and coffee break**

Room: amphitheater A2

Closed-door meeting

Teams audition #3 *Public session (15min presentation + 15 min discussion)*			
Time	**Room**	**Team Number**	**Presentation by**
17h15 – 17h45	amphitheater A2	**PROTECT**	**B. Ghaleh**
17h50 – 18h20	amphitheater A2	**DYNAMIC**	**F. Botterel**

18h15 – 18h45 **Committee debriefing**

Room: amphitheater A2

Closed-door meeting

18h45 **End of day 1 Interview**

20h15 **Dinner**

Location: "Le Swan" restaurant (271 avenue Daumesnil, 75012 Paris)

Committee alone

Interview day 2: 5th of December 2024
8h50 at the IMRB gate, 8 rue du général Sarrail, 94000 Créteil

Teams audition #4 *Public session (15min presentation + 15 min discussion)*			
Time	**Room**	**Team Number**	**Presentation by**
9h00 – 9h30	amphitheater A2	**Translational Neuropsychiatry**	**S. Jamain**
9h35 – 10h05	amphitheater A2	**Physio. Glomerular Diseases**	**D. Sahali**
10h10 – 10h40	amphitheater A2	**DREAMS**	**P. Bartolucci**

10h45 – 11h15 **Committee debriefing and coffee break**

Room: amphitheater A2

Closed-door meeting

Meeting with unit staff *(In the absence of managing staff)*			
Time	**Room**	**Committee Number**	**Meeting**
11h15 – 12h15	116 (1st floor)	1	Meeting with ITAs (*in French*)
	amphitheater A2	2	Meeting with researchers
	112 (1st floor)	3	Meeting with PhD students and postdoctoral fellow

12h20 – 13h30 **Lunch break and committee debriefing**
Room: 314 (3rd floor)
Closed-door meeting

Teams audition #5 *Public session (15min presentation + 15 min discussion)*			
Time	**Room**	**Team Number**	**Presentation by**
13h30 – 14h00	amphitheater A2	**Virus, hepatology, cancer**	**J.M. Pawlotsky**
14h05 – 14h35	amphitheater A2	**Moon-LYT**	**N. Ortonne**
14h40 – 15h10	amphitheater A2	**EpiDermE**	**E. Sbidian**

15h10 – 15h45 **Committee debriefing and coffee break**
Room: amphitheater A2
Closed-door meeting

Teams audition #6 *Public session (15min presentation + 15 min discussion)*			
Time	**Room**	**Team Number**	**Presentation by**
15h45 – 16h15	amphitheater A2	**MUSE**	**F. Relaix**
16h20 – 16h50	amphitheater A2	**StemRepairNF**	**C. Colnot**
16h55 – 17h25	amphitheater A2	**Muskether**	**E. Malfatti**
17h30 – 18h	amphitheater A2	**GEIC2O**	**S. Lanone**

18h00 – 18h30 **Committee debriefing**
Room: amphitheater A2
Closed-door meeting
18h30 **End of day 2 Interview**
20h15 **Dinner**
Committee alone

Interview day 3: 6th of December 2024
8h50 at the IMRB gate, 8 rue du Général Sarrail, 94000 Créteil

9h15 – 10h15 **Meeting with institutions representatives**
Room: Salle du Conseil (3rd floor)
Closed-door meeting
10h15 – 11h00 **Coffee break**
Room: Salle du Conseil (3rd floor)
Public session
11h00 – 12h15 **Meeting with the unit direction**
Room: Salle du Conseil (3rd floor)
Closed-door meeting
12h15 – 13h30 **Lunch break and committee debriefing**
Room: Salle du Conseil (3rd floor)
Closed-door meeting
13h30 – 16h00 **Redaction of the final report**
Room: Salle du Conseil (3rd floor)
Closed-door meeting
16h00 **End of the interview**

GENERAL OBSERVATIONS OF THE SUPERVISORS

UNIVERSITÉ
PARIS-EST CRÉTEIL
VAL DE MARNE

Connaissance - Action

Vice-Présidence de la recherche et de la commission de la recherche :
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Créteil, le 7 mars 2025

Objet : Observations de portée générale sur le rapport d'évaluation Hcéres - E2026-EV-0941111X-DER-ER-DER-PUR260025110-SVE4-IMRB (Institut Mondor de Recherche Biomédicale, UPEC, Inserm U955)

Nous tenons tout d'abord à remercier le conseiller scientifique qui a accompagné le processus d'auto-évaluation et l'évaluation elle-même pour son écoute et la bienveillance dont il a fait preuve durant l'ensemble du processus. Nous adressons également nos remerciements les plus sincères aux membres du comité d'experts et à son président pour le rapport d'évaluation de l'IMRB dont nous partageons le diagnostic et, pour l'essentiel, les recommandations.

Nous remercions les membres du comité d'avoir souligné les éléments distinctifs du positionnement et des orientations stratégiques de l'IMRB avec son identité forte en recherche translationnelle sur différents axes (*Translational Psychiatry and Neuroscience, Muscle Biology and Physiopathology, Vaccinology/Immunology/Infectiology and Senescence, Metabolism and Chronic Diseases and Diseases and Environmental Aggressions*).

Nous ne formulons pas d'observations de portée générale sur ce rapport d'évaluation. La direction de l'IMRB a fait des remarques que vous trouverez à la suite de ce document.

Nous prendrons note des recommandations et en tant que tutelles, nous nous efforcerons à soutenir l'IMRB pour lui permettre de répondre aux axes d'amélioration tout en restant attentifs aux enjeux posés par les changements des contextes de la recherche.

Nous vous prions d'agréer, Mesdames, Messieurs, nos salutations distinguées.

Carole Hénique

Vice-présidente de la recherche et de la commission de la recherche

Hélène Maury

Déléguée régionale Paris Inserm

INSTITUT MONDOR DE RECHERCHE BIOMÉDICALE

Créteil, March the 6th 2025

OBJET : Remarques portée générale sur le rapport d'évaluation
DER-PUR260025110-SVE4-IMRB - Institut Mondor de recherche biomédicale

I. EVALUATION OF THE CENTRE

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The direction of IMRB would like to thank the HCERES Committee for the very detailed and constructive analysis of the unit's past activities and trajectory. IMRB very much appreciated the positive global assessment of the unit and its five-year trajectory.

The Committee made several comments that we grouped by subject and, each time, made a unified response. Collectively, the direction of the IMRB fully agrees with the spirit of the comments.

Area 1:
Profile, Resources and Organisation of the Unit
The Committee states that" It remains unclear whether the 19 clinical research programs funded by the Assistance Publique – Hôpitaux de Paris (APHP), totaling 5 M€, also contribute to the Institute's basic and translational research efforts". Indeed, yes, these clinical research programs contributed to fund research programs involved in IMRB activity.
The Committee noticed that team leaders for the next contract "falls short of the goal of gender parity". We fully agree with this comment. As stated in the auto evaluation document, in the next contract we will intensify gender equality policy to reach gender equity among future team leaders.

Attractiveness
The Committee noticed that "despite innovative and high technologic tools, some core facilities suffered from a lack of staff". We agree with this comment. In spite of different recruitments in platforms during the last contract, we request 1 staff positions to Inserm and 1 to UPEC to reinforce respectively imaging platform and animal facility.
The Committee has concerns about "the heterogeneous success to obtain highly competitive international grants among the IMRB teams". We agree with this statement. The purpose of the IMRB Grant Office will be to support those teams with low rate of success to international grants to overcome this limitation.

Scientific production
The Committee considers that "There is a potential risk of overlapping or confusion between the presentation of publications from the CIC and those attributed to the IMRB, which should be carefully clarified during evaluations". The activities of CIC and IMRB are deeply intricated, therefore is difficult to clearly separate publications from both structures. However, we will give more attention to this distinction in future evaluations.

The Committee recommends to "ensure that the newly integrated teams maintain high standards of both quality and quantity in their publications". This is a critical issue. The new direction will yearly evaluate the new teams to ensure that their integration in IMRB is as best as possible. The advice of the IMRB Scientific Advisory Board will be requested at mid-term to consolidate this process.

The Committee noticed that “It appears a problem of visibility for some non-principal investigators. Each one should be engaged in nonacademic interaction”. We fully agree with this recommendation, and as suggested by the Committee we will promote media training, and more delegation of representation, among young PI.

II. COMMENTS OF THE TEAMS (Teams whose comments are not listed below did not wish to add comments on the report)

Team 1. Transfusion and pathologies of the red blood cells (Ms France Pirenne)

We would like to thank the evaluation committee for their work and constructive criticism.
One project of the team regarding the origin and specificity of the anti-red blood cell humoral response in patients with autoimmune hemolytic anemia (AIHA) was not mentioned in the report. This project will be led by the "Antibodies and Blood Cells" group (Dr. Etienne Crickx) in collaboration with the coordinating reference center for autoimmune cytopenia (coordinated by Prof. Godeau), which is affiliated with the unit. Building on our previous work on the humoral response in patients with autoimmune thrombocytopenia, we plan to decipher the mechanisms leading to tolerance breakdown in AIHA using spleen samples obtained from patients who underwent therapeutic splenectomy for active disease. Specifically, we will isolate B cells reactive against red blood cells to analyze their immunoglobulin repertoire and affinity, to better understand the role of germinal center maturation in this disease.

Team 5. Pharmacology and technologies for cardiovascular diseases, PROTECT (Mr Bijan Ghaleh)

Despite participating in multiple international projects as Work Package Leader, the team has not yet secured leadership of a European projet
We fully agree with this remark. The development of our activity over the years and the recognition by international collaborators represent an important opportunity to build ambitious projects that will be the basis for European grant applications. Furthermore, the group of Stephane Germain has experience in obtaining and leading European grants. Altogether, we believe that we will have the assets for obtained European grants in the future.

The PROTECT team’s expertise in pathophysiology is strong, but molecular and cellular approaches need to be further developed.
We acknowledged this weakness in our autoevaluation HCERES document. The development and investigation of large animal models is resources consuming (researchers, trainees and technical staff). The arrival of Stephane Germain’s group, an expert in molecular and cellular approaches, is a great opportunity for the team to reach a higher level in our mechanistic approaches.

An effort should be done to maintain large animal expertise within the group in regard of the ageing of the technical staff
This is a major challenge for the team. During the past years, we could welcome and promote young researchers that are now PIs (Prof Matthias Kohlhauer, Prof Romain Gallet, etc..). Welcoming young technical collaborators is one of our major goal to achieve for the future. Thanks to the proximity of IUT of Creteil (technicians university school) and other training programs, we have and will have the opportunity to welcome such young technicians and, in relationship with our supervising bodies, working in an effort to promote them within the team. Renewal

of the technical staff is indeed a very important aspect for both University and INSERM to maintain this important expertise in the Research Center.

Team 6: From Pathophysiology towards Immune-based interventions in HIV (Mr Yves Lévy).

We appreciate the reviewers' observation regarding the team's current structure and opportunities for young researchers. While recognizing the limited number of permanent positions at INSERM and CNRS, we are actively addressing this issue.

We have recently recruited two fully qualified senior post-docs with strong track records. These individuals are serious candidates for future permanent research positions. We are committed to providing them with the support and mentoring they need to improve their competitiveness for positions at INSERM in the medium term. In addition, we are actively exploring other funding options to create more opportunities for young researchers. This includes seeking grants that specifically support scientists at the start of their careers (junior prof chairs).
We recognize the importance of recruiting young researchers to ensure the team's long-term future. We believe that the recent recruitment of talented senior post-docs, coupled with our proactive approach to securing additional funding, demonstrates our commitment to ensuring the long-term sustainability of our team.

We acknowledge the reviewer's comment regarding the authorship of publications. We understand the importance of providing PhD students and post-docs with opportunities to lead publications.
Over the past five years, our team has successfully trained eight PhD students, who have published an average of 1.9 first-author articles. Additionally, we have mentored four post-doctoral fellows, who have published an average of 1.3 first-author articles.
We are committed to fostering an environment where our trainees can develop their scientific writing and leadership skills. We actively encourage them to take the lead in writing and submitting manuscripts, and we provide them with the necessary guidance and support throughout the process.
While the PIs may have taken the lead on some publications, this does not diminish the significant contributions of our PhD students and post-docs to the research. We believe that our publication record, coupled with our strong training program, demonstrates our commitment to the development of young researchers.

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