

EVALUATION REPORT OF THE UNIT
PHERE - Physiopathologie et épidémiologie des
maladies respiratoires

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Université Paris Cité - UP Cité

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

EVALUATION CAMPAIGN 2023-2024
GROUP D

Rapport publié le 03/06/2024



In the name of the expert committee¹ :

First Name, Last Name, Chairman/Chairwoman of the committee

For the Hcéres :

Stéphane Le Bouler, acting president

Pursuant to 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 chairs 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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	Ms Virginie Kaulek, Centre hospitalier régional et universitaire de Besancon - CHRU Besancon
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CHARACTERISATION OF THE UNIT

- Name: Physiopathologie et épidémiologie des maladies respiratoires
- Acronym: PHERE
- Label and number: UMR-S-1152
- Composition of the executive team: Ms Marina Pretolani

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement
SVE6 Human physiology and Physiopathology. Ageing
SVE4 Immunity, Infection and Immunotherapy
SVE3 Living molecules, Integrative Biology, Cell and Development biologist for animal science
SVE7 Prevention Diagnostic and Treatment of Human Diseases

THEMES OF THE UNIT

The "Physiopathology and Epidemiology of Respiratory Diseases" unit aims to decipher the personal and environmental factors involved in severe respiratory diseases, identify and validate new diagnostic markers and therapeutic targets, and explore new therapeutic strategies.

Research within Team 1 (Pathophysiology of Severe Asthma and Obstructive Bronchial Disease) focuses on the role of epithelium and smooth muscle in airway remodeling during severe asthma, and whether the crosstalk established between these cellular partners may constitute new therapeutic targets or biomarkers. Thanks to unique collaborations with clinicians and on the basis of large national and international cohorts, Team 1 has developed solid translational research exploring new biomarkers and innovative strategies, particularly in severe asthma and lung transplantation.

Team 2 (Lung inflammation and fibrogenesis) aims at elucidating the mechanisms involved in idiopathic pulmonary fibrosis and rheumatoid arthritis-associated interstitial lung disease, with a focus on the dialog between epithelial cells and fibroblasts in the setting up of fibrosis, at determining the role of fibrosis as an early cancer driver and at exploring the genetics aspects of fibrosis.

Team 3 (Innate immunity and anti-infective pulmonary defense) is mainly interested in the characterization of mechanisms of subversion allowing lung colonization by pathogens, the development of innovative immunomodulatory (cell-based) and anti-infectious (vaccines) strategies.

Importantly, a large part of the research projects of the unit PHERE rely on strong collaborations with clinicians of the Bichat University Hospital.

For the next period, most of the members of the PHERE units will integrate the CRI.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The unit PHERE is located at the Bichat Medical Faculty and Bichat university hospital. PHERE was created on January 2005 and was renewed in January 2009. The unit was then created again in January 2014 and renewed in January 2019 with endorsement from Inserm and Université Paris-Diderot (PRES Sorbonne Paris Cité).

The unit is composed of three teams since 2019: Pathophysiology of severe asthma and obstructive bronchial disease (Team 1), Lung inflammation and fibrogenesis (Team 2) and Innate immunity and anti-infective pulmonary defense (Team 3).

The unit was directed by Dr Pretolani until October 2020 and then by Pr Crestani as an interim director.

In the next period, most of the members of PHERE will join the Centre for Research in Inflammation (CRI), either as a de novo group or by integrating existing teams of the CRI. This merging will allow the extension of fields of interest in CRI, with PHERE bringing its expertise in lung pathology. At the horizon of 2028, all teams including clinical and basic research will be relocated on a new campus with support from AP-HP and UPC.

RESEARCH ENVIRONMENT OF THE UNIT

The PHERE research programs rely on strong translational research to generate original results in fundamental and medical research. Most of the projects involve access to relevant experimental models, technical facilities, human cohorts and biocollections. This interface is facilitated by the proximity of the Bichat Medical School and the Bichat Hospital.

PHERE is integrated in different national and international networks, including the multicenter longitudinal French "COhort of BRonchial obstruction and Asthma" (COBRA) that was developed on-site by Team 1, and the nationwide RAMSES cohort (severe asthma patients treated by biologics in 53 French centers).

PHERE was a founding member of the Laboratory of Excellence (Labex) "INFLAMEX" and of the Fédération Hospitalo-Universitaire (FHU) APOLLO (that took over from the Département Hospitalo Universitaire (DHU) FIRE) coordinated by Pr Crestani. INFLAMEX and APOLLO constitute driving forces of collaboration with CRI.

PHERE has a wide range of clinical (pneumology, thoracic Surgery, intensive Care) and biological (Tissue pathology, biochemistry, immunology) expertise. PHERE participates to the French OrphaLung and RespiFil networks and is involved in international task forces in rare pulmonary diseases (familial pulmonary fibrosis, alveolar proteinosis) and is involved in European networks (EurIPFnet, EurILDregistry). Clinicians of Team 1 received the "Centre of Excellence" label from the World Allergy Organization and Pr Taillé is a founding member of the Severe Asthma CRISALIS-FCrin network.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	15
Maîtres de conférences et assimilés	5
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	7
Cliniciens (praticiens hospitaliers)	10
Sous-total personnels permanents en activité	39
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	4
Post-doctorants	4
Doctorants	2
Sous-total personnels non permanents en activité	12
Total personnels	51

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

Nom de l'employeur	EC	C	PAR
UNIVERSITÉ PARIS-CITÉ	18	0	3
Inserm	0	2	6
Autres	0	8	0
Total personnels	18	10	9

GLOBAL ASSESSMENT

PHERE is working on severe and rare respiratory diseases and aims to decipher the molecular, cellular and physiopathological mechanisms associated with severe asthma and bronchiolitis obliterans, pulmonary fibrosis and anti-microbial pulmonary immune defenses. The projects are supported by a unique and strong continuum from the clinic to basic research thanks to the involvement of clinicians, national and international clinical and academic collaborations and access to cutting-edge technologies. The scientific production is excellent, notably in high-ranked journals. The overall assessment is excellent to outstanding.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Recommendations on scientific production and activities

The unit should aim at increasing its number of high IF publications in generalist journals.

The unit should enhance its action in the field of public outreach.

These recommendations were not totally fulfilled. Nevertheless, one can mention some publications in leading generalist journals, such as FASEB J (n=2 including one as major contributor), Nat Commun (1 as major contributor) JCI Insight (2 as collaborator), Cell (1 as collaborator), NEJM, (7 including 1 as major contributor), Sci Transl Med (2), Lancet (1) and Sci Rep (10).

The unit maintained publication in excellent journals of speciality, including Am J Respir Crit Care Med (21), Eur Respir J (49), Lancet Respir Med (14) JACI (3) and Am J Physiol Lung Cell Mol Physiol (6 including 5 as major contributor).

Recommendations on the unit's organization and life

Recruitments of full-time researchers as well as PhDs would foster the collaborative projects at the unit level as well as the project of each team.

The unit must keep the pace and the current very positive organization.

The access to the platforms should be secured along with an appropriate number of technicians and full time researchers.

The number of full-time researchers remained stable over the period. It is important to mention that a junior scientist who was hired by Inserm during this period finally decided not to return to France. The merging of the PHERE unit with the CRI should facilitate the participation of CRI researchers in projects actually developed in PHERE.

The very good organisation of the unit has been maintained.

The access to the platform has been secured in term of number of technicians. The organisation of the platforms on the Bichat site into a UMS (2028) is expected to stabilise the personnel working in the facilities and to secure their fundings.

B - EVALUATION AREAS

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

Assessment on the scientific objectives of the unit

The scientific objectives of the unit are outstanding.

Assessment on the unit's resources

The ressources of the unit are excellent.

Assessment on the functioning of the unit

The functioning of the unit is excellent.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

PHERE is working on severe and rare respiratory diseases, with a focus on pathologies for which the clinicians are lacking therapies. The pathologies studied are (i) severe asthma and bronchiolitis obliterans, the main phenotype of chronic lung transplant rejection, (ii) pulmonary fibrosis, both idiopathic and rheumatoid arthritis-associated interstitial lung disease, as well as fibrosis as a cancer-promoting process, and (iii) anti-microbial pulmonary immune defenses.

All these projects are built on and supported by a continuum from the clinic to basic research. This translational research is supported by the involvement of clinicians in the projects and their integration in national and international networks. The Bichat Hospital's Pneumology Department in particular has an excellent international visibility.

Thanks to a scientific strategy focused on their specific areas of expertise, the unit has published in excellent journals and established strong networks of clinical and academic collaborations. In addition to clinical research, translational research projects are supported by relevant preclinical models and cutting-edge technical and technological approaches, notably through the LabEx Inflammex.

The PHERE unit has developed its own imaging expertise (histology platform, hosted in the Bichat hospital) and has access to facilities of the Bichat campus. The PHERE unit is also strongly involved in the training of future researchers through the LabEx and the FHU APOLLO.

Weaknesses and risks linked to the context

Most researchers of PHERE have a significant teaching and/or clinical activity, which can strongly impact their time commitment to research.

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

Strengths and possibilities linked to the context

The unit is composed of three teams and includes fifteen professors, one director of research, five associate professors, one researcher and seven technicians and engineers (plus 4 fixed-term contracts). During the period, PHERE hosted thirteen PhD students and ten post-doc scientists.

PHERE receives recurrent institutional funding (k€ 1.187 for the period 2017-2022). These resources are complemented by external competitive funding via national (k€ 2,900 for the period) and international agencies (k€ 377 for the period) and from industrial collaborations/contracts (k€ 532 for the period).

One of PHERE's main assets is the close cooperation with a number of clinical departments that are central contributors to the research programs and provide privileged access to patient samples. Research projects and expertise between teams are complementary, promoting productive collaboration. The strong community feeling and the excellent work environment are definitely major assets for the unit, and are key to the production of excellent research.

The unit also has the potential to attract junior clinicians to participate actively in scientific projects.

The relocalization into a new building (Campus Paris Nord) should alleviate the current need for modern and efficient lab spaces.

Weaknesses and risks linked to the context

Access to the facilities is sometimes limited by a lack of technical staff.

As the new campus is not expected to be operational for at least five years, the unit may not get the necessary logistical and infrastructural support during the transition phase.

Supervisory and affiliated institutions must remain vigilant to enable junior clinicians to take part in research.

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

Equal gender representation has been achieved in the entire staff, except in leadership positions (more acute since team 1 is led by Pr Aubier).

The team leaders constitute the directory of the unit; the self-assessment document does not mention the participation of technician/engineer and PhD student/postdoc representatives in the directory.

No dedicated working groups were constituted to work on work-life balance, research integrity and green lab. The implementation of health and safety procedures is managed by one permanent engineer. PHERE promotes education via the participation to master and PhD programs as well as LabEx and FHU programs.

Weaknesses and risks linked to the context

The unit has no set up dedicated committees to address these points, probably due to lack of time

The unit will benefit from the organization of the CRI which has already set up committees for Gender and Equality and for Mediation, Ethics and Scientific Integrity and has initiated actions to promote team (co-) leadership by female investigators and adoption of family-friendly policies for institutional activities.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the unit is very good to excellent.

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 PHERE members have a strong national and international recognition in the field of lung biology, pathology and therapy, as illustrated by more than 170 invitations or communications to congresses (The Thoracic Society of Australia and New Zealand Conference, ATS international conference, Lung Science conference, COST conference, ERS international conference, 2d International Symposium on ILD in Rheumatic diseases, Congrès de Pneumologie de Langue Française) and more than 160 posters (Gordon research conference on antimicrobial peptides, ERS international Conference, 15th ECFS Basic Science European Cystic Fibrosis, EULAR European Congress of Rheumatology (EULAR), International Conference of the American-Thoracic-Society, American College of Rheumatology Annual Convention, EAACI, AAAAI).

PERE manages and participates to several national and international biocollections (COBRA, EurIPFreg, COLT cohort, Cystic fibrosis cohort, and Emphysema cohort). The Bichat University Hospital is a Centre of Reference for rare lung diseases.

Some members of the PHERE unit were awarded (ERS Gold Medal for ILD, Doctor honoris causa UC Louvain, SPTC Young Scientist bursary) and participate to scientific societies (RCMB assembly planning committee of the ATS, COVID-19 research consortium at the University of Southern California, Société de Pneumologie de Langue Française SPLF) or to research steering committees (Fondation du Souffle).

Some clinicians are involved in the French OrphaLung network and the RespiFil network (rare pulmonary diseases) as well as in international task forces (Familial Pulmonary Fibrosis, Alveolar proteinosis, Connective tissue disease-ILD) and European networks (EurIPFnet, EurILDregistry). Prof Taillé is a founding member of the Severe Asthma CRISALIS-FCrin network, and coordinates the national severe asthma cohort RAMSES.

Members of the PHERE unit are involved in the Editorial boards of specialized journals (Info-respiration, Revue des Maladies Respiratoires). Pr Crestani is President of the Fondation du Souffle.

No information is provided on the organization of congress or symposium.

In terms of recruitment: PHERE has been able to recruit early career scientists (Chargé de Recherche Inserm, Junior Professor Chair at Université Paris-Cité), who have been given a starting grant. Unfortunately, the junior Inserm scientist ultimately did not accept this permanent position. In addition, the unit is faced with the recurrent challenge of replacing permanent staff who leave or retire.

In terms of funding: PHERE was successful in obtaining grants from National agencies (ANR, INCa, PHRC ARS) and foundations/charities (Ligue contre le Cancer, VLM, FRM, Fondation du Souffle) and succeeded in challenging international calls (Wellcome Trust Bill & Melinda foundation, international ANR with Germany). PHERE was also supported by several industrial contracts. The mean annual funding is about 800 k€ (328 – 1,279 k€).

In terms of formation: eight PhD were defended during the period and seven researchers were qualified for research supervision (Habilitation à Diriger des Recherches).

In term of access to technologies: in close collaboration with the Bichat Hospital, PHERE manages the Plateau de Morphologie of the Bichat Hospital with a dedicated Inserm assistant engineer. PHERE has its own facilities for running technologies (biochemistry, cellular and molecular biology, microscopy and image analysis, Multiplex analyzer). PHERE has access to platforms located in house, including videomicroscopy/TIRF, confocal and bi-photon microscopy, flow cytometry, animal imaging (scintigraphy, computerized tomography, magnetic resonance imaging). By the end of 2023, PHERE has access to a novel animal facility.

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

Difficulty attracting PhD students, post-docs and junior scientists. No specific programs have been developed to promote attractiveness.

Funding from national (and international) agencies is relatively low, considering the quality of the scientific output.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of the PHERE unit is outstanding, with publications in outstanding journals of speciality, especially in clinical research.

- 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

Members of the PHERE unit have published over 800 articles, including 88 reviews (59 in French-language journals), with around 1/3 as last-authors. Most articles have been published in leading outstanding generalist (Cell, JCI Insight, Nat Commun, NEJM) and specialized journals (ERJ, AJRCCM, JACI). The portfolio illustrates the translational nature of research at PHERE, which is the driving force of their scientific strategy.

Among the most remarkable productions, one can mention the demonstration of the role of the IL-33-ST2 axis in bronchial epithelial repair and implicating ST2 in the differentiation of monocytes into repairing myeloid cells

(Nat Commun) as well as the identification of new actors in idiopathic fibrosis (Am J Respir Cell Mol Biol). Collaborative genetic studies have demonstrated that the donor club cell secretory protein G38A polymorphism is associated with a decreased risk of severe primary graft dysfunction after lung transplantation (Transplantation), and identified genetic signatures associated with rheumatoid arthritis-Interstitial lung disease and pulmonary fibrosis (N Engl J Med, eLife). These studies illustrate the importance of establishing and developing patient cohorts, such as the RAMSES cohort (national severe asthma collection) and the COLT cohort, in the scientific strategy of PHERE. In the field of pulmonary infectiology, PHERE members have unraveled the mechanisms involved in nosocomial infections and exacerbations (Front Immunol), highlighted the role of IL-6 in the acquisition of a reparative phenotype by alveolar macrophages (Mol Ther) and analyzed, at molecular and cellular levels, the potential of nanoparticles as adjuvant in the protection against pulmonary infections (AmJ Respir Cell Mol Biol).

Although all three teams contributed to the overall production of the unit, their number varies significantly between the three teams. These differences are mainly explained by the team composition, with a high number of clinical publications in teams composed mainly of teacher-researchers with a clinical activity.

Members are strongly encouraged to be trained for scientific integrity and ethic.

The unit has strong rules concerning the reproducibility of the data and raw experimental data are discussed in a weekly basis. The Inserm rules for laboratory notes apply.

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

Publications in generalist journals remain limited compared to the weight of publications in medical journals. This probably reflects the limited human resources and time they can devote to laboratory work. Moreover, publications in high-ranked journals are mostly the result of collaborations with teams whose members are listed as contributors.

Inter-team publications, especially on joint projects, are limited.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The PHERE unit has established excellent and lasting interactions with the industry and is heavily involved in communication actions, especially with patient associations.

- 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

The PHERE unit has established strong collaboration with industries (13 contracts during the period). Some of these projects led to publications in high-ranked journals.

The contribution of PHERE members to research activities to society is very good. They participate to the « Apprentice Researchers » network) that aims young students to discover research and related job opportunities. PhD students are encouraged to participate to the education of children at the 'Cit  des Sciences. Members are also involved in information and education for general public in severe asthma (World Asthma day, Gregory Pariente Foundation day) and participated to national radio or TV shows (France Inter).

They organize the « Bichat Asthma day » for patients and their families and set up a website (<https://asthmateque.fr>), for patients and physicians information on the disease and clinical research. Members also participate to conferences organized by Inserm for the dissemination of knowledge (Conference "Souffle" Inserm/Bibliocit ). Clinicians provided weekly updates to the public via national media outlets on COVID19 pandemic.

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

Risk of reducing interaction with patients/families and stakeholders due to the time and resources required.

ANALYSIS OF THE UNIT'S TRAJECTORY

Over this period, the PHERE unit has been extremely productive. The unit's main asset is its excellent interaction with numerous clinical departments at Hôpital Bichat, and the strong involvement of clinicians in research. However, the PHERE unit has faced major challenges in maintaining technical and scientific staff, and has encountered difficulties in recruiting (junior) candidates with a scientific background. Despite these obstacles, PHERE has continued to develop its research activities.

For many years, PHERE has maintained close relations with the CRI unit, as evidenced by joint meetings and a number of collaborative projects and publications. In this context, some PHERE members have indicated their intention to join the CRI unit for the next period. Following a joint PHERE/CRI scientific meeting, this project has been validated by the supervising institutions.

Members of Team 1 and Team 3 will join Dr de Chaisemartin's and Dr Saveanu's teams of the CRI. These integrations will be accompanied by a focusing of their projects to fit with the objectives of the CRI teams. Team 2 will join the CRI as an independent team working on lung fibrogenesis and inflammation.

The committee evaluated this merger/integration project favourably, as it will allow PHERE researchers to continue their research projects in a more secure environment. Existing collaborations and knowledge of the staff, the CRI working methods and technological environment will ensure smooth integration.

This integration should also facilitate the recruitment of students and post-docs with a scientific background and reduce the workload of PHERE's permanent technicians/engineers and enable students and post-docs to join a wider community. PHERE researchers will benefit from a more structured management team, which should reduce their administrative workload.

RECOMMENDATIONS TO THE UNIT

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

PHERE members will have to be vigilant about their role in the scientific management of projects.

Recommendations regarding the Evaluation Area 2: Attractiveness

Recruitment of PhD students and post docs should be improved.
The number of institutional national and European grants should be increased.

Recommendations regarding Evaluation Area 3: Scientific Production

PHERE members should pay particular attention to publications in high-ranked generalist journals.
Collaborations with the industry should be maintained and even developed. The involvement of PhD students in these collaborative projects, through CIFRE contracts for instance, should be considered in order to offer further opportunities to junior scientists after their PhDs.
PHERE members should increase number of patents filed.

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

The committee encourages PHERE members to continue and strengthen their outreach activities and relationships with patient associations and stakeholders.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Physiopathologie de l'asthme sévère et des maladies bronchiques obstructives

Name of the supervisor: Ms Marina Pretolani

THEMES OF THE TEAM

The goal of the team "Pathophysiology of severe asthma and obstructive bronchial disease" is to improve the understanding of the personal and environmental factors, to decipher the physiopathological mechanisms involved in the onset and progression of severe asthma and lung transplantation and to identify or to test novel therapeutic approaches. Therefore, the team developed two distinct research axes: severe asthma and lung transplantation, using translational approaches combining the expertises of clinicians and fundamental researchers.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

A – Recommendations on scientific production and activities: Although already published in the very best journals in the respiratory field, the team should continue to produce results that can be published in generalist journals. The team should enhance its action in the field of public outreach.

B – Recommendations on the team's organization and life: Attracting full time researchers as well as PhDs would foster the project.

A) The team partially succeeded in improving the scientific impact of its publications with high-impact and original science published with excellent visibility in specific domains. They also succeeded in publishing in outstanding generalist journals such as Nat Comm (1), Science Trans Medicine (2), Blood (1), NEJM (3), Crit Care (10), JAMA (1) and Lancet (1). Team members are strongly involved in public outreach including: (1) teaching, (2) information and education for general public, and (3) through a dedicated website (<https://asthmateque.fr>), for patients and physicians information on the disease and clinical research.

B) The Team succeeded in recruiting a new full-time permanent researcher as CR Inserm. However, this person finally decided not to join the lab. No new PhD was recruited.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	12
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	15
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	0
Sous-total personnels non permanents en activité	1
Total personnels	16

EVALUATION

Overall assessment of the team

Despite major issues over the last years, team members have been really effective in terms of scientific production and valorization. The research projects that are developed within the team are relevant major health problems which could be addressed thanks to the unique structure of the team, combining clinical and basic research. Attracting full time researchers as well as PhDs would foster the projects. The overall assessment of Team 1 is excellent.

Strengths and possibilities linked to the context

The team 1 is developing excellent translational research.
The team members have an excellent scientific track record: the team published almost 400 papers in specialist journals and general ones.
They are able to financially support their projects, with a strong contribution from industries.
Moreover, they also have added value to their work by patenting their findings.
Another strong point of the team is their involvement in the knowledge transmission through a high activity of teaching.

Weaknesses and risks linked to the context

The team had to face several human resource problems over the last years. Several leadership problems might have interfered with the proper functioning of the team.
The team is mainly composed of clinical researchers, and no permanent staff is dedicated to develop the basic research side on the projects.
The team did not train any PhD students.
The team did not succeed so far in getting academic institutional funding.

Analysis of the team's trajectory

The actual team will no longer exist. Six persons out of eighteen will create a new team in the CRI by joining the group of Dr de Chaisemartin. The main objective of the InnaLUNG team will be to tackle clinical complications related to inflammatory lung diseases through the angle of innate immunity. The future Team aims to decipher inflammatory pathways to define new therapeutic targets and diagnostic/prognostic markers in two conditions: severe asthma and acute lung injury.
Several research axes of the team 1 will be discontinued. However, the future team is set up to continue research projects in severe asthma and primary graft dysfunction.
This fusion relies on the major involvement of three PAR who will perform the basic research work.

RECOMMENDATIONS TO THE TEAM

Implementation of new strategies for diversification of research project funding (institutional academic sources).

Implementation of an ambitious strategy to attract, develop and retain the best talents (permanent staff and students).

Integration of european and international networks.

Reinforcement of the he basic research to better balance the excellent clinical work.

Technical and technological transfer (make sure that the know-how is transmitted).

Team 2: Inflammation et fibrogenèse pulmonaire
 Name of the supervisor: Mr Bruno Crestani

THEMES OF THE TEAM

Team 2 led by Bruno Crestani focuses on elucidating the mechanisms involved in the development of pulmonary fibrosis (PF) and identifying new therapeutic targets.

There are 4 main research axes: (1) study of the pathological cross-talk between epithelial cells and lung fibroblast in Idiopathic PF (IPF), (2) investigating the mechanisms of carcinogenesis as a frequent comorbidity in lung fibrosis, discovering new genes associated (3) with PF and (4) with Rheumatoid arthritis-associated interstitial lung disease (RA-ILD).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

While clearly aware of the lack of tenured scientists and eager to solve this issue, the team was unable to succeed in recruiting new CR; however, one recent CPJ position has been recently granted.

The number of team members with the HDR did not improved significantly.

The team succeeded in targeting generalist journals for some publications and in enhancing its public outreach activity.

The adequacy between technical support (including workforce) and the number of projects appears adequate.

The team partially succeeded in further developing large international networks and obtaining European grants.

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

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

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

EVALUATION

Overall assessment of the team

The overall assessment of Team 2 is outstanding. While relatively small (1 CR and 1 CPJ, otherwise mainly clinicians (8 as of 31/12/2022)), the team is recognized as a leader in translational research on the pathophysiology/genetics of pulmonary fibrosis and is part of several important networks that promote excellent national and international visibilities. Team 2 obtained significant support from public and private sources (>1M€), published >200 articles with ~80 as first/last authors including top ranked journals (NEJM, Lancet Respir Med...) and trained good number of PhDs and post-docs.

Strengths and possibilities linked to the context

The team is focused on significant scientific objectives related to pulmonary fibrosis, with a strong clinical relevance. The team is mainly composed of clinicians, facilitating a translational approach and access to human samples (including their own biobank). The team is developing new in vitro tools such as Human precision-cut lung slices (PCLS).

The team has a very good visibility, demonstrated through extensive collaborations, hosting international students, and participation in French/European research networks.

The team has successfully secured funding from various sources, including European projects, national funding, private foundations, and pharmaceutical companies.

The team has made major contributions to the fields of genetics of ILD and lung fibrosis pathophysiology, resulting in publications in high-impact journals.

The team was recently granted a CPJ position, demonstrating strong support from the institutions and important for the future of the team.

The team follows strong rules concerning scientific integrity, ethics, and open science, ensuring the reproducibility of data and compliance with guidelines.

The team actively engages with non-academic stakeholders, contributes to disease awareness, and collaborates with patient organizations.

Weaknesses and risks linked to the context

The team faces long-lasting limitations in the number of tenured scientists (1 CR, no DR), potentially affecting its future (no effective tenured Inserm position in the last 10 years).

The team faces chronic difficulties in recruiting students with a strong scientific background, particularly those with a biology curriculum, which may in part explain their issue to then have CR candidates.

The technical help is limited (only 1 permanent AI), and fixed-term contracts (CDD) do not stay for long periods.

Despite obtaining funding from various sources, the team expresses concerns about financial resources from the ANR, potentially impacting future research projects. The team also expresses concerns regarding the increasing cost of new techniques and animal facility expenses.

The effective contribution of research activities to society collaboration requires significant time and resources, which may impact other aspects of research activities.

Analysis of the team's trajectory

In contrast to the other two unitary teams, Team 2 will integrate the Center for Research on Inflammation (CRI) as an independent team with no major changes in staff members and leadership. They will address crucial questions related to lung fibrogenesis and inflammation, including the maintenance of the profibrotic phenotype by lung fibroblasts, new immune mechanisms in pulmonary fibrosis, the interaction between lung cancer and pulmonary fibrosis, and genetics of lung fibrosis.

With Bruno Crestani's potential retirement in april 2031, a co-direction plan involving Bruno Crestani and Arnaud Mailleux is proposed. Arnaud Mailleux is a candidate for a DR promotion and is positioned to coordinate the team in the future.

The team's future trajectory appears promising and its integration into the CRI clearly positive. The planned leadership transition demonstrates strategic planning for the team's sustainability. The team's commitment to collaboration, translational research, and societal engagement positions it well for continued impact in the field.

However, addressing challenges such as limited tenured scientists and issues to recruit students with a scientific background will be crucial for long-term success.

RECOMMENDATIONS TO THE TEAM

The team needs to continue its efforts to attract tenured scientists and students with scientific background.

It is important to pay attention on a continuous interaction between clinicians and other team's members to maintain team spirit and cohesion.

As far as possible, recruiting new technical staff (AI, IE) on fixed-term or permanent contracts will be a strong asset for the team.

The team will need to show that its integration to the CRI was beneficial.

Team 3: Immunité innée et défense pulmonaire anti-infectieuse
 Name of the supervisor: Mr Jean-Michel Sallenave

THEMES OF THE TEAM

Team 3, led by Jean-Michel Sallenave, investigates host-pathogen interactions and host responses against *Pseudomonas aeruginosa* and influenza virus lung infections and aims to develop (i) myeloid-centered cell therapy approaches to downregulate inflammation in lung infectious models and (ii) novel vaccination strategies to protect against lung infections. The impact of air pollution on anti-viral and host immune responses against influenza virus infection is also a topic of interest for part of the team led by Ignacio Garcia-Verdugo.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

It was recommended to pursue efforts in order to publish not only in excellent specialized journals, but also in more generalist journals. Team 3 has partially succeeded during the evaluation period, as their members signed ten original articles as first or last authors, mostly in specialized journals in the fields of immunology and respiratory medicine (Thorax, 2018; ACS Nano, 2018; Front Immunol, 2018 & 2020; Biomaterials, 2019; Mol Ther, 2022; Int J Mol Sci, 2022; Am J Respir Cell Mol Biol, 2022). One paper (Roussilhon et al. Sci Rep 2017) was published in a good generalist journal.

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

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

EVALUATION

Overall assessment of the team

Team 3 has a recognized expertise in cell biology, biochemistry, and immunology. Scientific projects, funded by ANR, FRM, VLM (total 1.5 M€), are clear across four themes. National and international visibility is very high with 188 publications, ten as first/last authors. Translational projects show progress. Outreach activities, carried mainly by one PhD student need a long-term strategy. Training includes three PhD students and one defended PhD. Communication within the team is excellent. While integration with CRI offers opportunities, future trajectories face challenges due to split into two groups, but team members are motivated to adapt. Overall, the overall assessment is very good to excellent, considering research, funding, visibility, and challenges.

Strengths and possibilities linked to the context

Team 3 has a recognized expertise in fundamental research in the fields of lung immunity and infections, as well as vaccination strategies, with a strong background in cell biology, biochemistry and immunology. The scientific objectives of the team performing fundamental research are clear and divided into four different themes. They have been reached thanks to an excellent and diversified funding (ANR, FRM, VLM) reaching a total of 1.500 k€ for the evaluation period. Team 3 has an excellent national and international visibility, with a total of 188 publications during the period, among which ten original articles have been signed with first or last authors as members of Team 3; five invitations to international meetings; and participation in evaluation, congress organization and editorial activities. The publication output is very good to excellent, given that four out of five permanent researchers are heavily involved in teaching activities, which can be time-consuming. The scientific production of the team respects the principles of scientific integrity, ethics and open science, as all results are kept in laboratory notebooks and are accessible, the institutional and training requirements are followed and the work of ITA is recognized by authorships in most of the publications. The communication within the team is excellent as per the discussions with the different groups of people (ITA, PhDs/Post-docs/Researchers).

The contributions of research activities to society are mainly related to the significant funding of the Team by "Vaincre la Mucoviscidose (VLM)" association. In this regard, the Team participate to annual satellite meetings with the patients, the one member of Team 3 sits at the scientific council of VLM. Besides, one PhD student actively participates to sharing knowledge and result dissemination via lectures at the "Cit  des Sciences" in Paris or contributions to "Apprentis chercheurs" program.

Weaknesses and risks linked to the context

The interactions between clinicians and fundamental researchers could be fostered and improved; however, they do exist as two translational original articles have been recently submitted (Gaudin et al., AJP-Lung & Front Immunol). A potential weakness of Team 3 within PHERE is that the thematic of Team 3 seems isolated to those of Teams 1 & 2. In this regard, very few interactions exist between Team 3 and the other two teams. The future integration of part of Team 3 to the CRI is a unique opportunity to integrate Team 3 activities in a broader context.

The outreach activities are mainly managed by one PhD student and their contribution to the global activities of the Team are arguably overestimated. A particular attention should be given to pursue such activities on the long-term.

Team 3 has trained three PhD students during the evaluation period, one of them completed the PhD in 2019, and the two remaining are in the process of defending their thesis in 2024 (4th year PhD). Hence, the number of defended PhD theses is relatively low given the number of HDRs in the Team. Two post-docs performed a one-year stay in the Team during the evaluation period. They did not sign a first-author publication but their work has been recognized through a co-authorship (Front Immunol, 2020; Int J Mol Sci, 2022). They were funded by 'Vaincre la Mucoviscidose' (VLM) and needed to re-apply the year after to secure 2 or 3-year fellowships, which they haven't done. The obtention of 2 or 3-year fellowships for postdocs might improve Team 3 productivity in the future. However, the attractiveness for postdocs is an issue, as there is funding for a 2-year post-doc position available but no suitable candidates so far. The integration to the CRI might increase attractiveness for postdocs and PhD students, even though it remains difficult to be competitive next to other Institutes (Pasteur-Curie-Cochin).

Analysis of the team's trajectory

Team 3 will no longer exist as it is in the near future, as Team 3 will be split into two different groups: J-M Sallenave's team will integrate Dr. Saveanu's Team within the CRI, while I. Guarcia-Verdugo will move to the Institut Cochin. The original rationale for the integration of the entire Team 3 to Dr. Saveanu's team was driven by previous collaborations between Team 3 and Dr. Guermonprez (member of Saveanu team). However, Dr. Guermonprez decided to move from the CRI to another Institute. Despite these challenges, members of Team 3 are eager and motivated to adjust their trajectory and adapt as much as possible to their future environment, at the benefit of their research activities and training objectives for junior scientists.

RECOMMENDATIONS TO THE TEAM

Following on the decisions to integrate the CRI (J-M Sallenave) and to move to Institut Cochin (I. Guarcia-Verdugo), both Teams should make sure to ensure an appropriate integration to their new environment in terms of existing and novel collaborations, access to technological platforms, scientific animation and scientific projects.

Publications in generalist journals should be encouraged.

Interactions between clinicians and fundamental researchers should be further explored to add a translational dimension to the fundamental work carried out by the team.

CONDUCT OF THE INTERVIEWS

Date

Start: 18 janvier 2024 à 09h00

End: 18 janvier 2024 à 18h00

Interview conducted: online

INTERVIEW SCHEDULE

18 Janvier 2024

9:00-9:10	<p>Règlement intérieur du Hcéres par A SEIGNEURIN (5 mn) Présentation du Comité par son président (5mn) <i>Séance publique (tous les membres de l'unité)</i></p>
9:10-9:50	<p>Présentation scientifique et administrative de l'unité (40 mn) 30 min présentation + 10 min discussion <i>Séance publique (tous les membres de l'unité)</i></p>
9:50-10:50	<p>Présentations scientifiques par les chefs d'équipe 15 min présentation 15 min discussion (soit 30 min par équipe au total) <i>Séance publique (tous les membres de l'unité)</i></p> <p>9:50-10:20: Equipe Physiopathologie de l'asthme sévère et des maladies obstructives bronchiques () (30 min) 10:20-10:50 Equipe Inflammation et fibrogénèse pulmonaire (B Crestani) (30 min)</p>
10:50-11:10	Pause (20 min)
11:10-11:40	<p>Présentations scientifiques par les chefs d'équipe 11:10-11:40 Equipe Immunité innée et défense pulmonaire anti-infectieuse (JM Sallenave) (30 min)</p>
11:40-12:00	<p>Rencontres avec les chercheurs (20 mn) <i>En l'absence de tout personnel d'encadrement (directeur, chefs d'équipe)</i></p>
12:00-13:30	Pause
13:30-13:50	<p>Rencontre avec les post-docs, doctorants et les étudiants (20 mn) <i>En l'absence de tout personnel d'encadrement (directeur, chefs d'équipe)</i></p>
13:50-14:10	<p>Rencontre avec les ITA (20 mn) <i>En l'absence de tout personnel d'encadrement (directeur, chefs d'équipe)</i></p>
14:10-14:55	<p>Rencontre collective avec les représentants des établissements (45 mn) <i>Réunion à huis clos</i></p>
14:55-15:10	<p>Rencontre avec le directeur et les chefs d'équipe de l'unité (15 mn) Réunion à huis clos</p>
15:10-17:00	<p>Débriefing du comité <i>Réunion à huis clos</i></p>

GENERAL OBSERVATIONS OF THE SUPERVISORS

Le Président

Paris, le 23 Avril 2024

HCERES
2 rue Albert Einstein
75013 Paris

Objet : Rapport d'évaluation de l'unité DER-PUR250024200 – PHERE – Physiopathologie et épidémiologie des maladies respiratoires.

Madame, Monsieur

L'université Paris Cité (UPCité) a pris connaissance du rapport d'évaluation de l'unité PHERE – Physiopathologie et épidémiologie des maladies respiratoires. Ce rapport a été lu avec attention par la direction de l'unité, par le vice-doyen Recherche et le doyen de la Faculté de Santé d'UPCité, par la vice-présidente Recherche d'UPCité et par moi-même. L'ensemble des acteurs UPCité remercie le comité pour son travail d'évaluation.

Présidence

Nous vous signalons une erreur factuelle, liée au départ à la retraite de Bruno Crestani, qui n'interviendra qu'en avril 2031, ce qui lui permettra bien d'assurer la responsabilité pleine de l'équipe « Lung fibrogenesis and inflammation »

Référence

Pr/DGDRIVE/2023

Affaire suivie par
Christine Debydeal –
DGDRIVE

Adresse

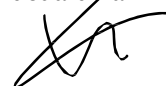
85 boulevard St-Germain
75006 – Paris

Le doyen de la Faculté de Santé et moi-même souhaitons souligner que l'unité de recherche Physiopathologie et Épidémiologie des maladies respiratoires est une unité de recherche translationnelle collabellisée par UPCité et l'INSERM. Son activité de recherche va du fondamental à la clinique en passant par des modèles pré-cliniques. Elle a su maintenir son dynamisme et son excellence malgré les difficultés liées au décès de sa directrice. L'intérim a été assuré par Bruno Crestani et les tutelles ont ensuite procédé rapidement à sa nomination. Le fort soutien de l'université s'est par ailleurs traduit par la mise en place d'une Chaire Professeur Junior. Pour le prochain contrat, l'unité rejoint le Centre de Recherche de l'Inflammation, démarche soutenue par l'ensemble des tutelles.

www.u-paris.fr

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

Édouard Kaminski



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