

Research evaluation

EVALUATION REPORT OF THE UNIT  
H&P – Hypoxie & Poumon : pneumopathies  
fibrosantes, modulations ventilatoires &  
circulatoires

UNDER THE SUPERVISION OF THE  
FOLLOWING ESTABLISHMENTS AND  
ORGANISMS:

Université Sorbonne Paris Nord  
Inserm

---

**EVALUATION CAMPAIGN 2023-2024**  
GROUP D

Rapport publié le 10/01/2024



In the name of the expert committee<sup>1</sup> :

Jorge Boczkowski, Chairman of the committee

For the Hcéres<sup>2</sup> :

Stéphane Le Bouler, acting president

Under the decree n° 2021-1536 of 29<sup>th</sup> November 2021:

<sup>1</sup> The evaluation reports "are signed by the chairperson of the expert committee". (Article 11, paragraph 2);

<sup>2</sup> The president of the Hcéres "countersigns the evaluation reports established by the expert committee and signed by their chairperson." (Article 8, paragraph 5).

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

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

## MEMBERS OF THE EXPERT COMMITTEE

<b>Chairperson:</b>	Mr Jorge Boczkowski Université Paris-Est Créteil Val de Marne - UPEC ()
	Ms Isabelle Dupin Université de Bordeaux
	Ms Halima Kerdjoudj Université de Reims Champagne-Ardenne - URCA
	Ms Véronique Montcuquet Université Paris Cité (supporting personnel)
<b>Experts:</b>	Mr Jean-Louis Pepin Communauté Université Grenoble Alpes (representative of CNU)
	Mr Mustapha Si-Tahar Institut national de la santé et de la recherche médicale – CSS3 INSERM

## HCÉRES REPRESENTATIVE

Ms Sophie Ezine

## REPRESENTATIVE(S) OF SUPERVISING INSTITUTIONS AND BODIES

Mr Raymond Bazin, IT PMN, Inserm  
Ms Claire de Marguery, DR Centre Nord, Inserm  
Ms Pascale Molinier, Université Sorbonne Paris Nord

## CHARACTERISATION OF THE UNIT

- Name: HYPOXIE & POUMON (HYPOXIA & the LUNG)
- Acronym: H&P
- Label and number: UMR 1272
- Composition of the executive team: Ms Carole Planes, head of the unit

## SCIENTIFIC PANELS OF THE UNIT

SVE6: Human Physiology and Physiopathology, Ageing  
SVE7: Prevention, Diagnosis and Treatment of Human Diseases

## THEMES OF THE UNIT

UMR1272 Hypoxie & Poumon (H&P) is a multidisciplinary, single-team, unit dedicated to the study of rare pulmonary diseases: interstitial lung diseases (ILDs, mostly idiopathic pulmonary fibrosis–IPF– and pulmonary sarcoidosis) and large airway transplantation.

The unit is structured into three interconnected and complementary research axes:

- Axis 1. Epidemiological and (bio) clinical approaches to identify risk and prognostic factors in Interstitial Lung Diseases (ILDs)
- Axis 2. Experimental comprehensive approaches to decipher the impact of hypoxic microenvironment in cellular models of ILDs
- Axis 3. Innovative strategies to facilitate the repair, regeneration, replacement of airways tissues

## HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

H&P was founded in 2014 as a university research unit (EA2363). Historically, EA2363 research unit was created in 1992 (and directed until 2013) by Pr. Jean-Paul Richalet (PU-PH Physiology, CNU 44.02) under the name 'Réponses Cellulaires et Fonctionnelles à l'Hypoxie'. During this period, the main field of research was the study of physiological and pathological responses to hypoxia in various organs and systems, with a focus on high-altitude illnesses.

In 2014, Pr. Carole Planès (PU-PH Physiology) became Director of the unit which was renamed 'Hypoxie & Poumon', and substantial changes occurred in the organization and the scientific policy of the unit. The research program more specifically focused on the study of hypoxia and its consequences on the respiratory system. Indeed, a new axis of research on the role of hypoxia in the pathophysiology of fibrosing Interstitial Lung Diseases (ILDs) was developed thanks to the expertise of the Pulmonary Department of Avicenne University Hospital closely linked to the unit. Progressively, research on ILD pathophysiology became the overarching research theme of the unit.

In 2017, Pr. Emmanuel Martinod (Head of Thoracic Surgery Department, Avicenne University Hospital) and his team joined the unit. Pr. Martinod is a pioneer in the field of large airway replacement with cryopreserved cadaveric aortic matrices (first-in-human in 2009), the only efficient surgical procedure in patients with extended tracheal damages. This innovative therapy raises some intriguing scientific issues (for instance, by which mechanisms transplanted aortic matrices progressively transform themselves into functional large airways with *de novo* generation of cartilage rings). Therefore, H&P had the unique opportunity to combine the expertise of renown thoracic surgeons and the skills of basic scientists specialized in lung biology to develop translational and experimental studies in tissue therapy and bioengineering of large airways aiming at improving innovative tracheal surgery procedures. Thus, the unit proposed a new research axis entitled 'repair/regeneration/replacement of lung tissues' for the ongoing contract (2019–2024), very complementary to our research on lung chronic injury caused by ILDs, and applied for the first time for an INSERM label.

H&P was labelled by INSERM as UMR 1272, Université Sorbonne Paris-Nord (previously Paris 13) on 01/01/2019 (ex *nihilo* creation).

H&P is located in the 'Unit of Formation and Research' 'Santé, Médecine, Biologie Humaine' (UFR SMBH), Sorbonne Paris Nord (SPN) University, located itself in the University Campus of Bobigny in the Northern area of Paris.

## RESEARCH ENVIRONMENT OF THE UNIT

The research environment of the unit is composed by interaction with the following structures and research programs:

- IFRB (Institut Fédératif de Recherche Biomédicale), a federative institute for biomedical research labelled and funded by SPN University (UMR 1125). H&P is member of this structure and H&P director is member of the Bureau and of the Executive Committee of IFRB. Fruitful interactions with IFRB are developed by the unit, particularly with EREN (Equipe de Recherche en Epidémiologie Nutritionnelle) exploring the potential impact of nutrition in the incidence and outcomes of pulmonary sarcoidosis and IPF thanks to the creation of specific e-cohorts on the NUTRINET-Santé web platform (NUTRISARC study and NUTRINET-IPF study funded by Fondation du Souffle and AFEFPI, the French Association of patients with IPF). Indeed, IFRB funding by SPN University allows buying collectively 'medium' equipments (ultracentrifuge for instance) and to launch every year a research call to promote collaborative research on-site. Moreover, members of H&P unit are strongly involved in research management bodies both at site level and at the University level.
- Different research federations and platforms. H&P unit has partnerships with CYPS Sorbonne University Platform, large platform of Alain Carpentier Foundation located in the centre of Paris and POLLURISK Platform located at UPEC University Créteil.
- PIA projects: two H&P members are members of label GrEx and the unit participates in PIA program RaDiCo (Rare Disease Cohorts) through RaDiCo-ILDs, a national cohort of interstitial lung diseases in children and adults.
- Finally, H&P unit has the long-standing and strong link with care structures, i.e. Hôpitaux Universitaires de Paris Seine-Saint-Denis (Avicenne & Jean-Verdier HUPSSD, APHP). The fact that MD PhD teacher researchers involved in the unit are also working in/directing either care services (Thoracic Surgery Dept headed by the one of the responsible for axis 3, Pulmonary Dept headed by co-responsible for axis 1, Radiology/Thoracic Imaging or medical-technical platform – Physiology Platform including – clearly facilitates the continuum between laboratory research and care, and the development of translational research on well-phenotyped patients. Indeed, the Pulmonary Dept of Avicenne Hospital, the services/platforms working with it (thoracic imaging, PFT, thoracic Pathology...) and H&P axes 1 & 2 constitute a Reference Centre for Rare Pulmonary Diseases in Adults – CRMOR ORPHALUNG, site constitutif – labelled in 2017 (directed by the responsible for axis 1).

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

Catégories de personnel	Effectifs
Professeurs et assimilés + praticiens hospitaliers	10 + 5
Maîtres de conférences et assimilés	10
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	3
<b>Sous-total personnels permanents en activité</b>	<b>28</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	
Personnels d'appui non permanents	1
Post-doctorants	2 (ATER)
Doctorants	5
<b>Sous-total personnels non permanents en activité</b>	<b>8</b>
<b>Total personnels</b>	<b>36</b>

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

Nom de l'employeur	EC	C	PAR
UNIVERSITÉ SORBONNE PARIS NORD	17	0	2
AUTRES	0	0	7
INSERM	0	0	1
<b>Total personnels</b>	<b>17</b>	<b>0</b>	<b>10</b>

## GLOBAL ASSESSMENT

The unit H&P – three axis – develops a strong translational approach.

During the evaluation period, the H&P unit has maintained an excellent scientific production in the field of respiratory medicine – 235 original articles, with 30% in PDC position, 30% of this last category published in generalist journals such as *JAMA 2018* and *JCI Insight, 2018*, and in the best journals in respiratory medicine such as *European Respiratory Journal*, *American Journal of Respiratory and Critical Care Medicine*, and co-authors *Lancet Respiratory Medicine* and *Thorax*. However clinical and epidemiological studies were published in more impacting journals than basic research studies.

Major achievements of the unit, illustrated by the following items, reflect the high quality of its research activities which respond to very important medical and societal issues:

- i) demonstration of the roles of environmental factors on the prevalence and course of interstitial lung diseases – *European Respiratory Journal 2017, Thorax 2018*, experimental studies going on with a project funded by ANSES – , ii) evaluation of new therapeutic strategies to treat exacerbations of idiopathic pulmonary fibrosis (*Lancet Respiratory Medicine 2022*),
- iii) new image analysis tools based to assess lung fibrosis in patients with interstitial lung diseases (*European Respiratory Journal 2020*, creation of a national consortium, 2 ANR projects, 1 as PI),
- iv) innovative surgical research on large airway replacement with cryopreserved aortic allografts leading to successful clinical applications in patients (*JAMA 2018*, clinical and experimental studies going on, 2 ANR projects, 1 as PI), and
- v) consolidation of a platform devoted to study hypoxia, a unique platform in Ile de France region and supported by Sorbonne Paris Nord University.

The H&P unit has an excellent reputation in the field of respiratory diseases at the European level as revealed by the following functions in scientific European institutions: Heading of the group 'Sarcoidosis' at the European Respiratory Society (ERS); Co-chairing of the ERS Sarcoidosis task force for the elaboration of clinical practice guidelines; Vice-chairing of the ERS Early Career Committee. Moreover, a member of the unit takes part of the Scientific Advisory Council of the Foundation for Sarcoidosis Research at the USA.

Unit members received 83 invitations to give conferences in international meetings of the field, among which the most relevant are: American Thoracic Society annual meeting, European Respiratory Society annual meeting...

The attractiveness of the unit is very good and on an excellent trajectory: members applied for competitive national grants (including ANR, ANSES and PHRC), resulting in a consistent increase in projects funded by these agencies as compared to the previous contract, i.e. 6 ANR projects funded, with two as coordinators vs two as partners for the previous contract, and two ANSES projects as coordinators vs 0 in the previous contract. Overall, the total budget of the unit increased by 128% as compared with the previous contract. However, no funding from European agencies was obtained. The unit was very active in its recruitment policy, with 6 Associated Professors recruited during the contract. Fifteen PhD students were hosted, and 9 PhD thesis defended for twelve HDR. Members direct three Master programs. However, no permanent Inserm investigator was recruited, and no full-time research postdoc was hosted.

The interaction with the industry shows significant positive outcomes. The unit established successful R&D partnerships with two companies at the national (MECCELIS Biotech and OTR3) and with another at the international level (i.e. Baker Ruskin). A collaborative ANR-PRCE project was obtained with OTR3 in the field of regenerative medicine. The H&P unit has developed and set up a computer-controlled system to expose rodents to intermittent hypoxia through an R&D partnership with Baker Ruskin).

Inclusion of the unit's research in society is outstanding as evidenced by developing a participative research project, a strong interaction with patients' association (idiopathic pulmonary fibrosis), and participation in society dissemination events like 'Fête du Savoir' and 'Apprentis Chercheurs'.

The life and organization of the Unit are unanimously well appreciated by all members of the Unit. In total, H&P unit has carried out excellent projects, recognized by the academic and medical communities, with a very strong contribution to the society.

## DETAILED EVALUATION OF THE UNIT

### A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Three main recommendations were performed in the previous report: to further increase collaborations especially in basic science, to increase administrative and technical support for the unit and to develop novel methods allowing continuing successful experimental or translational research work on ILD Globally, the unit answered satisfactorily to these recommendations.

Concerning the first recommendation, new academic and industrial collaborations (ANR consortia) were set up allowing the unit to increase the number of proposals granted as partners and as coordinators, as compared to the previous contract: 6 ANR projects funded (2 as coordinators) vs two as partners for the previous contract, two ANSES projects as coordinators vs 0, and 7 PHRC (3 as coordinators). The unit is also currently filing a first patent thanks to the collaboration with biomechanicians & computer scientists. Moreover, the unit developed new partnerships with two bioengineering companies: Mecellis Biotech, OTR3 (an ANR PRCE partnership was established with this last company). Collaboration with academic laboratories in basic science was also performed (UMR955 Inserm-UPEC and UMR CNRS 7583 CNRS-UPEC for pulmonary fibrosis and air pollution, and with IPMC, Nice University for lung single cell-RNAseq analysis).

Concerning the second recommendation, the administrative support increased by the recruitment of a half-time Inserm secretary. Two additional engineers were recruited through the funding obtained through research projects.

Finally, concerning the third recommendation, the Professor recruited with a full-time research dedication developed different new experimental models: a 2D culture of monocyte-derived macrophages from sarcoidosis patients and control subjects, and an original 3D culture model of sarcoidosis granuloma using patients PBMC (monocytes & lymphocytes) and human normal lung fibroblasts is under development, two models of lung granulomatosis in mice induced by *Propionibacterium acnes* extracts or carbon nanoparticles inhalation respectively, chronic models of lung fibrosis induced by repeated treatment with low-dose BLM reproducing most of the features of human IPF, a unique model of tracheal replacement with aortic cryopreserved allograft in mice, reproducing the tracheal 'regeneration' observed in patients. Moreover, members of axis 3 (mainly surgeons) will develop a perform tracheal transplantation preclinical model thanks to the support of Alain Carpentier Foundation.

### B – EVALUATION AREAS

Considering the references defined in the unit's evaluation guidelines, the committee ensures that a distinction is made on the outstanding elements for strengths or weaknesses. Each point is documented by observable facts including the elements from the portfolio. The committee assesses if the unit's results are consistent with its activity profile.

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

##### Assessment on the scientific objectives of the unit

The scientific objectives are remarkable and meet unsatisfied needs in terms of respiratory health (the study of rare pulmonary diseases and large airway transplantation) and societal needs (the effects of air pollution and exposomes on ILDs progression). The unit has unique expertise in these fields at the national level.

##### Assessment on the unit's resources

The unit resources are excellent regarding the increase in funding, the recruitment of professors and the obtention of two ANR as PI. However, a full time Inserm investigator is still lacking in the unit.

## Assessment on the functioning of the unit

Excellent function of the unit in terms of health and safety, environmental issues and the protection of scientific assets. However, regular scientific meetings in English are lacking to the life of the unit.

### *1/ The unit has set itself relevant scientific objectives.*

#### Strengths and possibilities linked to the context

The scientific objectives of the unit are well defined and meets unsatisfied needs in terms of respiratory health: the study of rare pulmonary diseases: ILDs (mostly IPF and pulmonary sarcoidosis) and large airway repair. Moreover, some research topics, such as the influence of environmental factors in ILD progression is in a direct link with major societal issues concerning pollution and its relationship with climate change.

To achieve these objectives, the H&P unit set up a strategy based on developing a solid translational research approach thanks to strong interactions between clinicians and basic scientists taking in advantage of the very close link of the unit with the Respiratory Diseases and Thoracic Surgery departments of Avicenna University Hospital. Moreover, the unit promotes multidisciplinary approaches bringing together clinicians, surgeons, epidemiologists, biologists, biomechanicians and computer science scientists. In this context, the inclusion of Axis 3 for the present contract was a logic development taking the expertise of the Director of the Thoracic Surgery Department of Avicenne Hospital into account on tracheal replacement surgery which fully fitted with this multidisciplinary approach developed by the unit.

The internal scientific organisation of the unity allows the implementation of the strategy of the unit: Axes 1 and 2 are devoted to study ILD with complementary approaches, and Axis 3 ensures the full development of a translational approach on large airway transplantation.

The unit upgraded the Hypoxia Platform which was labelled 'SPN University Platform' in 2019. This is an important asset of the unit because of this platform gathers different technologies, allowing a translational approach of physiopathological consequences of hypoxia exposure.

#### Weaknesses and risks linked to the context

The collaboration between axes 2 and 3 is not enough developed.

### *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 recruited several members during the present contract: 4 university-hospital Associate Professors (2 MCU-PH Pulmonology and 2 MCU-PH Physiology), two university Associate Professors (MCF) of Physiology, five clinicians (3 PH in Pulmonology, 1 PH in Pathology, 1 PH in Thoracic Surgery), and two biological engineers.

The unit obtained from the UFR SMBH an additional Laboratory room (25 m<sup>2</sup>), which allowed to increase and diversify the biological research activities following the creation of research Axis 3 in 2019.

#### Weaknesses and risks linked to the context

Recurring endowment form SPN University and INSERM (555 k€ between 2017 and 2022)) represented 22% of total financial resources of the unit.

The unit has not recruited a permanent EPST scientist as proposed by the last evaluation committee.



### 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

H&P permanent workforce presently consists of nine women and ten men, which respects gender equality.

The general organization of health and safety in the laboratory is managed by a unit council, made up of the unit director, the prevention assistant, and the various projects and/or platform managers. This local committee meets several times a year.

The unit organizes training around workplace safety for new arrivals (internal rules, general operation), whether they are staff or students.

A proactive policy was set up by the unit to facilitate integration and mentoring of new staff members (priority for applications to grants from the university, rapid investment in a collective task, incitation to follow specific training to upgrade their technical skills, mentoring by an established investigator to supervise students, etc.).

In addition to the mandatory annual interview, technicians and engineers are strongly encouraged to follow specific training to upgrade their technical skills and to attend scientific meetings/events.

PhD students are strongly encouraged to present their work once or twice a year in national and international meetings and to follow specific training programs. The mean number of articles per PhD student is 4 (2.1 as 1st author): mean duration of PhD thesis is 41.8 months for students with a scientific background and 56 months for students with medical background doing part-time research (COVID pandemic has to be taken into account in this calculation).

A business continuity plan is regularly updated to guarantee the preservation of samples and the proper functioning of equipment.

The unit aims to reduce the carbon footprint related to transport by limiting airplane travels (videoconferencing if possible, otherwise favouring certain means of transport for responsible travel), but also by grouping together orders for laboratory equipment and supplies. Other measures already implemented and related to energy consumption, the reduction in the use of paper and ink (dematerialization, shared and secure space).

The life and organization of the Unit are unanimously well appreciated by all members of the Unit.

#### Weaknesses and risks linked to the context

A steering committee devoted to discuss the scientific aspects of the life of the unit in a regular basis is lacking in the organizational chart.

H&P permanent workforce respects gender equality and a referent for 'Parity & Professional Gender Equality' has been recently appointed; however, there are no details about actions devoted to promote gender equality among all the categories of members of the unit to ensure that the present situation is not only the result of chance.

Regular scientific presentations and meetings in English are lacking.

## EVALUATION AREA 2: ATTRACTIVENESS

### Assessment on the attractiveness of the unit

The unit has an excellent reputation at the national and international level in the field of respiratory diseases, particularly clinical research on pulmonary interstitial diseases and airway transplantation.

The unit was very active in: i)-recruiting fifteen new permanent members. However, no foreign PhD students or postdocs were recruited; ii)-obtaining competitive projects funded by ANR, ANSES, and PHRC; however European funding is lacking; iii)-9 PhD were defended, for twelve HDR; iv)-the unit consolidated its state-of-the-art platforms (hypoxia and microscopy), the former being a unique platform in Ile de France Region, which is frequently used in collaborative studies.

Overall, these different elements show that the attractiveness of the unit is 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

**1. The unit has an attractive scientific reputation and contributes to the construction of the European research area.**

The unit is recognized in the field of respiratory diseases at the European level as revealed by the following functions in scientific European institutions: PIs are head of the group 'Sarcoidosis' at the ERS (2020–2021); write guidelines for the elaboration of clinical practice guidelines (2021); member of the Scientific Advisory Council of Foundation for Sarcoidosis Research (USA); etc.

Unit members received 83 invitations to give conferences in international meetings, among which the most relevant are the following: Am. Thoracic. Soc. meeting (ATS, n=2), European Respiratory Society (ERS, n=5), Association for Sarcoidosis and Other Granulomatous diseases (WASOG, n=4).

The unit also has a well-established national visibility reputation as revealed by participation of its members in different French scientific societies and foundations (presidency and of the French Society of Exercise & Sport Medicine, presidency of the Groupe de Sarcoïdose Francophone, co-coordination of the transversal and interdisciplinary working group of SPLF 'Pollution & Climate', ...

**2. The unit is attractive for the quality of its staff hosting policy.**

The unit recruited fifteen members during the present contract: four university-hospital Associate Professors (2 MCU-PH Pulmonology and 2 MCU-PH Physiology), two university Associate Professors (MCF) of Physiology, five clinicians (3 PH in Pulmonology, 1 PH in Pathology, 1 PH in Thoracic Surgery), and two biological engineers.

In addition, the unit hosted 4 visiting scientists from Chile and Peru (one of them spent 5 short periods in the unit), fifteen PhD students (9 PhD thesis defended) for 7 HDR investigators and three HDR defended during the last five years, and 6 'postdoctoral' fellows through university positions (ATER).

**3. The unit is attractive because of the recognition gained through its success in competitive calls for projects.**

The unit developed a proactive policy applying to competitive national grants – including financial supported by ANR, ANSES and PHRC –. Since 2019, two-to-3 letters of intent for ANR calls in various categories have been submitted every year, either as coordinator or as partner. This approach was successful inasmuch as the unit markedly increased the number of projects funded by national competitive calls as compared to the previous contract: 6 ANR projects funded – two as coordinators, 15K€ and 275k€ – vs two as partners for the previous contract, two ANSES projects as coordinators vs 0, and 7 PHRC – three as coordinators –. Moreover, the unit obtained eight grants from foundations and national academic societies. Overall, the total amount obtained for the unit was 1443 k€ – the total budget of the unit for the period under consideration was 2539 k€ –. These successes were the result of the development of fruitful national scientific collaborations and research 'consortia' in the fields of biology and bioengineering/biomaterials – 5 main collaborations –.

The unit obtained an international funding from ECOS-Sud – travel award 15 k€ –.

**4. The unit is attractive for the quality of its major equipment and technological skills.**

Thanks to various academic funding sources, the research unit progressively acquired a complete set of devices to expose cells or rodents to acute/chronic hypoxia and to intermittent hypoxia: a hypoxic station for exposing cells and tissue explants – *In Vivo* O<sub>2</sub>, Baker Ruskin® –; an original set up developed by the unit in partnership with Baker-Ruskin and devoted to expose rodents to intermittent hypoxia including the hypoxic/normoxic chambers, the computer with specific software and the nitrogen concentrator (*Iconic*, Baker Ruskin®). A double-chamber plethysmograph to study rodents' ventilation is also available in the laboratory. In addition, ventilatory and cardiovascular responses to hypoxia at rest and at exercise can be studied in healthy volunteers and patients in the Physiology & Sport Medicine Department of Jean Verdier University Hospital – under the direction of a member of the unit –. Taken together, these set-ups/facilities constitute the SPN University 'Hypoxia Platform', which is unique in Paris area. It has been recognized as a research platform by SPN University in 2019 and is funded by the university since that time. The Hypoxia Platform is open to the scientific community – SPN University units and external units –, it allowed the unit to set up 5 fruitful scientific collaborations.

Members of H&P unit possess specific skills such as 2D or 3D cell culture of primary lung cells; complex model (lung fibrosis, lung granulomatosis, tracheal replacement (and preclinical models) tracheal replacement).

Finally, the unit hosts biological samples (blood, urine, lung tissue biopsies) and clinical/epidemiological data from well-phenotyped patients with rare pulmonary diseases or tracheal replacement, thanks to past or ongoing cohorts/studies with biobanking and data banking (6 well characterized cohorts).

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

Nine PhD theses were defended for twelve HDR, with only seven PIs involved during the last mandate.

Besides participating in the bodies of European medical scientific societies, the unit does not participate in European research steering bodies such as the ERC or H2020. The unit lacks significative funding from international sources, specially from European agencies.

No foreign students or postdocs were hosted by the unit during the contract. Moreover, no full-time research postdocs were noticed, as such funded by national or international grants.

The unit is not involved in heading or participating in PIA projects.

## EVALUATION AREA 3: SCIENTIFIC PRODUCTION

### Assessment on the scientific production of the unit

The unit publishes original articles either in the best generalist journals – *JAMA*, *JCI Insight* – and in the best speciality respiratory medicine journals (*Lancet Respir Med*, *Am J. Respir Crit Care Med*, *Eur Respir J*). Thirty percent of original articles were published in PDC position, and 72% in open science journal. However, a certain degree of heterogeneity is observed among publications, between axis.

Mean number of publications per teacher researcher and per PhD students was excellent (1.4 PDC article/year/teacher researcher, and two articles in 1<sup>st</sup> position for PhD students).

Overall, scientific production of the unit in the field of respiratory medicine is excellent.

*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

#### **1. The scientific production of the unit meets quality criteria.**

The unit published 235 original articles (including 5 research letters), 72 original articles in PDC, 25 of whom (35%) were published in the best speciality journals such as *Eur Respir J*, *Lancet Respir Med*, *Am J. Respir Crit Care Med*, *JAMA Dermatol* and in generalist journals such as *JAMA* and *JCI Insight*.

Moreover, members of the unit were involved in the writing of sixteen guidelines or consensus conferences including international guidelines on sarcoidosis treatment by the European Respiratory Society.

Major achievements of the unit reflect its high expertise in the field of ILD and tracheal replacement along with the ability to develop a really translational strategy, going from clinic to basic research (projects on pollution and IPF and in tracheal replacement). In detail, these major achievements are i) the study of the role of atmospheric pollution on the natural history of IPF (article of a member of the unit in 1<sup>st</sup> position in *Thorax* in 2018, experimental studies going on with a project funded by ANSES), ii) research on Artificial Intelligence and image analysis in pulmonary fibrosis (national consortium, 2 ANR projects, 1 as PI), iii) ongoing projects on risk factors on

sarcoidosis, iv) ongoing projects of tracheal replacement project (article in JAMA in 2018, clinical and experimental studies going on), and finally v) the development of the hypoxia platform.

## **2. Scientific production is proportionate to the research potential of the unit and shared out between its personnel.**

Mean number of publications (2017–2022) per teacher researchers was important,  $27.5 \pm 27.8$ , and mean number for PDC articles was  $8.6 \pm 5.8$  (corresponding to 1.4 PDC paper/year/teacher researchers, or to 3.3 PDC/year/full-time research equivalent). It must be noted that clinicians (especially the most experienced of them) have generally more publications than basic scientists, mostly because they are involved in clinical collaborative networks.

Concerning junior researchers, the mean number of articles/PhD thesis defended was 4, and three HDR were also defended (12 HDR in a whole in the unit). The mean number of articles signed by PhD students was 2.1 in first position, which is a very satisfactory data. The committee appreciates the long-standing policy of the unit stipulating that support technical staff are systematically co-authors of the papers in which they participate.

## **3. The scientific production of the unit complies with the principles of research integrity, ethics and open science.**

An 'ethics referent' has been appointed which received in 2021 a specific training concerning scientific integrity. She regularly attends meetings gathering ethics referents from different research units organized by SPN University.

Studies on the human person are performed in compliance with the Public Health Code, the Jardé law and its subsequent decrees. Confidentiality of patient data is preserved.

In accordance with the regulations in force, experiments with GMOs, tissues and human cells are carried out under cover of obtaining authorizations and with the approval of the ethics committees.

Since 2020, a data management plan is set up between H&P researchers and external collaborators for the traceability of the data used and generated as part of each research project in order to facilitate data sharing, re-use and sustainability.

Concerning the publication policy, particular attention is paid to SCImago indicators and Clarivate bibliometrics (WOS and JCR) to identify predatory journals and direct publication to the most ethically appropriate journals. Concerning authorship contributions, PhD students sign the publications directly linked to their thesis in first position, and the PhD supervisor in the last position. When a researcher with no HDR yet supervises a PhD student in collaboration with a senior researcher with HDR, both supervisors may sign papers as co-last authors if their contributions are equivalent. If the younger researcher with no HDR had a greater contribution than the senior with HDR, he/she will sign as last author and the senior researcher as penultimate author.

Concerning Open Science, SPN University signed the DORA agreements (2021), established an open science charter (2021), and since then an Open Science working group has been advocating actions related to University Research Committee. COARA was signed in 2022.

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

The repartition of the number and level of publications between the three axes is heterogeneous. Most of the original article relies on the production of axis 1 (72% of unit publications). More in detail, top 10% articles in axis 1 are above, and percentage in leading position is below, the level of the unit (49% and 21% respectively). This last point reflects an important number of articles coming from collaborative studies in this axis.

In addition, the percentage of top 10% among PDC articles in axis 1 is higher than the unit (54% vs 35% respectively). Indeed, most of the top 1% publications of the unit cited above relies on axis 1.

Axis 2 publications represent 20% of the unit, 60% of publications in PDC but only 13% are in the top 10% (13%).

Finally, the number of original articles emerging from the new axis 3 is low (8% of the unit), but near half of these articles are in PCD, and 43% of these articles are in the top 10%.

In a whole, axis 1 produced most and the more impacting original articles of the unit.

The particularities in original articles publication between the axis are not directly related to the workforce and probably reflects the historical development of the unit with an initial core around the subjects of axis 1. Indeed, axis 1 is composed essentially of seventeen medical doctors (11 of whom are university-hospital professors and 6 are clinics); axis 2 is composed of twelve members (5 university-hospital professors, 5 university professors and 2 engineer); finally axis 3 is composed of ten members (3 university-hospital professors, three university professors, 2 clinicians, 1 postdoc and 1 engineer). Some members are included in several axes. Therefore, although numerically speaking axis 1 is the larger one, in terms of full-time equivalent investigators, axis 2 is the larger, followed by axis 1 and axis 3 (6.5, 4.2 and 2.7 respectively).

The particularities in original articles publication between the axis could neither be fully explained by the financial resources obtained by each axis. Indeed, without considering clinical funding (grants from the

'Programme Hospitalier de Recherche Clinique, PHRC', obtained in axes 1 and 3) funding obtained by axes 1 and 3 was similar (981 k€ and 821 k€ respectively) whereas publication profile was different. Funding obtained by axis 2 was lower than above-cited axes (311 k€).

Historical reasons (the unit was initially focused on clinical research on ILDs) and the newly emerged axis 3 can explain this heterogeneity.

No HAL document was furnished.

## EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The 'H&P' laboratory has performed 9 clinical trials and initiated three with three PHRC as PI, obtained three industrial contracts and collaborative innovation (2 companies, 1 ANR-PRCE). However, no patent or start-up company was created during the contract. Members were very active regarding societal interactions (patients' associations and public outreach). The overall assessment is excellent.

*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

#### **Standard 1: The unit stands out by the quality and quantity of its non-academic interactions**

The unit engagements with the socio-economic world and patient associations have yielded significant positive outcomes, which are summarized below.

*R&D partnerships:* The unit established successful R&D partnerships (3) with both national (MECCCELLIS BIOTECH®, ORT3) and international entities (Baker-Ruskinn®, the UK). Of note is that this latter partnership exemplifies adaptability and problem-solving skills of the laboratory in equipment modification (Hypoxia platform).

*Collaborative science activities:* The collaboration with OTR3–Matrix Therapy Company is the evidence of the laboratory's capacity to secure external funding (235 k€ through an ANR PRCE-2022 grant for the 'MAT-PL project' as partner) and showcases the unit's commitment to advancing regenerative medicine research.

*Interactions with pharmaceutical companies:* H&P clinicians were involved in 9 national clinical trials with three as PI. The unit also participated in 4 medical continuing education courses and patient-focused meetings, granted by industry (including Roche, Sanofi, Boehringer and BMS).

*Interactions with patient associations:* H&P clinicians interacted with three patient associations, namely APEFPI/AFPP, SARCOIDOSE INFO and AFPCA. Recognition as a 'Center of Excellence' for Sarcoidosis by the Foundation for Sarcoidosis Research also acknowledges the unit's leadership in this domain.

#### **Standard 2: the unit develops products for the cultural, economic, and social world**

The H&P unit has developed and set up a computer-controlled system to expose rodents to intermittent hypoxia in vivo through a R&D partnership with BAKER RUSKINN® (UK).

#### **Standard 3: The unit shares its knowledge with the general public and takes part in debates in society.**

The unit was involved in programs like 'Fête-le-Savoir' and 'Apprentice Researchers / Tree of Knowledge'. These initiatives contribute to a more informed society and inspire future generations of scientists. Through its research on crucial public health matters, such as atmospheric pollution and respiratory diseases and tracheal replacement, the laboratory has also positioned itself as an authoritative source of information. Its active

contributions to the medical press, to the mainstream media as well in interviews contributes to better information of the society.

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

**Standard 1: The unit stands out by the quality and quantity of its non-academic interactions & Standard 2: the unit develops products for the cultural, economic, and social world**

While the unit demonstrates remarkable strengths as proved by industrial collaborations and ANR-PRCE project, it also faces specific weaknesses and risks in the context of Standards 1 and 2. Although the units showed good interactions with industrial partners that support continuing education courses, neither basic nor clinical research interaction with industrial was established.

*Risk = conflicts of interest:* The laboratory's engagement in clinical trials financed by pharmaceutical companies carries inherent risks of conflicts of interest. Indeed, it could compromise the laboratory independence and creativity. It could also undermine public trust since such research findings could be influenced by the interests of the funding organizations.

**Standard 2: the unit develops products for the cultural, economic, and social world**

No patent or start-up company was created during the contract.

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

The unit efforts to share knowledge with the various audiences and engage in public events, as addressed in Standard 3, present some weakness.

*Weakness = time and resource constraints:* The unit faces challenges in allocating sufficient time and human resources to maintain consistent and impactful public commitments. Indeed, balancing research engagements with public communication efforts can put a tension in the available human resources, potentially compromising the effectiveness of both research performance and knowledge dissemination.

Finally, the non-clinical staff of the unit should be more actively involved in scientific outreach activities within specialized communities as well as in public communications.

## ANALYSIS OF THE UNIT'S TRAJECTORY

- The project of the unit capitalizes on the main success of the present contract: analyses of the role of environmental factors on the natural history of ILDs through clinico-epidemiological studies; implementation of translational studies aimed at deciphering the molecular mechanisms underlying these phenomena; multi-scale modelling of lung fibrosis from HRCT imaging, and development of experimental models devoted to study the mechanism of tracheal repair. The project of the unit proposes to further develop and go in deep into these subjects, maintaining the 3 axes implemented during the present contract. This is an ambitious project, going from epidemiological to basic science approaches, that responds to important medical and societal needs, and is in agreement with the strategy of tutorial bodies. The project is feasible since it takes into advantage the techniques, infrastructures, and cohorts available in the unit and relies on several national collaborations, partnerships with actors of the socio-economic world (start-up OTR3 and MECCELLIS Biotech). However, two points of concern are the current lack of infrastructure and human resources in the unit concerning methodology, statistics and large-scale data analyses, and the lack of a full time Inserm investigator with expertise in basic science.
- The project will benefit from the input of a new group which will be incorporated to the unit in 2025. This group, called 'Biotherapies & Glycoconjugates' (BG), is composed of 7 SPN University staff and is specialized in the field of glycobiology and intercellular communications. This group is currently located in the UFR SMBH campus (like the unit), although it now belongs to another Inserm unit located mainly in Bichat hospital campus, in the north of Paris. It is expected that this integration will strengthen and energize axis 2. and 3. In particular, a new program regarding the role of proteoglycans (PGs) in the development of pulmonary fibrosis is planned. The investigation on the role of (PGs) in IPF is supported by preliminary data, also demonstrating the ability of researchers from the different units to work together. Obtaining grant is, however, absolutely required to support this program and guarantee a successful integration of the BG group. Moreover, axis 3 will also benefit from the expertise of some researchers of the BG group in bio-prosthesis engineering, to test novel biomimetic substitutes for tracheal replacement. The trajectory of the unit will be thus reinforced by the arrival of this group either in terms of staff and in terms of expertise in cellular biology. Of note, one of the members of the group obtained the very prestigious 'Institut Universitaire de France' Junior Chair, in 2022, and another member of the group is the Dean of the UFR SMBH.
- Therefore, the incorporation of the BG to the unit is very interesting and timely operation. However, the situation is challenging as it usually occurs when two research structures merge. Governance of the unit and research of financial support will be critical issues to ensure the harmonious inclusion of the new group. Moreover, some degree of prioritisation in the projects will be beneficial for allowing the unit to reach the highest degree of success.
- In terms of international recognition and visibility, the unit is setting up an ambitious strategy to integrate European networks, such as promoting active participation of junior members in committees of the European respiratory Society and sending junior scientists to do fellowships in European laboratories.
- Overall, the unit's project is ambitious and challenging, responding to important medical and societal needs, feasible and in agreement with the strategy of tutorial bodies. The unit should pay attention to the points of concern listed below to ensure the success of the project.

## RECOMMENDATIONS TO THE UNIT

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

In spite of the important number of recruitment achieved during the present contract, a single full-time investigator (a Professor dedicated to this activity) could be a limiting step in the continuous development of basic and transactional research.

Actions for protection of the environment could be further developed.

A steering committee devoted to discussing the implementation of scientific orientations on a regular basis will further improve the function of the unit. Permanent workforce respects gender equality but a detailed gender parity policy is necessary to ensure the perennial of this situation.

### Recommendations regarding the Evaluation Area 2: Attractiveness

Although the unit has a well-established scientific reputation, its contribution to the construction of the European research area should be improved.

### Recommendations regarding Evaluation Area 3: Scientific Production

The unit should be in a trajectory ensuing that the number and impact of the original articles will be more homogeneous between the axis.

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

Special attention must be paid to detect conflicts of interest related to studies sponsored by the pharmaceutical industry.

The non-clinical staff of the unit should be more actively involved in scientific outreach activities within specialized communities as well as in public communications.



## TEAM-BY-TEAM OR THEME ASSESSMENT

**Axis 1:** Epidemiological and (bio) clinical approaches to identify risk and prognostic factors in Interstitial Lung Diseases (ILDs)

Name of the supervisor: H. Nunes

### THEMES OF THE TEAM

Axis 1 research is essentially conducted 'at bedside' with clinical research aiming at identifying risk/progression factors of Interstitial Lung diseases (ILDs) with a particular focus on environmental causes (outdoor and indoor pollution, occupational exposures), socio-economic status and comorbidities (sleep apnea and COVID-19). Axis 1 is supported by established well-phenotyped cohorts. Axe 1 has demonstrated capabilities in leading multi-centre clinical trials to better define the respective indications of different medications classes in IPFs care pathways including management of acute exacerbations. Axis 1 also develops innovative tools for characterizing disease progression by validating pulmonary physiology functional parameters and artificial intelligence algorithms applied to imaging and thoracic HCRT-scans.

### CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations were given at the level of the unit and not for the axis.

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

Catégories de personnel	Number
Professeurs et assimilés + praticiens hospitaliers	9 (+ 2 shared with other axes)
Maîtres de conférences et assimilés	4 (+ 2 shared with other axes)
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	0
<b>Sous-total personnels permanents en activité</b>	<b>13 (+ 4 Shared)</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	2
<b>Sous-total personnels non permanents en activité</b>	<b>2</b>
<b>Total personnels</b>	<b>15 (+ 4 shared)</b>

## EVALUATION

### Overall assessment of the team

Axis 1 is outstanding demonstrating a long-standing and worldwide-renown expertise in Interstitial Lung diseases (ILDs). This is substantiated by leading and participating in scientific committees in the official respiratory medical societies in Europe and the US, publications in leading journals in the field (Am J. Respir Crit Care Med, Eur Respir J., Lancet Respir Med with unit members as PI), invitations to give conferences in the meetings of these societies and in international laboratories and universities (Taiwan University, Milan Research Hospital, CHUV Lausanne and CHU Erasme Bruxelles) and national competitive academic funding (ANR, ANSES, PHRC) with 4 contracts with members of the unit as PI and five as partners. Contributions are broad in the different field dimensions covering new contributive factors to ILDs progression, new therapeutic interventions with evidence established by collaborative pharmaceutical trials and identification of potential new actionable targets.

### Strengths and possibilities linked to the context

#### *Composition of the group*

Axis 1 is composed of clinician scientists and clinicians, with very strong links with the Hôpitaux Universitaires de Paris Seine-Saint-Denis (Avicenne & Jean-Verdier HUPSSD, APHP), thanks to their clinical activities. The axis was successful in recruiting two PhD students at permanent positions of MCU-PH.

#### *Scientific outputs and activities*

Scientific production of axis 1 is abundant and overall, of high quality with 178 scientific articles. More than 85 original articles have been published in top10% specialized journals in respiratory medicine, radiology and physiology fields such as Lancet Respir Med, AJRCCM, Eur Resp J., Thorax (PCD position), Radiology, and CHEST, (co-authors). Best publications of the Unit, Jama 2018 and JCI Insight 2018.

One major asset of axis 1 is the possibility to share biological samples (blood, urine, lung tissue biopsies) and clinical/epidemiological data from well-phenotyped patients with rare pulmonary diseases.

#### *Academic collaborations, reputation and appeal*

Axis 1 has developed strong and fruitful national and international academic collaborations. This is objectively documented at different levels: (i) scientific publications included various external multidisciplinary collaborations; (ii) A very good track record collaborative funding including ANRs and PHRCs (4 contracts as PI, 4 as partners) (iii) participation in national and international guidelines.

#### *Interactions with the non-academic world, impacts on economy, society, culture or health*

Axis 1 has developed numerous partnerships with industrial companies through clinical trials and associated funding. Members of the unit participated in numerous radiobroadcasts, magazine and newspaper interviews or TV shows. Dissemination of the unit's work is highly visible at the societal level with major collaborations with patients' association and impact in patients care.

The team obtained competitive funding successfully as promoter, from ANR (2 grants PI; 563 k€ and 15 k€ for H&P, 1 grant as collaborator), ANSES (1 grant PI, 199 k€ for H&P), PIA (1 grant PI, 57 k€ for H&P), foundations (1 grant PI form Fondation du Souffle, 75 k€; 1 grant PI form Fondation de France 65 k€).

#### *Involvement in training through research*

Axis 1 is involved into a careful training for students both in terms of quantity and quality. The axis has attracted 4 university-hospital Associate Professors and three clinicians during the last contract. Two PhD defences can be more specifically associated with axis 1. They are all MD students, and their PhD work was mainly founded by USP/APHP. They significantly contributed to the scientific production of the team (6 articles in first author position).

### Weaknesses and risks linked to the context

The axis has limited success in obtaining European academic grants (H2020, ERCs).

Regarding the true potential of the axis, valorisation activities merit to be extended in terms of patents and start-up creation.

Attractiveness might be improved by recruiting international postdocs

## Analysis of the team's trajectory

The valid strategy of axis 1 is to integrate social and environmental determinants of health as modifiable risk factors for progression of IPF/ILDs through an exposome approach (ANSES EXPOSOM-IPF project). This will provide unique and original epidemiological and clinical research datasets supporting new knowledge, funding and multi specialities academic collaborations. This strategy in axis 1 is parallelized by the development of preclinical models accounting for these exposures and complexity. Also, a better phenotyping including multi-scale modelling of lung fibrosis from HRCT imaging will reinforce the quality of the prospective cohorts. The integration of these new actionable risk factors will redirect intervention to inclusion of nutrition, physical activity and sleep. The committee is strongly valuing this strategic trajectory.

## RECOMMENDATIONS TO THE TEAM

The links between axes 1 and 2 are obvious, and a continuum of research appears quite clearly. In contrast, strengthening the links between axes 2 and 3 could reinforce axis 2, in particular by providing access to innovative in vitro models and bioengineering techniques. Fostering collaborations with basic scientists and establishing new interdisciplinary collaborations, as well as fully exploiting the precious cohorts of biological samples should help to upgrade the level of research and their valorisation. The team leader should encourage researchers of her group to apply for national (and international funds) as PIs and continues her effort to recruit permanent scientists for the next contract. Obtaining specific funding to support the new projects brought by the arrival of the BG group is required to guarantee their integration.

**Axis 2** Experimental comprehensive approaches to decipher the impact of hypoxic microenvironment in cellular models of ILDs

Name of the supervisor: C Planes

## THEMES OF THE TEAM

The aim of the axis 2 is to investigate experimentally the impact of chronic/intermittent hypoxic environment in cellular models of ILDs (sarcoidosis and idiopathic pulmonary fibrosis). Lately, the impact of air pollution on ILDs exacerbations was also included, following clinical studies carried out by the axis 1 of the unit, in particular the one from Sesé et al. (Thorax 2018), showing a correlation between air pollution and increased risk of exacerbations of idiopathic pulmonary fibrosis. Researchers from the axis 2 have also developed realistic preclinical mouse models of chronic pulmonary fibrosis and sarcoidosis. Research on innovative strategies for sarcoidosis treatment is also ongoing, with promising results regarding the possibilities of targeting the JAK/STAT pathway.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations were given at the level of the unit and not for the themes.

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

Catégories de personnel	Number
Professeurs et assimilés + praticiens hospitaliers	3 (+ 2 shared with other axes)
Maîtres de conférences et assimilés	1 (+ 4 shared with other axes, including the MCF with full-time research dedication)
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	2 (+ 1 administrative assistant shared)
<b>Sous-total personnels permanents en activité</b>	<b>6 (+ 7 Shared with other axes)</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	1 (ATER)
Doctorants	2
<b>Sous-total personnels non permanents en activité</b>	<b>3</b>
<b>Total personnels</b>	<b>9 (+ 7 shared)</b>

## EVALUATION

### Overall assessment of the team

This is a group that produced very good and high-quality translational research. The group is composed of teacher researchers and clinician researchers, and has a national visibility. Members succeeded in producing 29 articles as PDC in subspeciality journals (for example, Sci Rep 2018, Respir Res 2018, Am J. Physiol Lung Cell Mol Physiol 2018) and obtaining funding from ANSES and grants of the Fondation du Souffle. Two former PhD students were hired permanent clinician researchers.

### Strengths and possibilities linked to the context

This axis is fully complementary to the axis 1, and represents the translational and experimental side of the research undertaken by the unit on ILDs. It is composed of mostly teacher researchers, and clinician researchers,

from various disciplines (physiologist, pulmonology, histology, molecular and cell biology), which is a real strength to promote research in direct links with clinical challenges associated with ILDs. Some of the members are also members of the axis 1 (4 researchers) and 3 (3 researchers).

Six PhD defences can be more specifically associated with axis 2. They are mainly funded by MENRT (3 PhD), foundation (FRSR, 1 PhD), Franco-Peruvian consortium (1 PhD) + by USPN/APHP (1 MD-PhD). They significantly contributed to the scientific production of the team (14 articles in first author position). Concerning their future, one (MD-PhD) was recruited at a permanent position in the unit, only two of them had a position of postdoctoral fellow (1 in France, 1 in the UK), the other ones being project manager for Genethon, CDD Engineer in Biology in an Inserm lab, and one began medical studies ('Passerelle Médecine'). Six postdocs/ATER were also funded, mainly by the university (mainly ATER positions).

The work of axis 2 is nationally recognized in the domain of ILDs. It also has a unique position on sarcoidosis research, with the centre being the only centre in France recognized as 'Center of Excellence' for Sarcoidosis by the Foundation for Sarcoidosis Research (FSR). Research of axis 2 is well implanted in national networks (ORPHALUNG, RESPIFIL, GST networks).

The position on the research stage is shown by 49 original research articles published between 2017 and 2022 in eminent general or specialized journals, including 29 as first and (co-) last authors (for example, Sci Rep 2018, Respir Res 2018, Am J. Physiol Lung Cell Mol Physiol 2018, JCI Insight 2018, Front Immunol 2021, Physiol Rep 2022 Front Physiol 2022).

Numerous communications were done at international congresses (ERS congresses) and national congresses (CPLF, J2R 2022).

The axis 2 leader, also unit director, is strongly invested. three researchers are involved in several steering committees (Univ Paris13/USPN, AP-HP, INSERM CSS3...) scientific societies (ERS...)

The hypoxia platform, an original structure allowing in vivo and in vitro controlled exposure to hypoxia, is used by members of the unit, and is also accessible to other researchers outside the unit, is a real asset. The platform was upgraded with two new devices for in vivo and in vitro exposure, and successfully labelled as an 'SPN University Platform' in 2019.

A R&D collaboration with Baker-Ruskinn® (UK) was started to develop hypoxia exposure system for rodents. Although this collaboration could not lead to finance a CIFRE thesis as initially planned, this privileged relationship could in the future in more concrete interactions with the private sector.

The team obtained competitive funding successfully as a promoter, from ANSES (1 grant PI, 165 k€ with 45 k€ for H&P), foundations (3 grant PI form Fondation du Souffle, 2 × 60 k€ and 35 k€), scientific societies (2 grants as PI, 35 and 16 k€), ECOS SUD (1 grant PI 15 k€).

Members of the axis 2 are also strongly involved in clinical trials (EXAFIP I and II PROGRESSION-IPF, and EVER-ILD PHRC), and coordinating some, such as the 'QUIDOSE' PHRC. Results obtained by axis 2 may have important clinical applications to treat ILDs, such as the work performed on the role of the JAK/STAT signalling pathways in sarcoidosis.

This axis is deeply involved in scientific dissemination, towards patients and professionals (Association Fibrose Pulmonaire France...) and young public (programme Apprentis Chercheurs...). As pollution is a major societal issue, researchers from H&P are more and more solicited to communicate on this particular topic. Being very active in communicating their knowledge on this particular topic to mass media (France Inter...) and patient associations, they are becoming reference interlocutors on the subject.

## Weaknesses and risks linked to the context

There is still no full-time researcher, who could introduce new approaches and methods and reinforces the group. The departure of one PI could weaken the team, although strategies to cope with this event have been well explained and seem very realistic (in particular, the possible recruitment of an Associate Professor with the same profile as the leaving PI – MCF CNU 64/65).

Experimental results obtained by the axis 2 are published in 'intermediate' journals and not high-notoriety. Although the number of applications and the success rate at competitive national calls for grants have increased relatively to the last HCERES evaluation, it is still low.

## Analysis of the team's trajectory

The unit trajectory proposes the integration of the group 'Biotherapies & Glycoconjugates' (BG) in 2025, mostly into the axes 2 and 3. This group is composed of 7 SPN University staff and is specialized in the field of glycobiology and intercellular communications. It is expected that this integration will strengthen and energize axis 2. In particular, a new program regarding the role of proteoglycans (PGs) in the development of pulmonary fibrosis is planned. The investigation on the role of (PGs) in IPF is supported by preliminary data, also

demonstrating the ability of researchers from the different units to work together. Obtaining grant is, however, absolutely required to support this program and guarantee a successful integration of the BG group.

Researchers from axis 2 also plan to continue to investigate the role of urban pollution on IPFs (FIPOLL study), and launch in new projects to analyse the consequences of long-term silica exposures on the lung (this latter could be supported by an ANR grant PUF-ARENA full proposal submitted to ANR aapg-2023). This is in connection with the axis 1, and is fully coherent with the scientific politics of the unit.

Regarding sarcoidosis, the focus is on the investigation of HIF-alpha and JAK-STAT signalling pathways. The methods (innovative *in vitro* 3D models, pertinent models) together with the access to human samples are good indicators of success, and clinical utility to treat sarcoidosis can be expected from this work.

## RECOMMENDATIONS TO THE TEAM

The links between axis 1 and 2 are obvious, and a continuum of research appears quite clearly, at least from axis 1 to axis 2. Strengthening the links between axis 2 and the other axis of the team could reinforce axis 2, in particular by promoting the 'bench to bedside' research (axis 2 to axis 1), and by providing access to innovative *in vitro* models and bioengineering techniques (axis 3 to axis 2), respectively.

Introducing a level of priority between the different projects, as well as fully exploiting the precious cohorts of biological samples should help to upgrade the level of research and their valorisation. The team leader should encourage researchers of her group to apply for national (and international funds) as PIs and continues her effort to recruit permanent scientists for the next contract as well as increase the level of publication in more visible journals. Obtaining specific funding to support the new projects brought by the arrival of the BG group is required to guarantee their integration.

**Axis 3:** Innovative strategies to facilitate the repair, regeneration, replacement of lung tissues (scientific supervisors)

Name of the supervisor: E Martinod & V Besnard

## THEMES OF THE TEAM

The scientific topic of the axis 3 is focused on the development of innovative strategies for lung and large airway repair, using regenerative medicine approaches: (i) based on cell therapy, the alveolar repair and regeneration aims to decipher the potential paracrine role of human bone marrow derived mesenchymal stem cells on AT2 cells submitted to hypoxia, showing that MSC's conditioned media was able to reverse the deleterious effects of hypoxia on AT2 cells; (ii) based on tissue engineering, the team aims to repair and regenerate large airways (translational studies) using, among others, biomimetic prosthesis. Furthermore, clinical research from 'bedside' aims at improving cadaveric aorta conditioning for tracheal regeneration.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations were given at the level of the unit and not for the themes.

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

Catégories de personnel	Effectif
Professeurs et assimilés + praticiens hospitaliers	2 (+ 2 shared with other axes)
Maîtres de conférences et assimilés	1 (+ 2 shared with other axes, including the MCF with full-time research dedication)
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	0(+ 1 administrative assistant shared)
<b>Sous-total personnels permanents en activité</b>	<b>3 (+ 5 shared with other axes)</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	2
<b>Sous-total personnels non permanents en activité</b>	<b>3</b>
<b>Total personnels</b>	<b>6 (+ 5 shared)</b>

## EVALUATION

### Overall assessment of the team

The scientific output of the theme is remarkable as it demonstrated major innovation in lung repair and regeneration. The team developed a strong *in vitro/in vivo* expertise aiming to validate innovative strategies. Their pioneering work in understanding cytoprotective mechanisms, bioengineering tracheal substitutes, and unravelling cellular events in tissue regeneration showcases significant contributions to the field. Despite these assets, the team has to increase collaborations between basic scientists and socio-economic actors and its attractiveness with the recruitment of additional permanent researchers and PhD students.

### Strengths and possibilities linked to the context

The team is composed of clinicians (3), clinician scientists (3) and scientists/enseignants-chercheurs (2). Clinicians involved in the team have a strong interaction with the Thoracic surgery department of Avicenne hospital. This

axis involves two PhD students – MD/PhD students – . This strategy facilitates integration between translational, clinical and health services research.

Translational research is a key strength of axis 3, supported by the clinical research leadership of the co-axis responsible who is Head of Thoracic Surgery Department at Avicenne hospital, the access to cutting-edge facilities like the 'Hypoxia Platform,' and the establishment of a transgenic mouse model for tracheal replacement.

Furthermore, the Head of Thoracic Surgery Department at Avicenne hospital possesses expertise in surgery and has access to the Alain Carpentier platform facility. It is engaged in innovative clinical/preclinical surgery, experimental approaches, and bioengineering in collaboration with L. Trichet from LCMCP.

Notable contributions in clinical settings include scientific publications that advance understanding of airway replacement using stented aortic matrices – JAMA, 2018 and Am J Transplant. 2022) as PI.

Finally, the axis actively participates in clinical trials – TRITON 01 and TRITON 02 – and contributes to guidelines papers – J Visc Surg. 2021).

Academic collaborations, reputation and appeal

Theme/Axis 3 built a strong national network in biomaterials and large airway regenerative medicine through collaborative grants totalling 120 k€ from ANRs – 3 ANR projects with one as PI and one PRCE – , a 300 k€ PHRC grant, and support from national societies worth 105 k€. Axis 3 has developed partnerships with industrial companies (2) through preclinical/clinical trials and PRCE funding. The axis also participates in national and international guidelines.

## Weaknesses and risks linked to the context

While members actively participate in selective national grants, including three ANR programs – one as PI – and PHRC – two – , the total funding secured remains relatively modest when compared to the number of permanent scientists involved in this ambitious program. The requested budget should include postdoc financial support to increase the attractiveness.

Besides, there are no junior members – lecturer – serving as PI and there is a notable absence of industrial collaborative funding for stem cell therapy approach and alveolar regeneration.

The proportion of collaborative publications is also disproportionately high compared to publications produced solely by the team – five versus thirteen – .

The absence of both scientific PhD students and postdocs within this axis 3 weakening the work.

## Analysis of the team's trajectory

The trajectory of this Axis focused on the replacement and regeneration of large airways, has been marked by significant achievements and promising avenues for future research. It aims to enhance its expertise in two key areas. In the first area, the focus is on repairing alveoli, which involves the use of heparan sulfate mimetics through an industrial collaboration funded by ANR-PRCE, as well as exploring the potential of mesenchymal stem cells. In the second area, efforts are directed towards improving the success rate of large airway replacement, with a particular emphasis on enhancing the performance of cryopreserved aortic allografts – PHRC TRITON 02 – and evaluating the suitability of new medical devices like collagen and glycosaminoglycane-based coatings. Furthermore, with the goal to decipher how the immune system influences tracheal regeneration using aortic matrices, a powerful transgenic mouse model will be developed, supported by ANR funding. This axis 3 strategy will therefore be running in parallel to the clinical programs.

## RECOMMENDATIONS TO THE TEAM

Building connections between axes can enhance the foundation of both basic and translational knowledge and research strategy. This, in turn will increase the attractiveness and the recruitment of full-time tissue engineering researchers and scientific PhD students. Encouraging the pursuit of European funding to support axis 3 ambitious projects is also strongly recommended.



## CONDUCT OF THE INTERVIEWS

### Date

**Start:** 09 octobre 2023 à 8 h 30

**End :** 09 octobre 2023 à 18 h 30

**Interview conducted : on-site**

### INTERVIEW SCHEDULE

9 Octobre 2023

8 h 30 – 8 h 45 Arrivée des experts et installation/café

9h-10:45 a.m. *Présentations : Bilan et Trajectoire*

1) Bilan de l'unité (15 min) et discussion (15 min)

2) — Axe1 : H Nunes (10min/axes et 5 min questions)

Axe2 : C Planes

Axe3 : E Martinod et V Besnard

3) Présentation de la Trajectoire de l'unité par la directrice (15 min) et Discussion (15 min)

10 h 45-11 h Entretien avec les ITA (3) — Lead: Veronique Montcuquet

11h-11h30 Entretien avec les étudiants : Lead: Halima + all

11 h 30-12 h Entretien avec les chercheurs : Lead: Mustapha + all

12 h-12 h 30. Rencontre avec les tutelles

**Université Sorbonne Paris Nord**

VP recherche actuelle : Pascale Molinier [vpcr@univ-paris13.fr](mailto:vpcr@univ-paris13.fr)

Précédente : Pr Anne Pellé [vpcac@univ-paris13.fr](mailto:vpcac@univ-paris13.fr) ABSENTE

**Inserm**

DR Paris-IDF Centre Nord [claire.de-marguerie@inserm.fr](mailto:claire.de-marguerie@inserm.fr)

IT PMN. Raymond Bazin [raymond.bazin@inserm.fr](mailto:raymond.bazin@inserm.fr)

12 h 30-13 h 30 Lunch et discussion et préparation des questions au DU (huis clos)

13 h 30-14 h 30 rencontre avec le DU

15 h-17 h Travail sur le rapport Hceres : huis clos du comité

17 h 30 Départ

### PARTICULAR POINT TO BE MENTIONED

NA

## GENERAL OBSERVATIONS OF THE SUPERVISORS

Monsieur Eric Saint-Aman  
Directeur du département d'évaluation de la  
recherche  
Hcéres  
2, rue Albert Einstein  
75013 PARIS

Villetaneuse, le 27 novembre 2023

*Objet : Rapport d'évaluation DER-PUR250024489 - H&P - Hypoxie & Poumon : pneumopathies  
fibrosantes, modulations ventilatoires & circulatoires*

Cher Monsieur,

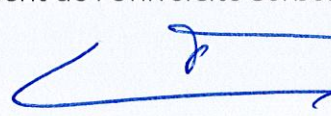
Nous faisons suite à votre courriel du 16 novembre 2023 par lequel vous nous avez transmis le rapport d'évaluation de l'unité de recherche Hypoxie & Poumon dirigé par le Pr Carole Planès.


L'université Paris XIII – Sorbonne Paris Nord souhaite remercier au nom de l'ensemble des personnels de l'unité de recherche Madame Sophie Ezine, Déléguée du HCERES, Monsieur le Professeur Jorge Boczkowski, Président du Comité, ainsi que les membres du Comité pour la qualité des échanges lors de la visite d'évaluation effectuée sur site en présentiel le 9 octobre 2023, ainsi que pour la qualité du rapport provisoire d'évaluation de l'Unité. Nous n'avons pas d'observation de portée générale à formuler sur ledit rapport.

Nous nous réjouissons de voir confirmer les grandes qualités de cette équipe, en particulier son expertise reconnue sur le plan international dans les domaines de l'hypoxie et des pneumopathies interstitielles diffuses. L'université se félicite également de voir mis en évidence l'excellence des résultats et le très bon dynamisme de la vie de l'unité.

Je vous prie de croire, Monsieur le Directeur, en mes sincères salutations.

Le Président de l'Université Sorbonne Paris Nord

  
Christophe Fouqueré



The Hcéres' evaluation reports are available online: [www.hceres.fr](http://www.hceres.fr)

**Evaluation of Universities and Schools**  
**Evaluation of research units**  
**Evaluation of the academic formations**  
**Evaluation of the national research organisms**  
**Evaluation and International accreditation**



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

[hceres.fr](http://hceres.fr)

[@Hceres\\_](https://twitter.com/Hceres_)

[Hcéres](https://www.youtube.com/Hceres)