

Research evaluation

EVALUATION REPORT OF THE UNIT P3Cell - Pathologies pulmonaires et plasticité cellulaire

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université de Reims Champagne-Ardenne Inserm

EVALUATION CAMPAIGN 2022-2023 GROUP C

Rapport publié le 25/01/2023



In the name of the expert committee¹ :

Esther Barreiro, Chairwoman of the committee

For the Hcéres² :

Thierry Coulhon, President

Under the decree n° 2021-1536 of 29th November 2021:

¹ The evaluation reports "are signed by the chairperson of the expert committee". (Article 11, paragraph 2); ² The president of the Hcéres "countersigns the evaluation reports established by the expert committee and signed by their chairperson." (Article 8, paragraph 5).



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

Chairperson:	Mrs Esther Barreiro, Hospital del Mar-IMIM, Universitat Pompeu Fabra, Barcelona, Spain
Experts :	Mr Patrick Berger, Université de Bordeaux Mrs Sylvia Cohen-Kaminsky, CNRS, Le Plessis-Robinson (representative of CSS Inserm) Mr Bruno Crestani, Université Paris Cité (representative of CNU) Mrs Beatrice Eymin, INSERM, La Tronche Mrs Stéphanie Venteo, INSERM, Montpellier (supporting personnel)

HCÉRES REPRESENTATIVE

Mrs Sophie Ezine



CHARACTERISATION OF THE UNIT

- Name: Pathologies pulmonaires et Plasticité Cellulaire
- Acronym: P3Cell
- Label and number: UMR-S 1250
- Composition of the executive team: Myriam POLETTE

SCIENTIFIC PANELS OF THE UNIT

SVE6: Physiologie et physiopathologie humaine, vieillissement

SVE4: Immunité, infection et immunothérapie

SVE7 : Prévention, diagnostic et traitement des maladies humaines

THEMES OF THE UNIT

UMR-S 1250 is a single-team unit attached to the Multi-Organism Thematic Institute (Itmo) "Physiopathology, Metabolism, Nutrition" (PMN).

The unit is interested in respiratory diseases such as cystic fibrosis, chronic obstructive pulmonary disease (COPD), non-small cell lung cancer (NSCLC) and upper airway cancer (UAC). UMR-S 1250 has focused its activity on the plasticity of the respiratory epithelium along two axes: epithelial transdifferentiation in the remodeling mechanisms of the respiratory epithelium in cystic fibrosis and COPD, and epithelial dedifferentiation in the processes of tumour progression in NSCLC and cancers of the VADS. Although the mechanisms observed are sometimes different, many common molecules and pathophysiological processes are involved in the plasticity of epithelial cells and have been the subject of cross-disciplinary work between the two themes of the unit.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The Inserm UMR-S 1250 unit, "Pulmonary Pathologies and Cellular Plasticity" was jointly created by Inserm and the University of Reims Champagne-Ardenne (Urca) on January 1, 2018. The UMR-S 1250 has a significant experience in the respiratory field since more than 30 years with the creation of the Inserm 314 unit directed by Dr Edith PUCHELLE.

The team is located within the Reims University Hospital where it occupies a three-storey building of 1,400 m². The equipment of the unit and the Bioimaging Platform ("Plateau Technique d'Imagerie Cellulaire et Tissulaire", PICT) of the Urca are located on the ground floor. The first floor houses the administrative sector. The upper floor is divided into work spaces and dedicated offices.

RESEARCH ENVIRONMENT OF THE UNIT

On a local level, the unit is part of the "Cap Santé" Federative Research Structure (SFR Cap Santé) supported by the Urca and which brings together teams working on the issue of health and quality of life (1 Inserm unit, 3 CNRS units, 1 UMR INERIS, 1 UMR ANSES and 11 university teams). The main missions of the SFR Cap Santé have been to develop a common scientific policy, to plan scientific strategies and to financially support cooperation projects between the members of the SFR.

In terms of scientific activity, four federative thematic axes are developed, two of which are co-coordinated by members of the unit (the Health/Environment axis and the Regeneration / Cancer / Ageing" axis)

Members of the unit play a role in the operation of several Urca platforms (the Cellular and Tissue Imaging Platform (Pict), Cytometry and Animal Care). Three senior researchers are members of the Cellular and Tissue Imaging Platform (Pict) which holds an IBiSA endorsement; the three platforms Health, Pict, Cytometry and Animal Care. Two senior researchers are also involved in various bodies, namely the President of the Research and Innovation Commission of the University Hospital and the Biomedical and Public Health Research Committee.

On a regional level, the unit participated in the creation of a University Hospital Federation (FHU CURE "CUring and pREventing chronic inflammatory condition"). This structure aims to bring together teams working on the clinical and fundamental aspects of inflammation in the Grand Est region and to develop an integrated approach to care, research and training. It brings together clinicians and staff from the Nancy and Reims university hospitals, as well as researchers and teacher-researchers from several research teams (universities,



CNRS) and Inserm research units, including UMR-S 1250. This project is part of the inter-regional approach to structuring research on inflammation with the creation of the European Institute of Inflammatory Diseases (E3I) of the Grand Est region, which is supported by the universities, university hospitals and research units of Strasbourg, Nancy and Reims.

UNIT WORKFORCE: in physical persons at 31/12/2021

Permanent personnel in active employment	
Professors and associate professors	9
Lecturer and associate lecturer	9
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	16
Subtotal permanent personnel in active employment	36
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	3
Post-docs	2
PhD Students	6
Subtotal non-permanent personnel	18
Total	48

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: NON-TUTORSHIP EMPLOYERS ARE GROUPED UNDER THE HEADING "OTHERS".

Employer	EC	С	PAR
Université de Reims	18	0	5
CHU Reims	0	0	8
Inserm	0	2	3
Total	18	2	16



UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	801
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	1 800
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	732
Own resources obtained from international call for projects (total over 6 years of sums obtained)	90
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.)	249
Total in euros (in K€)	3 672



GLOBAL ASSESSMENT

The P3Cell unit is a monothematic unit with three major axis (chronic obstructive pulmonary disease -COPD-, cystic fibrosis, and lung cancer) that conduct research on pulmonary pathologies at the fundamental and clinical levels.

The main scientific objectives of the unit are excellent. They aim to better characterize the molecular mechanisms that support cellular plasticity during the remodelling of the bronchial epithelium which occurs during respiratory diseases such as COPD, cystic fibrosis and cancer in order to define biomarkers and novel therapeutic targets.

The unit's resources are excellent, since the unit's members have a very strong anchorage in the local, regional, and national pulmonary field landscape. This is exemplified by the involvement of the unit in the regional CAP Santé and FHU CURE networks as well as the E3I inter-regional networks.

The unit showed some success in obtaining funds from various institutional partners and associations. Three international contracts (as PI in OMS and in 4 PHC Tournesol; as partner in NIH-RO1, total amount $90K\in$), ten national contracts (3 as PI in 1 STIC-Revolens and 7 as collaborators in 4 PHRC, 1 IRESP-INCa 2020, 1 ANR 2019, 1 ANSES,... total amount $732K\in$); eleven regional (8 as PI in 1 Reims FEDER, 5 allocations doctorales,...) and 36 foundations (33 as PI in 8 Ligue régionale contre le cancer, 3 Vaincre la Mucovicidose, 4 Lions Club, ...) with a total amount $1800K\in$).

Funding from industrial contracts (6 in total, Laboratoires CHEMINEAU, AstraZeneca,... total amount 249k€) is very good (the know-how of the unit is exploited through one contract with Astra-Zeneca) and the unit has a policy of valorisation of their results (2 patents in 2018 and 2020), which is currently limited to patent filing.

The scientific publications of the unit are of very good quality, with 15% articles published in the best peerreviewed journals. In the last period, members of the unit have published a total of 295 articles, of which 67 articles as PI (first or last authors, in 35 scientific articles, 19 clinical articles, 13 reviews) with one EBioMedicine, one J. Pathol, one Cancers, one JAMA, one CHEST, one Eur Respir J, one Am J Respir Critical Care Med and co-PI in one Nat Comm).

However, publications in generalist journals remain low and a strategy aiming at supporting high-risk emergent projects has not been clearly defined.

The attractiveness of the P3Cell research unit is very good. P3Cell demonstrates a strong implication in the training of students (39 Master students, 19 PhD) and young scientists (11 license) through research. Nonetheless, the number of PhD students who defended during the mandate is low with respect to the number of senior scientific staff (13/20) and the number of HDR (14). No foreign PhD, post-doctoral fellows or visiting professor were hosted.

The functioning of the unit is also excellent. The management of human resources (participative management, gender parity, promotion, prevention of psycho-social risks, and security of the staff) is recognized by both the whole staff and the local supervisory authorities. The ethical guidelines for research and the data management and protection of the unit are clearly defined. Despite these strengths, the size of the unit remains small (only 9.5 full-time equivalent) and applications to international or European contracts are still insufficient. The unit has to deal with highly competitive fields for each axis.

The unit shows moderate participation and organisation in congresses and is not yet involved in European or international networks. Meanwhile, it has strengths in terms of its involvement in the scientific evaluation of research projects at the national level (300 projects reviewed) and international (295 articles reviewed). The unit also participates in scientific/academic boards (45 boards) at the regional and national levels. The unit benefits from easy access to the expertise and cutting-edge technological environment (13 technical platforms) in which members actively participate (steering committees).

The overall inclusion of the unit's research in society is very good. The unit P3Cell has demonstrated an excellent interaction with the socio-economic environment through its involvement in the associative world (general assemblies with various patients' associations), its ability to popularise science (welcoming pre-baccalaureate students (17 since 2016), as part of their discovery of the research world). The unit also uses mass media such as local radio (*France Bleu Champagne programmes* 2017, 2018, 2019, 2021), and the written press ("*Paris Match*" in 2016, various articles, interviews and videos on the Internet in *ORL/Pneumologie/Allergologie Pratique* and in the daily news-paper "*Le Quotidien du Médecin*").

Overall, the P3Cell unit should reinforce the design of projects that include common objectives to the three main themes and increase its international visibility.



DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The unit has considered the recommendations of the previous Hcéres evaluation. Indeed, the unit has improved the following 3 points:

- The unit has expended its expertise in omics-based strategies. In particular, the unit has (i) identified essential genes in P aeruginosa infection of the epithelium of healthy, CF or COPD patients using transposon sequencing; (ii) evaluated the endogenous microbiota of COPD patients; (iii) compared healthy and COPD epithelia using exome sequencing and transcriptomic approaches.
- The unit has also extended its participation in international networks, in particular through the European Respiratory Society and Epithelial-Mesenchymal Transition international Association. The unit has also started collaboration with UK and US colleagues. However, the unit does not lead international network but collaborate within the R01 project on bacterial resistance.
- New industrial collaborations has been started with private partners such as AstraZeneca, ManRos Therapeutic, and Laboratoires Chemineau.

B - EVALUATION AREAS

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

Assessment on the unit's resources

The unit's resources are excellent since (i) the unit's members have a very strong anchorage in the local, regional and national pulmonary field landscape (involvement in CAP Santé, FHU CURE, E3I); (ii) a large number of permanent technical staff (i.e., 10 persons representing 7,6 full-time equivalent; (iii) the number of full-time researchers is 2 (CR Inserm) for a small team; the allocation of human resources is well-distributed between the different thematic axes; (iv) 4 MCU-PH and 1 MCU have been recruited during the last period ; (v) the financial resources of the unit (i.e., 3.6 M€) which have to be normalized according to the number of full-time equivalent staff researchers (i.e., 9.5) have been obtained from 10 national grants (3 as PI in 1 STIC-Revolens, collaborators in 4 PHRC, 1 ANR, 1 ANSES and 1 INCA), 11 regional projects (8 as PI) and 36 supports from charities / foundations (33 as PI including 1 FRM, 10 Ligue régionale contre le cancer, 4 Vaincre la Mucoviscidose, 9 Association des Amis de l'American Memorial Hospital) ; (vi) the unit's equipment is remarkable and includes various platforms (cytometry, bacteriology, ...), this latter being recently funded by the Reims Champagne Ardennes University (Urca) for 300 k€.

Assessment on the scientific objectives of the unit

The main scientific objectives of the unit are excellent and are divided in three axes. They aim to better characterize the molecular mechanisms that support cellular plasticity during the remodelling of the bronchial epithelium which occurs during pathologies such as COPD (axis 1), cystic fibrosis (axis 2) and both lung and ENT cancers (axis 3) in order to define biomarkers and novel therapeutic targets. This represents a critical need to improve the management of the patients. The global scientific aims are clear and very well-supported by the well-recognized expertise of the unit's members, the very strong complementarity between biologists and clinicians of the unit, the access to highly relevant patient samples and the published results.



Assessment on the functioning of the unit

The functioning of the unit is excellent. The management of human resources (participative management, gender parity (19 M and 21 F including the director of the unit who is F), promotion (2 CRHC, 2 PU-PH, 1 Al Inserm), prevention of psycho-social risks, security of the staff) is recognized by both the whole staff and the local supervisory authorities. The ethical policy rules of research and the data management and protection of the unit are clearly defined.

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

Strengths and possibilities linked to the context

The scientific activity of the unit relies on the development of translational research projects focused on the remodelling of respiratory epithelium in the context of COPD, cystic fibrosis (CF), Non Small Cell Lung Cancer (NSCLC) and Head and Neck (ENT) cancers.

The scientific activities of the unit are fully supported by a very strong regional and national anchorage in the respiratory field. Over the last period, the unit has strengthened its regional network through its participation in the CAP Santé federative research structure led by University of Reims (Urca) and the creation of a University Hospital Federation (FHU CURE "CUring and pREventing chronic inflammatory condition"). The unit is also part of an inter-regional approach aiming at structure research in inflammation with the creation of the European Institute of Inflammatory Diseases (E3I) of the Grand-Est region, supported by the Universities, CHU and research units of Strasbourg, Nancy and Reims.

The scientific activities of the unit are also fully supported by a very strong complementarity between biologists and clinicians from the University Hospital of Reims who are full members of the unit and promote translational and clinical research (involvement of unit's staffs in 54 clinical trials). During the last period, the unit welcomed 8 new staffs in the field of bacteriology (4 HU and 4 H) from the former EA4687 team. These new members have been successfully integrated in existing projects in link with COPD and CF. Trans-disciplinary projects aiming at investigating the role of infection by Pseudomonas aeruginosa on the remodelling of pulmonary epithelium in COPD and CF have already been set-up.

Owing to the strong collaboration with clinicians, one of the main strengths of the unit is the accessibility to human samples through collaboration with the various clinical departments of the University Hospital of Reims (pneumology, thoracic surgery, oto-rhinolaryngology). The unit also has access to samples from the pathology department's tumour collection managed by the Biological Resource Centre. In addition, the unit works in close collaboration with the paediatrics department and the Cystic Fibrosis Resource and Competence Centre (CRCM).

The global organization of the unit (space, equipments, and human resources) is fully in line with its scientific activities. As an example, the unit anticipated the arrival of the bacteriology team and built a second L2 laboratory entirely dedicated to bacteriological experiments with the support of Urca. Achievements of scientific objectives are also ensured by the unit's access to all the resources of the URCA technological platforms [Cellular and Tissular Imaging platform (PICT, IBISA label), cytometry (URCACyt), molecular analysis (P3M), animal facilities (URCAnim)]. Four members of the team are members of the Scientific Organisation Committees of three platforms (PICT, cytometry and animal facilities). Over the last six years, the unit has also acquired new scientific equipment (automate for fixation, electrophysiology system in Ussing chamber, cell counting/viability system) and renewed others (incubators, NanoDrop spectrophotometer, cytocentrifuge, chemical hood, real-time PCR system), all from its own resources.

Over the last six years in support to its activity, the unit has increased the number of permanent staffs from 24 to 36, showing a strong and continuous development of the unit. The current composition of the unit is 48 members including two Inserm CRHC, fourteen HU, five U, and eight PH, eleven ITA/Biatss, six PhD students and two post-docs. During the last six years, three permanent staffs have left the unit (2 retired, 1 on extended leave), thirteen permanent staffs have joined the unit (1 MCF, 1 PR, 4 MCU-PH, 2 PU-PH, 5 PH), two permanent staffs (1 IR Urca, 1 Tech Inserm) and eight non-permanent staffs (2 post-docs, 1 PHU, 2 tech Inserm/Urca, 2 IR Inserm/CHU, 1IE Urca) have been recruited. The diversity of expertise of the members of the unit covers different fields such as cellular biology, bacteriology, pathology, histology, emergency medicine, paediatrics, informatics and physics.



During the last six years, the unit has demonstrated a strong research training policy (10 PhD students, 39 Master students, 14 Bachelor/BTS students and 17 pre-baccalaureate trainees)

The unit finances its research from its own resources for about 80% (not including wages). In 2021, this represents 539K€. Over the past six years, these own resources were obtained from three international contracts (as partner in NIH, as PI in OMS, as PI in PHC Tournesol, total amount 90K€), ten national contracts (3 as PI, including 1 STIC-Revolens); seven as collaborators in four PHRC, one IRESP-INCa 2020, one ANR 2019, one ANSES 2020 total amount 732K€), 46 regional and 36 from foundations contracts (33 as PI, total amount 1800K€), six R&D contracts with industry as PI (total amount 249k€). From 2018 to 2021, the funding from national calls has increased testifying the unit's ability to successfully respond to competitive national and international calls.

Weaknesses and risks linked to the context

The size of the unit remains small (only 9.5 Full-time equivalent).

Concerning the permanent staff members, the unit is mainly made up of clinicians (MCU-PH, PU-PH, PH) whose involvement in research is in fact partial and includes only two full-time researchers (CRHC Inserm). Although gradual increase in the past six years, applications to national contracts, in particular ANR to promote the recruitment of PhD students/post-docs, are still insufficient. Noteworthy, three new ANR grants have been obtained in 2022 (including 1 coordinated by a unit's member). Application to international or European contracts are still limited.

2/ The unit has set itself scientific objectives, including the forward-looking aspect of its policy.

Strengths and possibilities linked to the context

The unit's activities are centred on the study of the plasticity of the respiratory epithelium along three axes, epithelial transdifferentiation in the remodelling mechanisms of the respiratory epithelium during cystic fibrosis and COPD, and epithelial dedifferentiation in the processes of tumour progression in NSCLC and ENT cancers. At the public health level, the scientific objectives of the unit perfectly fit within the major societal challenges in the field of these respiratory diseases that are to improve the management of patients, in the short and medium term, through the identification of predictive biomarkers as well as the development of personalised medicine and therapeutic innovation.

The unit has started to develop transversal and multidisciplinary projects between the different axes in link with: (1) Ciliogenesis in COPD, CF and NSCLC;

(2) Infection by Pseudomonas aeruginosa and remodelling of respiratory epithelium in COPD and CF.

These cross-cutting projects could strengthen the competitiveness of the unit in each field.

The scientific objectives for each axis are well-defined and the structuration of each axis in term of human and financial resources appears appropriated. The projects feasibility is very well-supported by the complementary expertise between biologists and clinicians of the unit and the access to pertinent and adapted cellular tools, animal models and human samples. In line with the unit's expertise, three staffs are members of specialized journal editorial boards (Frontiers in Oncology, Cancers, Pathogens, PLOS Pathogens, Clinical Respiratory Journal, Revue des Maladies Respiratoires).

Beside its regional and national partnerships, and following the recommendations of the last Hcéres evaluation, the unit has extended in the last six years its international academic network (University of Liege, Belgium; McGill University, Genome Center Montreal, Canada; Respiratory Biomedical Research Unit, Southampton, United Kingdom; Lunquist Institute for Biomedical Innovation, Torrance, United States).

The success of these international collaborations is attested by four publications (co-Pl in Nat Commun 2021, Cancers 2019, Cancer Res 2016, Oncogene 2020, 2 as Pl).

The unit participates in an international NIH-R01 project (50k€), which aims to establish the profile of bacterial resistance to antibiotics in pneumonia by studying volatile metabolites in exhaled air. The unit has also become more involved in international scientific networks and networks of excellence via its participation in working groups on COPD within the European Respiratory Society (ERS) and on EMT through the Epithelial-Mesenchymal Transition International Association (TEMTIA).

The unit is developing an explicit, participatory governance and offers multiple possibilities for staff involvement in decision-making affecting the life and priorities of the unit. The Director is assisted in her management by a management assistant and by a Laboratory Council (CoLab). The unit has also set up a Scientific Strategy Committee for the various theme leaders. The unit organises scientific seminars every fortnight with presentations by the unit's statutory researchers, by PhD students and by post-docs.



Weaknesses and risks linked to the context

Despite an overall increase in the last six years, the participation of the unit in international networks still remains low.

The unit has to deal with highly competitive fields for each axis.

3/ The functioning of the unit complies with the regulations on human resources management, safety, the environment and the protection of scientific assets.

Strengths and possibilities linked to the context

The unit has set up internal rules covering governance and decision-making, staff working conditions, health and safety, protection of scientific potential and management of the laboratory's resources.

The unit has implemented a staff training policy. The members of the unit participated in 175 training actions including security staff procedures, management of human and financial resources, and animal experimentation from 2016 to 2021, which represents a total of 235 days.

The unit supports staffs in the different campaigns of promotion organised by the supervisory authorities. During these 6 last years, five members of the unit have been promoted (2 CRHC INSERM, 2 PU-PH, 1 AI INSERM).

Gender balance is achieved for researchers, teacher-researchers (10 women, 11 men), for hospital practitioners (4 women, 4 men), and for the management structure (headed by a woman). The unit has recently appointed a laboratory correspondent within the framework of the INSERM Parity and Professional Equality Plan.

In terms of safety, the workspaces are very well-organised to divide the activities and limit the risks. The laboratory is equipped with two level 2 biohazard containment sectors, with activities related to eukaryotic cell models or class 2 bacteriological agents. At the end of 2021, a new referent for the two L2 laboratories has been appointed. A Local Health, Safety and Working Conditions Committee (CLHSCT), made up of the unit director and the two prevention assistants, meets twice a year and carries out an updated assessment of the risks associated with staff activities and proposes new preventive actions. In order to fully comply with health and safety regulations, the unit also benefited from Inserm's assistance in bringing the liquid nitrogen storage room into compliance.

The evaluation and prevention of Psycho-Social Risks (PSR) is integrated into the general risk prevention approach of the laboratory. The staff participate in the PSR assessment campaigns and a think tank meets, accompanied by the prevention advisors.

A data protection policy has been put in place (secure access to premises by badge). An IT charter has been drawn up for each new employee. Computer data storage with double daily back-up on on-site and external storage spaces exist.

The unit is committed to following environmental preservation measures (recycling, waste reduction, reduction in paper use, carbon footprint) and has recently appointed a sustainable development referent (end 2021).

A business continuity plan has been put in place and was put into action during the first wave of the SARS-CoV-2 pandemic.

Weaknesses and risks linked to the context No specific weaknesses have been identified.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the P3Cell research unit is rated very good.

P3Cell demonstrates a strong implication in the training of students and young scientist through research (19 PhD students and 50 trainees). The unit has strengths in terms of its involvement in the scientific evaluation of research projects on a national scale (300 projects reviewed) and of scientific articles (295 articles reviewed), its participation in scientific/academic board (45 boards) on a regional and national levels, its willingness to



welcome and train local young students and researchers. However, no foreign students or post-doctoral fellows were hosted during current mandate.

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

Strengths and possibilities linked to the context

The unit expertise is recognized at the international level, with regard to the tremendous number of scientific publications (295 total, 67 as PI).

Members have reviewed over the period 2016-2021 about 300 projects. The projects were reviewed for various institutional bodies (ANR, ANSES, INCa, ITMO Cancer, national PHRC, Cancéropôle Est/PACA) and charities (LCC, VLM, Cariplo Foundation, Endowment Fund for Respiratory Research) with more than 300

reports. The journals included top specialty journals (American Journal of Clinical Pathology, American Journal of Respiratory Critical Care Medicine, Antimicrobial Agents and Chemotherapy, Clinical Respiratory Journal, European Respiratory Journal Open Research, Journal of Antimicrobial Chemotherapy, Lung Cancer, Respiratory Research, Scientific Reports, Cancers, Journal of Chemotherapy, Histology and Histopathology, etc.), and 175 reviews were from five major publishers.

Weaknesses and risks linked to the context

The P3Cell unit shows moderate participation in congresses. There are six invitations at the international level (4 staff members involved), thirteen international and 29 national oral communications, 25 international and 28 national poster presentations, resulting in the coordination of 4 volumes of conference proceedings (all for SPLF "Société de Pneumologie de Langue Française"), and 28 papers published in conference proceedings.

The Unit staff has two Inserm Research associate (CRHC) and no Research Director (DR). Most (18/20) of the researchers in the unit have a teaching load, including nine professors and associate professors, nine lecturers and associate lecturers.

The unit has hosted only two post-doctoral students.

The unit is not yet involved in European or international networks, which would allow increasing its international visibility and attractiveness for foreign students. The collaboration with US-based groups (partner in a NIH R01 contract) and the participation of one member of the unit to a virtual networking event, aiming to connect French, Belgian and Dutch laboratories, companies and competitiveness clusters in the field of global health, organised by the French Embassy in Belgium, the French Institute of the Netherlands and the Campus France Agency are important initiatives for the future, to be further developed, namely at the European level. The unit has a French website.

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

Strengths and possibilities linked to the context

The policy of welcoming students and staff based on the scientific environment is excellent, including high training activity (175 training courses were attended, representing 235 days of training) to increase the skills and knowledge of staff and students. Training for risk prevention is also implemented by a dedicated prevention officer. The policy of student follow-up both during their stay in the Lab and after they have left the Lab, is very well described, with presentation of their work at thematic meetings, internal seminars, thesis monitoring committee etc. to assess their progression in the multidisciplinary environment of the Lab.

The policy for scientific integrity and open science is very well considered, organized, and controlled. Scientific and technical referents are appointed for each method developed and used in the unit, which guaranties homogeneity and scientific rigour within the Lab. An "open archive" referent has been appointed, who manages the deposit of the publication on Hal (106 documents deposited for 300 records), as well as a "data workshop" referent, in accordance with the FAIR principles.

The research unit shows strong involvement in health teaching (19 teachers-researchers, 9 academic disciplines) as well as teaching in Masters 1 and 2, and some dynamism for training in and through research for science and health students.



Four HDR (authorisation to direct research) were obtained during the last mandate with a total of fourteen HDR in the unit.

Weaknesses and risks linked to the context

Ten PhDs students defended their thesis during the mandate, which is low with regard to the senior scientific staff (20) and HDR (14). Many of the PhD students co-supervised in an interdisciplinary manner by members of the university hospital and the university.

The number of Master students is very high (39).

Members are not leaders of Master teaching.

The use of the English language during the training of students in the laboratory is not organized.

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

Strengths and possibilities linked to the context

The unit showed some success in obtaining funds from various institutional partners and associations (1.323 K€ to recruit post-docs and PhD students, 715K€ for functioning, and 189K€ for equipment).

They regularly applied for various ANR calls (13 applications to PRCI, PRC, JCJC, RACOVID, 2 have been funded). For the next mandate, three ANR project were in the second phase of evaluation when the HCERES self-evaluation was submitted, and all were funded in 2022, one as coordinator, and two as partners.

The unit has exploited successfully the specific funding opportunities for its topics (partner in 1 INCa, 1 ANSES), as well as the possibilities offered by its regional funding bodies (Grand Est region, Reims Métropole, the Reims University Hospital, the SFR Cap Santé and charitable associations such as Ligue contre le Cancer Interrégionale Est and Vaincre la Mucoviscidose.

The unit was able to be a partner in a NIH R01 contract (50K€, 2018-2023 AI138999-01). It has also contracted collaborations with a Belgian team by obtaining four PHC-Tournesol

Weaknesses and risks linked to the context

The laboratory poorly participates in international (particularly European) actions, projects, and networks which would allow increasing its international visibility and getting an additional important source of funding. In addition, it would enhance the attractiveness of the unit for international post-docs or PhDs.

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

Strengths and possibilities linked to the context

The unit benefits from easy access to the expertise and cutting-edge technological resources that make up its immediate environment and from a quality technological environment (13 technical platforms) in which it actively participates (steering committee of URCAcyt, PICT and URCAnim), and is also well equipped on site.

A monitoring strategy is implemented to maintain quality and foresee upgrading. During this mandate, the unit invested 188K€ of its own funds in the acquisition of new scientific equipment (automatic fixation system, electrophysiology system in Ussing chamber, cell counting/viability system) and renewed others (incubators, NanoDrop spectrophotometer, cytocentrifuge, chemical hood, real-time PCR system). There is dialog on a regular basis with Urca and Inserm (Ariane campaign) to get funding to obtain, maintain or repair equipment's. Urca is very supportive and invested in a second L2 cell culture platform (which is not taken into account in the annual budget of the unit).

Weaknesses and risks linked to the context

As mentioned in the document, the support obtained for equipment remains modest and does not allow for the acquisition of very large equipment, but this may not be necessary in the context of the platform-rich environment.



Assessment on the scientific production of the unit

The scientific production of the unit is of very good quality, with 15% articles published in the best peer-review journals. In the last six years, the members of the unit have published 67 articles as PI (first or last author) that represent 35 scientific articles, nineteen clinical articles, thirteen reviews. This includes one *EBioMedicine*, one *J Pathol*, one *Cancers*, one *Frontiers in Microbiology*, one JAMA, one *CHEST*, one *Eur Respir J*, one *Am J Respir Critical Care Med.*, and as co-PI in one *Nat Comm*, JAMA, etc.). Most work is published in specialized journals and publications in generalist journals remain few.

The unit's member have also contributed as co-author in high-quality journals including JAMA, Nat Comm, Chest, Cancer Cell, Nat Genet, Eur Respir J, Lancet Respiratory Medicine, J Pathol, Chemical Science, Cancer Res, Circulation, Thorax (one paper each).

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

Strengths and possibilities linked to the context

These last six years, through the development of well-focused research projects, the use of strategies, methodologies and tools well-adapted, and the existence of a strong synergy between biologists and clinicians which has led to transversal thematic projects such as the role of the cilium in bronchial diseases, the unit has done major contributions in the field of COPD, CF and lung cancers. These results have direct implications for the improvement of the patients' potential treatments.

Multidisciplinary projects have been successfully developed thanks to the arrival of new staff members with expertise in the bacteriology field (Pl in J Antimicrob Chemother 2017; Pl in Front Microbiol 2021)

In the last six years, four major contributions have been done in the context of COPD through:

- The identification of the role of polymorphisms of the human nicotinic acetylcholine receptor alpha 5 subunit in the smoking-independent COPD-like lesions (PI in Int J Mol Sci 2020; co-PI in Nat Commun 2021); these data highlight a5SNP as a potential therapeutic target;
- (2) The characterization of the role of altered airway microbiota in pejorative clinical symptoms of stable COPD patients (PI in Frontiers in Microbiology, 2021). These results could lead to a modification of the processing of COPD sputum in the practice of clinical microbiology laboratories;
- (3) The identification of the role of Hedgehog (HH) signalling pathway in the differentiation of airway epithelial cells and of its deficiency in airway epithelial cells from COPD patients providing the first evidence that Gli2 and the receptor Smo are key markers in COPD pathogenesis (PI in *EBioMedicine* 2019, PI in *Respir Res* 2020);
- (4) The development of innovative therapeutic strategy in severe emphysema [P-STI-Revolens clinical trial, (PI in JAMA 2016, CHEST 2019], and the contribution of staff members to international multicentric clinical studies for the development of targeted endobronchial denervation technique in COPD (BMC Pulm Med 2020).

Two major contributions have been done in lung cancer

- (1) To refine patient selection for immunotherapy (correlation between PD-L1 and vimentin expression with higher co-expression being significantly associated with poor overall survival (PI in Cancers 2019));
- (2) And to predict response to anti-HER2 molecules (characterization of a FHIT low/phospho-HER2 high expression signature) (PI in J Pathol 2020, Patent PCP/EP 2017).

Significant results were also obtained in the identification of the crucial role of CFTR in the regulation of the ciliogenesis, allowing for the identification of potential therapeutic strategies in CF to increase the repair of epithelium lesions and favour the differentiation of ciliated cells (Int Forum Allergy Rhinol 2016 + patent); the identification of new markers of NSCLC progression involved in angiogenesis and immune response (PI in FASEB J 2017, PI in Frontiers Cell Dev Biol 2021).

Weaknesses and risks linked to the context

The unit, which publishes in highly relevant specialized journals, has published only a few papers in generalist journals.

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

Strengths and possibilities linked to the context

During 2016-2021, the achievement of the overall research projects of the unit has led to 295 publications in



international peer-review articles. These included 117 scientific articles, 155 clinical articles and 23 reviews. Among these publications, members of the unit were PI (first or last author) in 67 articles that represent 35 scientific articles, nineteen clinical articles, thirteen reviews. Among the 35 original publications published by members of the unit as a first or last author, the committee underlines the scientific impact of publications in journals with a generalist readership such as *EBioMedicine*, one *FASEB J and J Pathol* or speciality journals, such as *Eur Respir J* (n=2), *Respir Res*, *Br J Cancer, Cancers, Frontiers in Microbiology, Frontiers in Cell Dev Biol, Diagnostics, J Microbiological Methods, J Anti Micro Chemo.*

The committee also underlines the co-publications with European and international collaborators including teams from McGill University Genome Center Montreal (Nat Commun 2021) or Liege University (Cancers 2019). The collaboration with Liege University also led to two other publications in Cancer Res (2016) and Oncogene (2020). Members of the unit also contributed as co-authors of other articles in high-quality journals including JAMA, Nat Commun, Chest, Cancer Cell, Nat Genet, Eur Respir J, Lancet Respiratory Medicine, J Pathol, Chemical Science, Oncogene (one paper each). For the reviews, unit members were in leading position in thirteen reviews including Eur Respir Rev, Cancers, Bioessays and J Clinical Virol. Among thirteen, six reviews were published in national peer-reviewed journals (Rev Maladies Respiratoires). A member was co-author in Nat Rev Clin Oncol.

Regarding clinical articles, nineteen clinical publications were published by members of the unit as a first or last author including JAMA (n=1), Am J Respir Critical Care Med (n=1), Eur Respir J (n=1), J Clin Virol (n=1) and five publications in national peer-reviewed journals (Annales Biologie Clinique, Rev Maladies Respir)

Members of the unit were also co-authors of other articles published in high quality journals including one Lancet Respir Med, one Circulation, one Thorax, one Respir Res.

Other publications of the unit include eight book chapters, four volumes of conference proceedings (Rev Mal Respir), 28 articles from conference proceedings (6 Am J Respir Crit Care Med, 2 Cancer Res, 1 Chest, 14 Eur Respir J), 21 articles in specialized professional and technical journals of pulmonology and nine recommendations for Inca, Haute Autorité de Santé or the French Microbiology Society.

The unit includes two researchers, nine MCU/MCU-PH/PU-PH, and eight PH who represent a total of 9.5 ETP. The ratio of publication was 10 articles/member or 31 articles/ETP. All permanent staff members contributed to the scientific production with a relative balance between scientific (35 as PI) and clinical articles (19 as PI)

Eleven articles were published from the results of PhD students and post-docs (12 total members) as first authors.

Weaknesses and risks linked to the context

There is a relative imbalance in the scientific production of the different axes.

Although the number of ETP is equally distributed between each axis, the COPD axis appears as the main driver of the unit for published articles, in comparison to the other ones.

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

Strengths and possibilities linked to the context

The unit has developed its policy in term of scientific integrity with a training and a sensitization of staff members to ethical rules.

The unit has established a register for all protocols to assess the quality of the methodology and has designed referees for each technique.

Regular meetings are organized to discuss the techniques and results.

The unit has developed the use of the electronic laboratory book to guarantee the traceability and the reproducibility of the results. Each member contributes to this lab book and includes protocols, results and raw data. Raw data are stored on an internal server.

To promote open science, pre-prints are encouraged, journals in open access are favoured.

Selection of the more appropriate journals is done according to SCImago and Clarivate (WOS and JCR). Contributions to each publication or scientific communication are discussed between each co-authors of the

study. Studies on human samples are carried out in accordance to official rules (Loi Jardé) and the patient's written

Studies on human samples are carried out in accordance to official rules (Loi Jardé) and the patient's written consent is obtained in each study.

Studies on animals are done in the respect of ethical rules in term of animal welfare All experiments are approved by the local ethical committee (one member of the unit is part of this committee). All experiments are performed under the supervision of PIs duly authorized to manipulate animals. One technician is trained and devoid to animal experiments.

CODECOH declaration is regularly up-dated.

Weaknesses and risks linked to the context

No specific weaknesses have been identified.



EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The global inclusion of the unit's research in society is very good. The unit P3Cell has demonstrated an excellent interaction with the socio-economic environment through its involvement in the associative world (patient associations, etc.), its ability to popularise science among the general public (by radio conferences, hosting young students)... Funding from contracts with the non-academic world is very good (the know-how of the unit is exploited through one contract with Astra-Zeneca) and the unit has a policy of valorisation of their results (2 patents in 2018 and 2020), which is currently limited to patent filing.

1/ The unit stands out by the quality of its non-academic interactions.

Strengths and possibilities linked to the context

The unit has developed numerous and various interactions with the non-academic world, in particular with patients' associations. The partnership established with patients' association, in particular, are intimately linked to the research questions of the laboratory, allowing progress in knowledge while responding to the societal challenges highlighted by civil society.

In total, thirteen research contracts have been concluded with associations such as the "Ligue contre le Cancer", "Vaincre la Mucoviscidose" or the "Association régionale d'aide aux insuffisants respiratoires de Champagne Ardenne", but also with international associations, national, regional or local associations serving society such as the WHO, the Philip Foundation, the Asthma Allergy and Inflammation Research Charity, the Foundation for Medical Research, the Lions Club, the Rotary Club and the Association of Friends of the American Memorial Hospital in Reims.

Remarkably, contracts with non-academic partners have allowed the funding of four PhD students, two postdoctoral researchers and six full-time equivalent technical staffs.

Partnership with the industrial world includes four projects (AstraZeneca, Laboratoires Chemineau and Visterra Inc. laboratories, as well as with the Champagne company "Agroindustrie Recherche et Développement (ARD)". The ARD collaboration allowed hosting of two female engineers within the Lab.

Weaknesses and risks linked to the context

The TRL (Technology Readiness level) of the research project developed is limited to TRL 1 or 2. The relationship with AstraZeneca is at an early stage. It seems that it is limited to funding research within the Laboratory in which the company has an interest, not to develop true collaborative R & D programs.

2/ The unit develops products for the socio-economic world.

Strengths and possibilities linked to the context

The unit has a policy of protecting intellectual property, with the filing of an invention declaration and two patents, directly related to its research themes over the 2016-2021 period.

One of the strengths of the unit is certainly its participation at the operational level to clinical research, to 50 clinical trials commissioned by pharmaceutical laboratories or patients' associations.

Members of the unit also act as experts for companies such as Accrelab, Sanofi, MSD or Roche, with the production of five technical expertise reports for the benefit of these laboratories.

The unit is strongly involved in drafting of guides and protocols for standardisation bodies (HAS, the National Network for the Prevention of Healthcare-Associated Infections (CClin - Arlin)) and also provides recommendations to numerous bodies and social actors (INCa, the French Microbiology Society, the French Language Infectious Pathology Society, HAS). Members of the unit also act (8 times since 2016) as advisors or experts for socio-economic players (ARS, HAS, Santé Publique France or the Ministry of Justice). They are also active members of decision-making bodies of societies or patients' associations (French Society of Allergology, French society of pulmonology, "Vaincre La Mucoviscidose"), thus influencing their thematic calls. The research production of the unit is thus regularly disseminated via the production of research activity reports towards all these different actors of their ecosystem.

Weaknesses and risks linked to the context

The total amount of financial resources obtained by the unit from valorisation, transfer and industrial collaboration was limited to 249 k€ during the six year-contract.



The TRL (Technology Readiness Level) of the research projects are limited to TRL1 or 2. There is no policy in advancing research and development towards TLR3 to 5, namely through applications to SATT Nord calls or through Inserm-Transfert as TTO, although there is the potential with regard to the typology of research projects, the patents filled and the already established collaborations with the pharma industry. This may also depend on the general agreements established between the unit and these TTOs.

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

Strengths and possibilities linked to the context

The unit has an outstanding interaction with the civil society on a regular basis (each year), through

- i) its participation in the organisation of territorial general assemblies of various patients' associations ("Ligue contre le Cancer" and "Vaincre la mucoviscidose"),
- ii) presentation of its results on bronchopulmonary cancer to various local associations (Crépy-en-Valois, Château-Thierry and Soissons Lions Clubs)
- iii) presentation of its results on cystic fibrosis ("Virades de l'Espoir" evening organised by "Vaincre La Mucoviscidose").

In 2018, the unit participated to the national day "researchers welcome patients" organised by Inserm, on the theme "allergic and inflammatory pulmonary diseases". Other dissemination media is the MT180 (my thesis in 180 seconds) challenge to which PhD students of the unit participate each year.

The unit also uses mass media such as local radio (France Bleu Champagne programmes 2017, 2018, 2019, 2021), and the written press ("Paris Match" in 2016, various articles, interviews and videos on the Internet in ORL/Pneumologie/Allergologie Pratique and in the daily news-paper "Le Quotidien du Médecin").

Finally, each year the unit welcomes pre-baccalaureate students (17 since 2016), as part of their discovery of the research world.

Weaknesses and risks linked to the context No specific weaknesses have been identified.

C - RECOMMENDATIONS TO THE UNIT

Recommendations regarding the Evaluation Area 1: Profile, resources and organisation of the unit

The unit should recruit at least one new full-time researcher during the next contract and lead international funding grants.

As requested by the students, lab presentation must be performed in English at least by PhD students. The lab website must be regularly updated and links with social networks must be built.

Recommendations regarding the Evaluation Area 2: Attractiveness

Members should participate to meetings organization and attend international workshops and congresses. The unit should also make a greater effort to collaborate with investigators of internationally-wide recognition. The unit should put in place initiatives to attract junior or senior staff to permanent research positions to balance with the teaching researchers.

The unit should consider leading European or international networks, which could allow increasing its international visibility and attractiveness for foreign students.

Recommendations regarding Evaluation Area 3: Scientific Production

The strategy already initiated aiming to develop multidisciplinary projects between the different axes (e.g. in relation with ciliogenesis) should be reinforced as it could increase both the synergy between the different staff members and the scientific production of the unit. The unit should struggle to reinforce the design of projects that include common objectives to the three main themes. The different staff members should participate more frequently in the publication of common original research papers. They should also struggle to publish articles in



the top-ranked journals of each speciality and in those of a wider audience. This would help increase the scientific impact of their publications.

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

The path toward innovation and technology transfer to the industry or through start-up creation has to be improved. In particular, the Unit should interact with the SATT Nord to consider funding eligible for pre-maturation and maturation programs.

The Unit might propose true R & D collaboration to its industrial partners, for example through the creation of LabCom Laboratory funded by the ANR LabCom Program.

RESPONSES TO SUPERVISING BODIES CONCERNS (IF ANY)

NA



CONDUCT OF THE INTERVIEWS

Date(s)

Start: 09 septembre 2022 à 08h3
--

End: 09 septembre 2022 à 18h30

Interview conducted: online

INTERVIEW SCHEDULE

08h30 08h45-09h20	Présentation du comité Présentation de l'Unité par la Directrice (20min présentation+ 20min questions)
09h20-09h40 09h40-10h00	Axe1 : Plasticité épithéliale et BPCO - Valérian DORMOY Axe2 : Plasticité épithéliale et mucoviscidose - Christelle CORAUX
10h00-10h20	Axe3 : Plasticité épithéliale et cancers des voies aériennes - Béatrice NAWROCKI-RABY
Pause - café :	
10h35-12h00	Réunion du comité en huis clos
12H00-13H00	Déjeuner du comité
13h15-13h45	Rencontre du comité avec les ITA (huis clos)
13h45-14h15	Rencontre du comité avec les étudiants + post-doctorants (huis clos)
14h15-14h45	Rencontre du comité avec les chercheurs (huis clos)
14h45- 15h15	Rencontre du comité avec les tutelles : huis clos Inserm : Eric SIMON VP Recherche URCA : Laurent LUCAS Directrice générale du CHU : Laetitia MICAELLI-FLENDER
Pause -café:	
15h30-16h00 16h00-16h30 16h30-18h30	Réunion du comité à huis clos Rencontre avec la Directrice et son adjoint Réunion du comité

PARTICULAR POINT TO BE MENTIONNED

NA



GENERAL OBSERVATIONS OF THE SUPERVISORS



Reims, le 20 DEC. 2022

Direction de la recherche et de la valorisation Affaire suivie par Karelle MASCRET 03.26.91.86.99 <u>karelle.mascret@univ-reims.fr</u>

Réf: 620 /RECH/NM/KM

Monsieur le président,

Je tiens tout d'abord au nom de l'ensemble des chercheurs et enseignants-chercheurs de l'université de Reims Champagne-Ardenne à vous remercier pour le temps et l'énergie consacrés à l'évaluation de nos unités de recherche.

Je vous remercie également pour la qualité du rapport d'évaluation ainsi que pour les échanges constructifs que nous avons eus avec le comité du HCERES. Les recommandations et les conseils formulés ainsi que l'intérêt porté au devenir de nos unités nous permettront de mener notre projet scientifique.

Suite à la réception du rapport du HCERES n° DER-PUR230023460 - P3Cell – « Pathologies pulmonaires et plasticité cellulaire », je vous confirme que l'établissement n'a pas d'observation de portée générale à formuler.

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



Monsieur Thierry COULHON Président du HCERES The Hcéres' evaluation reports are available online: 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

