

# Research evaluation

# EVALUATION REPORT OF THE UNIT

Canther - Hétérogénéité, plasticité et résistance aux thérapies des cancers OncoThai - Thérapies Assistées par Lasers et Immunothérapies pour l'Oncologie PhyCell - Laboratoire de Physiologie Cellulaire LPCM - Laboratoire de Physiologie Cellulaire et Moléculaire

# UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université de Lille,

Centre hospitalier régional et universitaire de Lille -CHRU Lille,

Institut Pasteur de Lille,

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

Centre national de la recherche scientifique - CNRS,

Centre Oscar Lambret - Centre régionale de lutte contre le cancer - CLCC Lille

# **EVALUATION CAMPAIGN 2024-2025** GROUP E

Rapport publié le 01/04/2025



# In the name of the expert committee :

Philippe Juin, Chairman of the Committee Sophie Tartare-Deckert, Co-chairwoman of the Committee

For the Hcéres :

Coralie Chevalier, president

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



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

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

# MEMBERS OF THE EXPERT COMMITTEE

Chairperson:	Mr. Philippe Juin, Inserm, Nantes
Co-Chairperson:	Mrs. Sophie Tartare-Deckert, Inserm, Nice
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# HCÉRES REPRESENTATIVE

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Mr. Alain Eychene, Inserm Mrs. Bénédicte Samyn-Petit, Inserm Mr. Patrick Blader, CNRS Mr. Régis Bordet, université de Lille Mr. Olivier Colot, université de Lille Mrs. Karine Faure université de Lille Mr. Yan Pennec, université Lille Mr. Fréderic Boiron, CHU Lille Mrs. Brigitte Courtois, CHU Lille Mr. Fréderic Gottrand, CHU Lille Mr Denis Postel, Université Picardie Jules Verne



# CHARACTERISATION OF THE UNIT

- Name: Hétérogénéité, plasticité et résistance aux thérapies des cancers
- Acronym: Canther, Unit 1
- Label and number: UMR 9020 CNRS, UMR 1277 Inserm
- Composition of the executive team: Isabelle Van Seuningen

# SCIENTIFIC PANELS OF THE UNIT

SVE6: Human Physiology and Physiopathology, Ageing

SVE4: Immunity, Infection and Immunotherapy

SVE7: Prevention, Diagnosis and Treatment of Human Diseases & ST5: Engineering ScienceSVE7: SVE7: Prevention, Diagnosis and Treatment of Human Diseases & ST5: Engineering Science

# THEMES OF THE UNIT

Research teams of the unit focus on the exploration of the mechanisms of resistance to various cancer therapies (chemotherapy, immunotherapy, radiotherapy) in both solid tumours and blood cancers. The unit is built on a multidisciplinary community of scientists and clinicians that conduct translational research using advanced preclinical models and exploration of clinical data, aiming to discover new diagnostic and therapeutic markers.

# HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The Canther research unit was established on January 1 2020, with the aim of unifying cancer research efforts in Lille (marking the first phase with the creation of the OncoLille Cancer Research Institute). This unit assembled three previous research teams (UMR8161 CNRS/M3T, U908 Inserm, UMR-S1172 Inserm/JPArc) and one university group from EA4483/Impecs, brought together after a process initiated in 2012 and supported by regional institutions and funding bodies. Canther's focus on tumour resistance and dormancy mechanisms were consolidated through the Siric OncoLille and CPER Cancer programs. Initially dispersed across several sites, all teams moved to the new OncoLille building on the Lille hospital campus (which now serves as the central location for the interdisciplinary research institute) in October 2022.

# RESEARCH ENVIRONMENT OF THE UNIT

Canther is part of a rich scientific and technological environment in the OncoLille Interdisciplinary Cancer Research Institute on the Lille hospital campus. Its proximity to Lille Hospital and Centre Oscar Lambret enables strong collaborations with clinicians and clinical departments, enhancing translational cancer research. As a Lille Pasteur Institute (IPL) unit, Canther also contributes to IPL's research on aging and age-related diseases, including cancer.

Canther has access to state of the art technology developped in the OncoLille Institute, such as the BioMEMS platform for microfluidic oncology applications, and several specialised laboratories (virology, microbiology, radioactivity). Canther also developed cutting-edge cancer research methodologies including: OrgaRes/OrgaLille (IBISA) that builds in vivo (PDX) and in vitro (3D culture, PDO) tumour models for studying tumour resistance and dormancy; PCBI that focuses on protein interactions to screen new therapeutic molecules; Metabolism Platform that analyses metabolic properties of cancer cells; Zebrafish Platform that develops unique cancer models; XAI Platform that uses AI to study regulatory networks for identifying biomarkers; and Single Cell Platform that investigates cancer mechanisms and tumour heterogeneity at the single-cell level.



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

Catégories de personnel	Effectifs
Professeurs et assimilés	49
Maîtres de conférences et assimilés	31
Directeurs de recherche et assimilés	12
Chargés de recherche et assimilés	13
Personnels d'appui à la recherche	80
Sous-total personnels permanents en activité	185
Enseignants-chercheurs et chercheurs non permanents et assimilés	10
Personnels d'appui non permanents	21
Post-doctorants	2
Doctorants	76
Sous-total personnels non permanents en activité	109
Total personnels	294

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

Nom de l'employeur	EC	С	PAR
U LILLE	60	0	16
Inserm	0	14	19
CHRU LILLE	8	0	18
AUTRE	12	0	9
CNRS	0	8	8
INST PASTEUR LILLE	0	2	5
CLCC LILLE	0	1	5
Total personnels	80	25	80



# **GLOBAL ASSESSMENT**

The Canther unit has successfully established itself as a prominent cancer research entity, combining cuttingedge investigation into resistance mechanisms against cancer therapies in both solid and blood cancers. With strong local and institutional support, Canther has fostered a multidisciplinary approach, uniting scientists and clinicians to identify new diagnostic and therapeutic markers. Its alignment with national strategies, particularly the 2021-2030 French "Cancer Plan," and regional health initiatives has enhanced its strategic focus. The unit's scientific objectives are very good to excellent. The unit is a key player in oncology research, notably through its affiliation with the OncoLille Cancer Research Institute.

The unit resources are excellent. It operates with an annual recurring budget of €670,000 supplemented by €3-5 million from successful grant applications. While its distribution policy for recurrent funding is pragmatic (redistributed amongst teams), the arrival of new teams will pose challenges on how to readjust this distribution proportionally. A hallmark of Canther's strategy has been the development of innovative models and platforms, such as organoids, tumour-on-chip technologies, and zebrafish cancer models which, combined with advanced translational research methods, have increased its workforce and enhanced its national and international recognition. However, the unit faces understaffing in administrative and technical positions, which risks straining team dynamics and platform functionality. Despite these challenges, Canther has grown from 180 to 210 members since its inception in 2020, attracting top talent and fostering career development through structured onboarding, welcome packages, and training opportunities. The unit functioning is thus very good to excellent.

Canther's scientific production is also very good to excellent, with 274 original publications, 52% of which were led by Canther members, including impactful contributions in Science Immunology, JCI, and Nature Medicine. However, there is room to increase publications in prestigious generalist journals. The unit actively adheres to principles of scientific integrity, open science, and sustainability, taking measures to reduce its environmental footprint.

The unit attractiveness is very good to excellent. It is bolstered by invitations to national and international meetings (Senescence Association Conference, European Cystic Fibrosis Conference), international collaborations, grants, and teaching. Researchers hold leadership roles in national and global scientific councils, contribute to curriculum development at the University of Lille, and host significant scientific events. Canther also supports numerous PhD and Master students, ensuring the next generation of cancer researchers.

Canther contribution to society is outstanding: it has contributed significantly to societal impact through collaborations with private companies, startups, and charity organisations, resulting in seven patents and two startup creations (Genvade Therapeutics, 2021 and SwitchKine Therapeutics 2023) during the current mandate. The unit obtained several contracts with private companies (Merck, Deuter Oncology, and AbbVie) on resistance mechanism to targeted therapies in oncology. Notably, they showed that the FDA-approved adenosine A2A receptor antagonist istradefylline (KW6002) protects from cisplatin-induced nephrotoxicity and neuropathic pain in mice, and even potentiates the antitumoural properties of cisplatin (JCl 2022). This work also led to an international patent. Public engagement has been a strong focus, with frequent participation in science fairs and outreach activities.

Looking ahead, the proposed merger with Phycell, Oncothai, and LPCM will create a unified oncology research structure for the 2026-2030 mandate, consolidating expertise in cancer resistance and dormancy. This integration aims to enhance regional and international visibility, translating innovative therapeutic strategies into clinical practice while fostering interdisciplinary collaboration. Canther's strategic ambition is to become a leading reference in cancer research globally, leveraging its extensive expertise, advanced methodologies, and commitment to societal impact. Losing CNRS support would threaten its interdisciplinary capacity.

Key recommendations are to improve governance transparency and inclusivity, foster internal collaborations through transversal scientific axes (e.g., ion channels, persistence), allocate an annual budget to support a unified scientific policy, support less experienced team leaders, and promote applications to national and international funding calls. A strategic plan should also be implemented to recruit external Pls. Installing these measures may help to boost European and international visibility of the unit.



# **DETAILED EVALUATION OF THE UNIT**

# A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

While there were no recommendations regarding scientific production and activities, there were some regarding the unit's organisation and life, as well as scientific strategy and projects.

Recommendations included "a good homogenisation of the publication signing policies within the unit". The committee noted that the unit ensures PhD students meet the requirements of the doctoral school and are actively involved in article writing to develop publication skills. Open access publications were encouraged.

The constitution of "an external scientific advisory board to decide which projects and cancers to focus on" was recommended. The unit's past and trajectories were reviewed by a SAB composed of 9 international experts on January 10 and 11, 2024. A report was subsequently drafted, and the teams took it into account. Notably the development of bioinformatics was allowed by the set up the XAI-Platform (the main scientific research project of the Emerging Computational Disco Team.)

# **B - EVALUATION AREA**

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

# Assessment on the scientific objectives of the unit

The scientific objectives of the unit are very good to excellent. The unit implemented a cutting-edge research program investigating the mechanisms of resistance to various cancer treatmentsincluding chemotherapy, immunotherapy, and radiotherapy—in both solid and blood cancers. The unit successfully brought together a multidisciplinary community of scientists and clinicians to identify new diagnostic and therapeutic markers in line with national and regional strategies. New teams emerged thanks to an incentive and concerted management.

### Assessment on the unit's resources

With strong local support, secured funding, and the acquisition of state-of the art equipment supporting platforms, the unti's ressources are excellent.

### Assessment on the functioning of the unit

The unit functioning has been very good to excellent in its ability to unite the forces in oncology research, making the thematic organisation of the unit dynamic and fostering the emergence of new teams. The unit's alignment with its institutional requirements regarding working conditions, safety, scientific procedures and reduction of environmental footprint is excellent.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

This unit aligned with national and regional health strategies and expanded with new teams since 2020 (Disco, NMD). Through in-depth group discussions, advertisements in scientific journals and strategic budget investments, it supported emerging projects. It established internal calls to fund innovative, high-risk ideas aimed



at securing national grants and fostering collaborations. Leveraging the OncoLille Cancer Research Institute methodologies and expertise, it generated significant scientific and translational research and supported interdisciplinary projects. Canther scientific objectives fit with the 2021-2030 national "Cancer Plan". They fully take into account the policies and strategic plans of University of Lille (Health strategy for the Lille area); CHU Lille (translational research fostered by a specific grant allocated to young clinicians); Centre Oscar Lambret (fundamental and translational research on breast, prostate, sarcoma and pediatric cancers) and IPL (research on aging and age-related diseases such cancers). They also align to the CNRS roadmap. It is important to highlight here the contributions of CNRS staff to publications and patents, to the design and development of funded projects (characterised by a remarkable use of interdisciplinarity) and to the very functioning of the OncoLille Institute which gathers numerous CNRS Units.

### Weaknesses and risks linked to the context

The loss of CNRS support represents a major risk for the functioning of the unit and for the maintenance of transversal skills and expertise. The committee regarded the latter as major assets for continuing to build interdisciplinary cancer research in Lille. In this context, a scientific strategy that explicitly interacts with the supporting institutions and sets clear goals for the research community will help consolidate the structure. Moreover, while the unit has developed advanced technical platforms for in-depth molecular and cellular analysis and for functional exploration, they seem to have struggled to recruit permanent staff to fully utilize these resources. This remains a challenge for future improvement and threatens to hinder development.

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

### Strengths and possibilities linked to the context

The unit has a recurring budget of nearly  $\leq 670\ 000\ (\leq 292,000\ from\ Inserm, \leq 195,000\ from\ the\ University, \leq 147,000\ from\ CNRS, and <math>\leq 36,000\ approximately\ from\ Lille\ Hospital$ ). In addition, successful grant applications (teams individual funding) contribute to  $\leq 3\ to\ \leq 5\ million\ annually$ . The steady increase in this latter figure since 2020 underscores the growing visibility and quality of the research conducted by the Canther teams.

The recurring budget is distributed in part to teams (60%,) and in part (40%) is used for common resources, including the annual Canther call ( $\leq$ 30k), welcome packages ( $\leq$ 5k for new arrivals), support for high-level projects, and common expenses, equipment maintenance, repairs, postal services, lab supplies, and more. This distribution seems rational and pragmatic.

### Weaknesses and risks linked to the context

With the arrival of new teams, there is concern that the budget from the supervising authorities may not be increased proportionally. The management may need to consider a redistribution of resources to individual teams using established criteria based on a robust and collectively accepted method. Administrative staff support appears to be below the unit's requirements.

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

Canther unit is well organised administratively, with a management team consisting of a Head assisted by the team leaders and the general secretary (Codir, monthly meetings). The Laboratory Council meets three times a year, or more if necessary, in the presence of all staff and has only an advisory role. The unit is as genderbalanced as possible, with women accounting for 58% of scientific and technical staff. All staff discuss their training needs at the annual interview with their direct supervisor and have access to the training offered by their institution. An officially appointed person is responsible for monitoring and providing information on genderbased and sexual violence and discrimination. A welcome procedure is in place for new arrivals, and a 'godfather researcher' is appointed for each student. Prevention, health and safety are effectively organised. This involves a safety and security assistants, three radio protection advisors, eight containment referents, one laser referent and three chemical waste referents. The unit has taken a number of measures to protect the environment, including regulating building temperatures, limiting travel and recycling plastic and electrical waste, and also respecting the 3Rs (Replacement, Reduction and Refinement) in animal experimentation.



Weaknesses and risks linked to the context

While the University's IT department is responsible for preserving and securing data, the latter is not stored in two separate locations and does not seem to be updated regularly.

# EVALUATION AREA 2: ATTRACTIVENESS

### Assessment on the attractiveness of the unit

The attractiveness of the unit is very good to excellent, as attested by invitations to national and international conferences (Senescence Association Conference, European Cystic Fibrosis Conference) and success of some teams in competitive European and national calls for projects (European Pearl doctoral program). The unit has hosted more than a hundred PhD students during the mandate. It attracted 28 permanent staff members, including CNRS and Inserm researchers, university teachers, medical teachers, and hospital practitioners. The quality of the unit's equipment and methodological development, such as OrgaRes/OrgaLille, IBISA labelled developing innovative in vivo and in vitro tumour models, is excellent. The support staff is qualified and needs to be strengthened.

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

Canther's efforts in organizing events, contributing to academic leadership, and participating in high-profile research projects underscore its arowing influence and recognition in the scientific community. Unit members are frequently invited to speak at major conferences, such as the International Senescence Association Conference and the European Cystic Fibrosis Conference. They also organize significant scientific events, including weekly seminars and international meetings such as the OncoLille Days and French Zebrafish Meeting. Canther researchers are heavily involved in editorial work, serving on boards such as Cancers and acting as guest editors for special journal issues. They also play leadership roles in national scientific councils, including CNRS and Inserm. The unit is committed to international collaboration, with members spending extended periods in laboratories across the USA, Japan, and Europe. In education, Canther researchers hold key positions at the University of Lille, directing programs such as the "Biology Health" Master and the Bilingual Bachelor Degree in Life Sciences. They are deeply involved in teaching and curriculum development. Canther has also been central to major research initiatives such as the CPER Cancer 2015-2020, and is involved in ongoing projects like CPER Resistomics 2021-2027. Unit members have received prestigious awards, including the Maurice Girard Award and the Grand Prix of Pharmaceutical Sciences. Canther performed well in attracting and retaining top talent, including scientists, students, and technical staff. To support new recruits, Canther offered a "welcome package". The unit's growth, was boosted, increasing its staff from 180 in 2020 to over 210 by the end of 2023. Canther has successfully attracted 28 permanent staff members, including CNRS and Inserm researchers, university teachers, medical teachers, and hospital practitioners. The unit also secured 39 advancements and promotions for its staff, reflecting its commitment to career development. New staff members are integrated into the Canther community through a structured onboarding process. The unit strategically responds to various research calls, ensuring the submission of proposals.

Canther has secured 274 grants, raising over €22.2 million. European funding includes Pearl international interdisciplinary PhD funding, one/three Feder grants as coordinator, one Interreg-Matisse as coordinator and one Era-Net Transcan-3 JTC-2021 as partner. The unit secured, as coordinator, one CPER contract (CPER Cancer 1348K€), 6/8 ANR and 5/10 INCA contracts. Members obtained eight ARC fundings (€1.028M) and >50 LNCC regional grants (5 K€-75 K€). The unit also plays a significant role in training, having supported 112 doctoral students and 121 Master's students since 2020.



The institute's organisation, with centralised state-of-the-art platforms, helps attract and retain staff by providing direct, cost-effective access to advanced equipment. Equipment development and maintenance are managed through regular discussions within Canther and the current CoDir of OncoLille Institute. Platforms allow innovative in vivo (Patient-Derived Xenografts: PDX) and in vitro (3D cultures, Patient-Derived Organoids: PDO) tumour models (OrgaRes/OrgaLille, IBISA label); protein-protein and DNA-protein interactions studies and screening new therapeutics (PCBI); metabolic analysis; the development of original cancer models using zebrafish; investigations of regulatory networks, (XAI Platform); single-cell level explorations. Canther also leverages the OncoLille institute's technological resources, including translational research, preclinical models, and Bio-Mems platforms such as microfluidic devices for oncology. Additional facilities include various specialised labs for microbiology, virology, and biochemistry. Technological seminars and demonstrations are held at least once a month to engage the local scientific community and promote equipment usage.

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

The number of full time-researchers is generally low, and for some teams crucially so. Overall, there is a shortage of permanent engineers and technicians within teams, platforms and the administration, which could result in psychosocial risk, stress, and tension between the teams and their administrative support, while also affecting platform operations.

# EVALUATION AREA 3: SCIENTIFIC PRODUCTION

# Assessment on the scientific production of the unit

The overall scientific production of the unit is very good to excellent (274 original scientific publications, including 52% signed in leading position), including some top-notch publications with clinical applications (e.g., JCI 2022). The unit has made several major contributions in the field of cancer, in particular on resistance mechanisms to therapy and the development of new therapeutic strategies, published in excellent general and specialist journals (Sci Immunol, J Clin Invest, Nat Commun, Blood, Leukemia, Elife), demonstrating its scientific competitiveness.

- 1/ The scientific production of the unit meets quality criteria.
- 2/ The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.
- 3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.

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

The unit published 977 publications during the mandate, of which 274 original scientific publications peerreviewed international journals and 142 (52%) signed as first or last author. The latter were published mostly in specialist journals (Br J Cancer, J Thorac Oncol, J Exp Clin Cancer Res, Sci Rep, BMC Bioinformatics, J Med Chem, Cell Death Dis, TIBS, TIPS, Cancers), and some in top generalist journals (Science Immuno, JCI, eLife). Unit members also signed both scientific articles (Nature Medicine, Nature Cancer, Nature, Science Signaling), and clinical studies (Lancet, NEJM) in top quality journal as collaborators. Of note, they reported the influence of acidic pH on the binding of IL2 to IL2R and its impact on the immune response (Science Immunol 2022); the similar antitumour effect of Istradefylline (an FDA-approved adenosine A2A receptor antagonist) to cisplatin without its well-known side effects in cancer patients (JCI 2022); or the MET receptor dependent signaling effect in cancer (eLife 2020). PhD students and postdocs published their work in proportion to their participation. Most of them had a first author publication from their main research project. The technical staff is clearly associated with research publications. The scientific production complies with the principle of science integrity and open science as much as possible, with clear, scientifically rigorous work. It complies with rules that satisfy the respect of human being and animal life. The unit respects the principles of open science by sharing publications, data and other elements. A strategy for long-term storage management of produced data is in place.



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

The number of publications in generalist journals is low given the size of the Unit, and there is a lack of publication in prestigious generalist journals (Cell or Nature press). Moreover, there is a clear imbalance in scientific production between teams. The quality of the PhD student publications is limited by the local doctoral school policy (1 main publication requested for the PhD graduation). The percentage of publications produced during the contract as open science papers was not optimal (70%).

# EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

Overall, the contribution of Canther research activities to society is outstanding. Canther has developed numerous and fruitful non-academic interactions and contributed to two successful start-up compagnies (Genvade Therapeutics, 2021; SwitchKine Therapeutics, 2023) as well as 2 Cifre contracts. Its staff members are very involved in general public events (Excur'Sciences, open door days...) and outreach actions (TV, radios local/national press interviews).

- 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

Throughout the reference period, Canther developed solid non-academic interactions with several institutions that include private companies, charity associations and foundations. These non-academic interactions were materialised by several collaborations and/or funding agreements. Two Cifre doctoral projects were finalised and partnerships with the Casden bank, Ligue Nationale contre le Cancer-comité du Nord, Cancéropôle Nord-Ouest were created for scientific animations and meeting organisation.

Seven Canther research projects are presently undergoing the patenting or maturation process by Inserm-Transfert or SATT Nord. The organisation on a regular basis of meetings with representatives of several National Industrial institutions (Inserm-Transfert, DGD-S CNRS Delegation, ...) has been very efficient in initiating and consolidating partnerships with non-academic institutions. Canther scientists created two start-ups companied during the evaluation period (Genvade Therapeutics, 2021; SwitchKine Therapeutics, 2023) and are involved in other startup companies that were created before the reference period (Lattice Medical, 17 awards since 2018). To communicate with the social, economic and cultural worlds, Canther uses both official channels (institution communication departments: University, Inserm,...) and social networks (LinKedIn, Twitter,...). Many Canther staff act as experts for both national grant awarding bodies and scientific institutions (ANR, INCa, Cancéropoles, Inserm, CNRS, Hcéres...) and international bodies (Research into Aging and Welcome Trust: GB; Research Foundation Flanders, ULB Brussels: Belgium; U Montréal, Canada) as well as private companies.

In addition to being involved in specific events for graduate students such as "OncoLille PhD student's Days" "OncoLille's open days", many Canther staff members and Ph.D students have a very dynamic outreach activity through their contribution to numerous scientific events dedicated to general public such as Lille science fairs, Escur-Science in 2023, yearly Fête de la Science, Sciences en fête organised by either the official institutions (university of Lille, CNRS, Inserm), annual open doors days (IRCL: Institut de Recherche contre le Cancer de Lille; IPL : Institut Pasteur de Lille and COL : Centre Oscar Lambret). Canther staff members have also contributed to many TV, radios local/national press interviews as well as press releases and a web site (https://nonsense.univlille.fr/) that displays some of the research undertaken by staff members.

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

No weaknesses were detected.



# **ANALYSIS OF THE UNIT'S TRAJECTORY**

By merging Canther, LPCM, Oncothai, and Phycell into a single cancer research unit, the over-reaching goal is to create a combined entity that will become more competitive and visible both nationally and internationally. This merger arguably represents a further step in structuring oncology research in northern France with full support from local institutions and regional bodies, a process initiated over a decade ago and validated by the successful Siric OncoLille label (2012-2017). This long-term process was also crystallised by the creation of the OncoLille Institute, an equipped building which was inaugurated in October 2022 and that houses seven research units (Canther, Phycell, Oncothai, LIMMS, LPP, LEM, and Scalab) in proximity to two major cancer hospitals (University Hospital Center and Cancer Center Oscar Lambret), and University's technological platforms (grouped in PLBS UAR2014 CNRS-US41 Inserm).

**Canther** was established in 2020, as a prominent cancer research unit with the dual Inserm/CNRS (UMR9020 CNRS-U1277 Inserm) label aiming to consolidate cancer research in Lille, uniting local cancer research efforts into one federative unit. Canther brought together researchers from the U908 Inserm, UMR8161 CNRS/M3T, UMR-S1172 Inserm/JPArc, and a University of Lille team, EA4478/Impecs. Initially comprising 180 members, Canther has since expanded to over 210 due to its increasing attractiveness, recruiting several researchers and clinicians. The Inserm U1003/Phycell unit, is internationally recognised for its work on ion channels in pathophysiology. Although initially not strictly aligned with Canther's research focus, Phycell's ongoing collaborations with Canther and other laboratories have highlighted the benefits of integrating Phycell's expertise in ion channels as therapeutic targets into Canther. The Inserm U1189/Oncothai unit has contributed significant expertise in onco-immunology and targeted photodynamic therapy. Oncothai's collaborations with Canther and Phycell, including joint publications and partnerships with medical departments, have underscored the value of merging with Canther. As a result, merging Canther, Phycell, and Oncothai into a larger cancer research unit for the 2026-2030 mandate is a strategic move to enhance regional and international visibility and performance in oncology. Additionally, it is proposed to integrate the LPCM unit from Amiens into this network which has a history of fruitful collaboration with Canther and Phycell.

To structure and foster cancer research in Northern France, the OncoLille Unit defined an explicit scientific strategy. Its ambition is to understand mechanisms of therapy resistance and dormancy, to discover new biomarkers, targets, treatments, and therapeutic strategies. This involves developing novel therapeutic molecules and technologies, such as targeted Photodynamic Therapy, with the aim of translating these innovations into clinical practice to enhance cancer treatment. The unit also engaged in the development of innovative models (organoids, OrgaLille; tumour-on-chip; vessel-on-chip; zebrafish models) as well as bioinformatics and AI.

The unit identified research challenges, associated with treating cancers with poor prognosis and treatment resistance. The unit aims to improve patient outcomes by enhancing early detection, reducing secondary effects, better targeting tumours, inhibiting resistance, increasing survival, decreasing pain, and improving quality of life. Translational/pre-clinical projects are encouraged through the involvement of clinician advisors in project management.

The unit fostered the emergence from existing teams-of four new research teams: NMD: Target non-sense mutations to find new cancer-fighting therapeutic molecules; Disco: Create a computational team to bridge high-throughput data and analytical tools, discover new regulatory networks, and develop Al-powered Bio-IT tools; Epicare: Explore epigenetic determinants involved in cancer risk and aggressiveness; Protect-L: Develop evidence-based strategies for treating pediatric hematological cancers. The unit also updated current themes on persistence as a contributor to resistance, ion channels as anti-cancer targets, and laser technologies

The unit implemented transversal projects to foster interdisciplinary collaborations with other units of the Lille ecosystem. The unit also plans to continue valorisation and transfer activities, to improve its international visibility and recruit new talents,

In sum, the OncoLille unit aims to offer an integrated approach to cancer research, encompassing fundamental biology, clinical studies, physics, mathematics, bioinformatics, and health technologies, with the aim of establishing itself as a leading national and international reference in cancer resistance.

# **RECOMMENDATIONS TO THE UNIT**

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

The committee felt that the key elements of governance were not always fully explicit for all staff members during the preceding mandate. The merger of four research structures presents an opportunity to implement a rigorous collegial decision-making process that allows everyone to participate in the functioning of the unit, while fostering a sense of community. To this end, organizing committees (that represent teams and professional groups—responsible for reviewing various matters related to the research structure (such as Shared Equipment



and Space, Health and Safety at Work, Scientific Animation, etc.)—prior to a decision-making Unit Council, held frequently (e.g., monthly), would be beneficial. This set of committees could allow the Team Leaders Committee to focus on strategic functions, rather than strictly operational ones. It will allow all unit members regardless of their status to contribute to the unit's life.

The dynamics of the structure should not be the responsibility of the direction alone; it is recommended that the different professional groups organise themselves in order to be a source of relevant proposals. As far as the scientific dynamism of the structure is concerned, the committee noted a high potential of synergy between some teams on specific subjects. The organisation of transversal scientific axes, for instance on ion channels or persistence, in addition to a translational pole of explicit modus operandi, are strongly recommended to foster interactions in a fruitful manner. To ensure an appropriate functioning of operational committees and scientific transversal axes, the unit direction might endow them with annual budgets (using funding from the supervisory bodies). This might involve less redistribution to the individual teams and more "common" money used as a genuine means to foster a unit scientific policy. The committee noted that numerous teams in the future unit will be led by dynamic scientists with relatively little experience in management. The aforementioned organisation with operational committees will allow these team leaders to focus on strategic actions and will relieve them of operational tasks to some extent. Moreover, the committee recommends the organisation of team leadership on the basis of duos whenever possible (see specific recommendations to teams below). Guidance by a small advisory group of senior PIs, and management training programs offered by the supervisory bodies are recommended for new team leaders.

# Recommendations regarding the Evaluation Area 2: Attractiveness

The committee feels that the unit should strengthen its research capabilities by more regularly sending applicants to the competitive recruitment of researchers by the supervisory bodies. Emerging teams who so far obtained essentially local funding should apply to national calls, while more established teams should apply to international ones. Indeed, increasing responses to international and European funding calls will improve global visibility and foster high-risk, high-potential projects. Improving international networking is essential on this aspect. The unit might capitalise on its expertise on ion channels, persistence, and key clinical aspects open to translation to do so. The committee found quite positive the emergence of new team leaders from the current units (with implications on management guidance mentioned above), yet also recommends the future unit to maintain available space and develop a structured plan to install new external PI's (e.g., Inserm Junior Professor Chair). For this type of operation to be useful to all, the team leader committee should work on defining a specific long term strategic plan and define the appropriate research profile(s) to target. This strategy will benefit from incorporating a commitment to maintaining an interdisciplinary approach to cancer. The recruitment of post-doctoral fellows could be improved and the unit needs to <u>develop a collective strategy for doing so</u>. Setting up a scientific advisory board dedicated to the unit, and not the OncoLille Institute as a whole, is recommended to obtain specific and expert input on the unit subjects and trajectory.

# Recommendations regarding Evaluation Area 3: Scientific Production

The committee noted that the publication track of the unit was heterogenous between teams. It is recommended that the unit implement a publication policy that ensures that predatory journals are avoided by diversifying publishers (Nature, Springer, BMC, Wiley, Elsevier...). The efforts of the unit to follow the doctoral school rules regarding PhD publications (e.g., one publication accepted before defence) are remarkable. However, the committee felt that these rules might eventually limit the quality of the teams' performance, especially for a unit that forms so many PhD. Other units have set up review committees aimed at improving the quality of manuscripts through internal critical reviews by qualified researchers. The unit could benefit from such a setup.

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

The unit should build on the outstanding contribution of its research activities to society to further increase its European and international visibility.

# RESPONSES TO SUPERVISING BODIES CONCERNS (IF ANY)

None



# **TEAM BY TEAM ASSESSMENT**

Team 1:	Mucins: Mucins, Cancer & Drug Resistance
Name of the supervisor:	Mrs. Isabelle Van Seuningen

# THEMES OF THE TEAM

The « Mucin » team aims to decipher mechanisms responsible for tumour resistance to chemotherapeutic treatments in the context of pancreatic and oeso-gastric cancers. Studies carried out during this period focused on understanding the role of mucins in cancer, evaluating the epigenetics and aggressive properties of digestive cancers, and developing interdisciplinary projects as well as innovative alternative models of cancer. More recently, the team has also been studying pancreatic neuroendocrine tumours.

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In response to recommendations made in the previous report, the "Mucin" team mentioned improved ties with the industrial world, mostly based on the development of the tumouroid OrgaRes platform. The previously mentioned absence of publication in high level journals, and the lack of foreign postdoctoral fellows persisted throughout the new evaluation period. Specific comments previously made concerning the scattering of the scientific program were addressed: the "Mucin" team refocused on pancreatic and oeso-gastric cancers, but projects on neuroendocrine pancreatic tumours were also recently developed.

Catégories de personnel	Effectifs
Professeurs et assimilés	7
Maîtres de conférences et assimilés	6
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	20
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	11
Sous-total personnels non permanents en activité	13
Total personnels	33

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



# Overall assessment of the team

The « Mucins » team carries out very good quality research with a very good national and international recognition in the field of "Mucins biology and Cancer", attested by a strong implication in national networks (CFP, AFRCP, FRAP) and good to very good scientific publications (Sci Reports, CDDis). The attractiveness is very good to excellent with two ANR contracts, one INCa COP, two PHRC, and one PRTK as promoters and one European grant (Pearl-Feder) as collaborator. The interaction with non-academic sector and society is excellent: one patent filed, IBISA labelled platform "OrgaRes" and numerous participations in science vulgarisation with over 30 TV/radio interviews. The team's reorganisation into two teams with specific projects represents a challenge to the consolidation of individual projects and their funding.

### Strengths and possibilities linked to the context

Over the past five years, the "Mucin" team confirmed its excellent visibility in the field of mucin biology, and specifically the implication of mucins in cancer aggressiveness and treatment resistance.

The team was successful in securing competitive national funding during the mandate as promoters: two ANR (MUC4 and Micro-Worms, 2018, 2022), one INCA COP (Fregat, 2022), two PHRC-K (Miro-2 and Needs Trial, 2023x2), one PRT-K (2023), > nineteen LNCC regionale (each 10-75 k€) as well as a Pearl-Feder, a European interdisciplinary PhD funding.

The team published a total of 283 publications, of which 35 in leading position, sixteen from collaborations and 232 from team clinicians. Publications in leading position were published mostly in good journals (Sci Reports 2019, CDDis 2020, Biology of the Cell 2021, Nutrients 2021). These publications illustrate the investment of the team in describing various mucins implicated in cancer, as well as their efforts to develop interdisciplinary projects involving chemists, physicists and bioinformaticians (development of a microfluidic tumour-on-chip model of pancreatic adeno-carcinoma (PDAC), numeric twin of PDAC cell signalling targeting, and refinement of PDAC classifications.

The attractiveness of the team was reinforced with the arrival of a physicist specialised in micro-technologies. Members of the team are strongly involved in the national structuration of pancreatic cancer research networks such as the FRAP network supported by the INCA (two members are project and task leaders). Team members are in the French Pancreatic club Council the Pancreatic Cancer French Association council. Unit members gave over 30 national and international conferences (16th international workshop Mucins in Health and Disease, Newmoon workshop, second Journée nationale "canaux ioniques et cancer"), participated in numerous council and steering committees (LNCC, INCA, IDEX, GDR "Micro & Nano-fluidique", CSS2 Inserm) as well as in the organisation of scientific meetings (CFP since 2021, ACHBT-SFCD, présidence of CECED). The PI maintained a strong activity in general public outreach activities (IRCL open doors, Fête de la science, articles in press and TV interview). The team is very well organised, with strong interaction between team members

### Weaknesses and risks linked to the context

The team has not published in journals of high visibility. This not only limits the attractiveness of the team (i.e., recruitment of qualified post-docs competitive in the national concours for permanent position), but also its ability to obtain major national and European grants as PI. The absence of a dedicated engineer for the OrgaRes platform is a weakness. For sixteen HDR in the team, nine PhD defenses were fulfilled.

### Analysis of the team's trajectory

The future PancRest (Chemoresistance and therapeutic targeting in pancreatic cancer) team project is a continuation of the actual Mucin team, with a specific focus on mechanisms of ion signalling and chemoresistance in PDAC and pNET. The new team will be joined by the LPCM unit, thereby strengthening the link between MUC4 and ion channels (more specifically TRPM7), for which the PI secured an INCA PLBio 2024. The team projects will be constructed around three major axes: 1) PDAC heterogeneity and chemoresistance; 2) identification of chemoresistance mechanisms through translational research; and 3) therapeutic targeting. The team composition will be equilibrated between researchers, lecturers and clinicians. The addition of LPCM's expertise will bring a rationale to the development of research on the role of ion channels in pancreatic cancer chemoresistance and cell transformation. The ongoing and future projects are innovative (with the development of multiples tools), but more importantly relevant to clinical needs. INCA PLBio secured funding will support part of the planned research. Although the expertise of team members as well as the proposed



projects are coherent, the PI should carefully evaluate the potential for scattering, in order to avoid manpower/financial support dispersion, and to create a positive and productive dynamic for this new team.

The second team to emerge from team 1, (Epigenetic mechanisms in cancer risk and resistance to treatment), will be led by a former group leader from the "Mucin" team. This team will consist of three researchers, one lecturer and five clinicians, and focus on chromatin-based mechanisms regulatory mechanisms associated with cancer risk and aggressiveness. The two main research axes are: 1) the identification of chromatin complexes involved in cancer risk and resistance to therapy and 2) the study of their environmentally-induced post-translational modifications (mostly by epimetabolites and hypoxia). The project is of great interest, especially in the context of pancreatic cancer, and involves the OrgaLille/OrgaRes organoid platform managed by the team leader, who in order to be more involved in the team management decided to share this responsibility. With regards to the trajectory document and the quality of ongoing work, as well as submitted publications, the committee consider that the team is on a positive and dynamic trajectory.

# RECOMMENDATIONS TO THE TEAM

### Team PancRest:

For the next mandate, the committee recommends that the team avoid potential scattering through the numerous projects, focusing on those that already secured funding. The valorisation of their research through high visibility journals, and the recruitment of international post-docs should be prioritised through stronger investment in the most promising projects. The team should take advantage of the innovative tools designed during the actual mandate. Regarding the two-sites team organisation, the committee recommends a codirection with the LPCM team leader. Considering the separation of this team on 2 sites (Amiens and Lille), and the lack of management experience of the proposed future team leader, the committee suggest that the direction of the team should be shared with the LPCM actual leader.

### Team Epicare

The committee recommends that the team focus on those projects already supported by grants. It should be particularly vigilant to avoid dispersion of projects, for example by taking full advantage of the innovative tools already developed (OrgaRes platform). The time dedicated by the PI to the OrgaRes platform should be reduced so as to concentrate efforts on team data valorisation. The investment of supportive institutions, with the recruitment of an engineer for the platform is necessary for the success of the emerging team.

Particular attention should be paid to ensure that the reorganisation into two teams does not lead to further dispersion of the manpower and financial supports of each team. The new team leader(s) should make special efforts to maintain the excellent team spirit and organisation, areas in which the former PI of the Mucin team has a strong expertise.



### Team 2:

Target: Efficacy & resistance to anti-tumour Targeted Therapies

Name of the supervisor: Mr. David Tulasne

# THEMES OF THE TEAM

The research team focuses on the development of targeted therapies in cancer, notably in lung and prostate tumours, with a specific focus on the therapeutic target and oncogenic role of MET receptor tyrosine kinase in non-small cell lung cancer (RTK MET in NSCL). The current team results from the merge of two distinct teams, expanding their research activity on the role of MET in prostate cancer to the cooperation of ETS transcription factors in this human disease. During the contract, the team hosted an emerging team focusing on mechanisms of tumour cell resistance to chemotherapy.

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team followed most of the recommendations from the previous evaluation. Notably, the teams that merged shared part of their research activities and interests by focusing on MET oncogenic activity in cancer. They implemented a strategy to recruit postdocs, resulting in the hiring a foreign postdoc during the contract and increase publication quality and visibility, with the example of a seminal paper published in Elife (2020), although the last goals have not been fully demonstrated yet.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	4
Maîtres de conférences et assimilés	5
Directeurs de recherche et assimilés	4
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	20
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	1
Post-doctorants	1
Doctorants	21
Sous-total personnels non permanents en activité	24
Total personnels	45

# EVALUATION

### Overall assessment of the team

The overall research activity and scientific production of the team is excellent, as attested by publications in generalist journals in leading position (Elife 2020, Nat Comm 2019, NAR 2020, Mol Therapy 2023). The attractiveness is also very good to excellent for the size of the team, as attested by two INCa and one ANR as coordinator. The interaction with the non-academic sector (e.g., Merck contract, 2 filled patents) and the society is excellent thanks to the clinicians incorporated in the team and their contribution to clinical trials focusing on a novel Meti (inhibitor) to treat a subgroup of patients with lung cancers (e.g., trial VISION).



# Strengths and possibilities linked to the context

The organisation of the team is coherent with the number of staff scientists (5 staff researchers, 2 PU/MCU, 8 PU/MCU-PH), staff engineers (4 permanent engineers), 1 postdoc and PhD students (4). During the contract, the team maintained a good balance between senior staff scientists and young researchers, with two postdocs and 9 PhD students during the mandate. This team was successful in securing competitive national funding: two INCa (2021 and 2022) and a one ANR grant as PIs during the mandate, which enabled the recruitment of two postdocs.

The team published 47 papers: 37 research articles and ten reviews. 25 original research articles were signed in first or senior position and published in journals of their specialty (e.g., J Th Onc, Br J Canc) and in generalist journals (e.g., NAR, ELife). Of note, they reported one seminal paper in Elife (2020) showing that MET is a dependence receptor with important phyio-pathological roles. They published a new resistance mechanism to MET-targeted therapy in lung cancer (J Thoracic Oncology 2020). Also, they identified Fascin as a potential biomarker and therapeutic target in prostate cancer (Br J Cancer 2023). The NMD team reported a low-toxicity drug with high-efficiency UGA nonsense mutation correction for the development of treatments for genetic diseases caused by nonsense mutations (Nat Commun 2020); and an unexpected phospho-AKT mechanism in nonsense mRNA decay (NAR 2021). The team's work is well-recognised nationally in their domain, as attested by organisation of international meetings (International Workshop "Signaling and targeting of the MET receptor in cancer", 11ème Symposium du Groupe Européen d'Étude des Métastases Osseuses, First Summer School Graduate Programme Precision Health). The team was successful in attracting four senior scientists (1 DR2 Inserm, 2 MCU-PH and 1 MCU) and young scientists (9 PhD students and 2 post-docs) and eight PhD defences were fulfilled with seven HDR.

The team is active in their participation in European societies (EACR, ESMO, European Association of Urology) and national societies (e.g., French Thoracic Oncology Intergroup, Société Française du Cancer). Team members acted as editorial board members of good journals of their specialty (e.g., Journal of Cellular Signalling, J Bone Miner Res). Two team members were involved in national research evaluation committees (Inserm) and the team is also active in communicating their findings and knowledge to the public (e.g., "Ia Fête de la Science"). The team filled two patents, obtained several contracts with private companies (Merck, Deuter Oncology, and AbbVie) on resistance mechanism to targeted therapies in oncology. The synergy between the laboratory and the clinical departments of pulmonology and urology has contributed to their visibility and facilitated their participation in large-scale international clinical trials in the field of targeted therapies (participation to 80 clinical trials), notably on MET-based therapy in NSCL patients (e.g., trial Vision)

### Weaknesses and risks linked to the context

The qualitative and quantitative scientific production does not fully match the research activity for the size of the team. The attractiveness of the team is not sufficiently demonstrated by recruitment of young foreign researchers and students relative to the number of senior scientists. The team did not capitalise on its research activity and network via European research projects yet. The translational potential of the research activity is not demonstrated by sufficient patent filing.

### Analysis of the team's trajectory

The team project is a continuation of the study of targeted therapy in solid cancer through the development of four specific projects: (i) underlying mechanism of Metex14del oncogene function in NSCL tumours and (ii) associated targeted therapy; (iii) an emerging project on targeting persistent cells in SCLC, and (iv) the targeting MET and EGFR-ER alpha signalling in aggressive prostate cancer. These projects are overall innovative and highly relevant to clinical research, including for poor prognosis cancers (e.g., SCLC), potentially leading to new therapies. The overall project is well-designed, well-supported by the current manpower and secured funding. The credibility of specific projects is well-supported by previous and recent unpublished data from the team. The team is also well integrated in identified axes of OncoLilleS project, and ongoing PIAs (e.g., Siric). The collaborative aspect of the project, notably in clinical research, is an important strength of the proposal. The NMD emerging team will focus on the development of anti-cancer therapeutic solutions through the study of small molecules that inhibit NMD or activate readthrough, alone or in combination with molecules interfering with the PD1/PD-L1 checkpoint, thereby capitalising on their previous results published in excellent journals (Nat Comm 2020, NAR 2021, Mol Therapy 2023).

# RECOMMENDATIONS TO THE TEAM

The committee recommends the team to continue their research activity and projects with their current staff and increase their excellence and attractiveness by recruiting young scientists in these new projects. The team is encouraged to apply for international funding, foster interactions with the private sector whenever possible, and keep on focusing on these well-identified projects. The committee recommends the team to promote



collaboration with colleagues on selected cancer types to fully integrate in the OncoLille Institute, increase synergy, and secure fundings.



### Team 3:

PLASTICITY; Cell Plasticity and Cancer

Name of the supervisor: Mrs. Xuefen Le Bourhis

# THEMES OF THE TEAM

The team is dedicated to the development of new therapeutic targets of two cancers in the brain, namely brain metastasis of triple negative breast cancer and, since 2020, high grade paediatric glioma. This team also hosts a working group (i3-BioNet) focused on the development of statistical and machine learning methods applied to more global cancer biology (emerging team in the next contract).

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team made significant efforts to follow the recommendations of the previous evaluation, notably by focusing its work on the brains tumour project with strong preliminary results. They also increased the quality of publications and the number of international grants. Nonetheless, the quality of the publications led by the team remains lower than that of collaborative publications, and no joint publication between the i3-BioNet group and the rest of the team has yet been published.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	9
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	10
Sous-total personnels permanents en activité	25
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	20
Sous-total personnels non permanents en activité	23
Total personnels	48

# EVALUATION

### Overall assessment of the team

The research activity and scientific production of the team is very good, as attested by publications in very good journals of their specialty in leading position (Exp Haemato & Onco 2023, Cell death Disease 2019, Faseb J), and excellent collaborative publications in generalist journals (e.g., Nat Commun, PNAS).

The attractiveness is very good for the size of the team, as attested by one INCa grant and one Siric grant as promoter.

The interaction with the non-academic sector (e.g., 1 licensed patent, 1 Cifre) and society (e.g., Lions club, interviews in newspapers) is also very good.



### Strengths and possibilities linked to the context

The size of the team is proportionate to its research activities and relies on a solid base of permanent staff (24 members).

This team was successful in securing research funding, obtaining national and regional grants (16 as coordinators, 9 as partner;  $1.4 \text{ M} \in$ ). At the national level, they secured competitive grants from INCa (1 as PI and 3 as partner), ANR (1 as partner), Siric (as PI), enabling them to conduct translational research and support doctoral training (7 fellowships). Additionally, they obtained one Cifre and 38 contracts with non-profit foundations (1,4 M $\in$ ).

The team published 128 articles, including 53 in leading position in journals with a good reputation in their specialty (e.g., Onc Letters 2019, Exp Haemato & Oncol, Faseb J, Cell Death& Disease, Bioinformatics), 33 as collaborations (including high-profile journals such as Nat Comm, Embo Mol Med, PNAS), and 42 clinical publications. Of note, they reported a critical role of TrkA as a therapeutic target in brain-metastasis of breast tumours (Onc Letters 2019, Exp Haemato & Oncol 2023). They developed cRegMap, a powerful web-based tool to provide researchers with rapid access to a unified coregulatory influence network view of cancer heterogeneity and plasticity. The team's work is well-recognised nationally, as attested by their participation/invitation to national meetings (OncoLille days, SUNRISE meeting) and, for some specific research activities, internationally (e.g., 8th world congress, Oxidative Stress, Calcium Signalling and TRP channels, Isparta Turkey 2023, International bladder cancer network (IBCN) 2022). Their recognition is also attested by active participation to national and international steering committees (La Ligue Contre le Cancer, Association Ruban Rose, Cancéropôle Nord Ouest, International Federation of ORL societies, European Science Foundation). Several team members had editorial responsibilities in specialised journals (e.g., Int. J. Mol. Sci, Cancers). The team was successful in the recruitment of new researchers during the mandate (2 PR, 2 MCF, 39 PhD students with 19 on-going theses, 5 post-docs). The team has established a robust scientific infrastructure and contributes to the development of technological platforms and novel tools (imaging, bioinformatics, animal facility), with structuring and federating impact. It also contributes significantly to the success of this infrastructure, not only through the acquisition of new and varied technologies but also promoting novel concepts and ideas such as alternative animal models (zebrafish facility with a capacity of ~1,000 individuals) or the use of machine learning and statistical analyses in cancer biology (Canther-XAI platform aimed at providing advanced machine learning-based computational tools). One patent of the team was licensed to Boehringer Ingelheim in December 2023.

### Weaknesses and risks linked to the context

The quality of the scientific production does not fully match the potential of the team, especially in terms of skills and know-how. The synergy between different competences (i.e., back-and-forth interactions between biology and informatics) and research projects developed in the team, both in experimental biology and in machine learning, is not fully reflected in the publication record. There is a lack of permanent technical staff, especially for the projects in breast cancer. Teaching occupies an important place in the team's overall activity, impacting its scientific production. The translational potential of the research activity is not fully exploited (insufficient number of patent applications, only one Cifre).

### Analysis of the team's trajectory

For the next mandate, the pediatric glioma group will join the EpiCARe "Epigenetic Mechanisms in Cancer Risk and Resistance to Treatment". The i3-BioNet group will create a novel and independent team (Disco, "Digital, Systems and Computational Cancer"). This team will leverage existing tools and develop novel machine learning methods for biological networks that will constitute the core of Canther.XAI (eXplainable AI engine to accelerate Cancer systems Therapeutics). The project is organised in three axes, each led by one permanent and distinct researcher with specific competences. The objectives of Disco project and their implication in other projects of the OncoLille unit are well presented. The rest of the team will continue their research project on brain tumours by studying the mechanisms underlying cell persistence and the ability of cancer cells to adapt to both treatment and the surrounding environment, ultimately contributing to the development of brain metastasis. This project consists of three axes: (1) targeted approaches, (2) unbiased approaches, and (3) functional ex vivo and in vivo validation. This multidisciplinary project incorporates innovative biological models and research tools, and capitalises on recent data produced by the team. The projects are overall innovative and relevant to clinical research, potentially leading to new therapies. It is well supported by the current manpower and secured funding. The team is also well integrated in identified axes of the OncoLille project, and ongoing PIAs (e.g., Siric). Nonetheless, the lack of sufficient focus and synergy between developed projects could affect the research output and its full success in a such competitive domain.



# RECOMMENDATIONS TO THE TEAM

The committee fully supports the team on the proposed project focused on brain metastasis with state-of-theart -omic methods and relevant biological models already developed. Nonetheless, given the competitiveness in this area of research, they recommend that the team focus on the most promising research result and try to publish in the best journals of this domain in order to increase their research excellence and attractiveness.

The committee recommends that the Disco team focus on the methodological aspects of the project, which thanks to ongoing collaborations with clinicians and/or biologists, have the potential to be published in excellent interdisciplinary journals (Nucleic Acids Research, Genome Biology, Genome Research, Nature Methods/Machine Intelligence, Cell Systems, etc...). This should help the team increase its attractiveness and its visibility, including participation in international conferences and in national/international computational biology committees. The Disco team may want to increase its interactions with the Laboratoire P. Painlevé. OncoLille may dedicate or request a permanent position, typically an engineer, to help biologists and clinicians use Canther.XAI and to free up research time for Disco members.

Given the socio-economic potential of the proposed projects, the teams, including Disco, should try to increase their interactions with industry in order to, for example, obtain more Cifre fellowships.



### Team 4:

SenFib; Senescence, Fibrosis and cancer

Name of the supervisor: Corinne Abbadie

# THEMES OF THE TEAM

The team investigates the contribution of fibrosis and senescence to cancer development and therapies. Research is organised into five axes that include understanding the regulation of pulmonary and renal fibrosis by non-coding RNAs, the potential role of senescence in tumourigenesis and anti-cancer therapies, and the potential cross-regulation of senescence and fibrosis.

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team made significant efforts to develop international collaborative networking through publications, grants and/or the organisation of conferences (European Sanofi eAward, European Pearl funding, Hubert Curien Partnership, Inserm International Research Project, organisation of the 2022 OncoLille days and 2019 3rd International Symposium Research on Healthy Ageing, with several invited international speakers from Switzerland, the Netherlands and Chile). By January 2022, the team was geographically unified and able to organize weekly meetings. Interactions with the non-academic world were developed, in particular through patent applications (two are being licensed) and contracts (Sanofi iAwards and several other contracts with private companies).

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

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	13
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	7
Sous-total personnels non permanents en activité	8
Total personnels	21

# **EVALUATION**



### Overall assessment of the team

The team published 43 articles in leading position in excellent journals (J. Clin Invest, ELife, Trends in Biochemical Sciences, Am J Respir Crit Care Med.). Collaborative publications were also of excellent quality (NAR, Oncogene). The attractiveness is excellent with regular funding: three Feder European grants (1 as coordinator), one Plan Cancer Hypoxia as coordinator, two ANRs and one INCa as partner, international collaborations (Germany, Belgium) and participation in national committees (Itmo, CNRS, CoNRS, CNU). The team established interdisciplinary collaborations (Inria). Interaction with the non-academic sector (Therakos, Hema. T Medical, Marvel Biotech) and society (e.g., internships of young students from colleges/lycées) are also excellent.

### Strengths and possibilities linked to the context

The team has a solid base of permanent staff (total of 13 researchers, clinicians and engineers/technicians). Two permanent researchers joined the team during the mandate.-.The team trained sixteen PhD students (including 3 of medical education). Staff with temporary contracts are accompanied in finding other positions in academic or non-academic structures. Nine PhD defenses were fulfilled with eleven HDR. The team secured national and regional grants (8 as coordinator, 2 as partner; ~4M€): 4 grants from Cancéropôle Nord-Ouest as PI, two ANRs and 1 INCa as partner. From charities and foundations, members obtained fourteen contracts as Pl including LNCC and Gefluc, as well as four PhD fellowships from the Ecole doctorale Biologie-Santé de Lille and the Namur University or Europe (European Pearl fundina). In addition, they obtained a total of 380k€ from collaborations with non-academic partners (Therakos, Hema, T Medical, Chiesi, Sanofi, Astellas, Novartis, Marvel Biotech). The team published 43 original research articles, including publications in excellent journals (J Clin Invest, Elife, Cell Death & Disease and Am J Respir Crit Care Med) in leading position, thirteen reviews (including in Trends in Biochemical Sciences) and eleven clinical articles. Notably, they showed that the FDA-approved adenosine A2A receptor antagonist istradefylline (KW6002) protects from cisplatin-induced nephrotoxicity and neuropathic pain in mice, and even potentiates the antitumoural properties of cisplatin (JCI 2022). This work also led to an international patent. A total of three patents have been deposited, two of which not yet licensed (negociations on-going between Inserm Transfert / Marvel Biotech (CANADA). The team is implicated in four clinical trials lead by the Lille Hospital and by the Centre Oscar Lambret. The team has responsibilities and activities in local (Cancéropôle Nord-Ouest, Ligue Régionale contre le Cancer, Association Lilloise pour le développement de la recherche médicale, Santélys Association) and national committees (ITMO, CNRS, CONRS, CNU).

### Weaknesses and risks linked to the context

The team has not yet sufficiently exploited its research activity and networks to acquire more national and international fundings. Interdisciplinary collaborations have been established (notably Mathematics with the Laboratoire Paul Painlevé, and Physics with the Institut d'électronique et de microélectronique du Nord) but not sufficiently developed. Axis 4 is rather competitive but seems less endowed in terms of personnel and finance compared to the other axes.

### Analysis of the team's trajectory

The team's future project aims to (i) study the contribution of fibrosis and senescence in age-related diseases, including cancer, (ii) decipher the role of senescence in cancer initiation, and (iii) investigate the potential of senescence and fibrosis modulation as anti-cancer treatments. This project is well organised, supported by the current staff, and has secured funding. In particular, it will draw on the expertise of established and newly recruited clinicians. Some of the subprojects currently developed are already addressing the weaknesses mentioned above (see Axis#2, Project #3). Overall, the project fits well with the objectives of the OncoLille institute, the Pasteur Institute and the University of Lille.

# RECOMMENDATIONS TO THE TEAM

The committee encourages the team to continue its excellent work. The team should leverage its research activity and network to acquire more international funding. We encourage PIs of the team to apply for competitive European grants. The team needs to be strengthened by recruiting full time researchers.



The team should also strengthen its interdisciplinary strategies, not only to analyse generated data, but also to generate experimental data and hypotheses from the outset of projects. This approach is already proposed for one axis (Axis#2, project#3) and could serve as a model for other ones. For instance, approaches based on CMap and/or David to analyse transcriptomic data and the role of non-coding RNAs (Axis#1, Project #2) could be refined with methods developed by the Disco team. Taking on team leadership should be used by the new team leader to justify teaching leave (CRCT, IUF) in order to disengage time for research, participation in international conferences, and fundraising.

Leukemia; Factors of Persistance of Leukemic Cells Messrs. Bruno Quesnel/Salomon Manier

# THEMES OF THE TEAM

The team studies the mechanisms of persistence of leukemia cells, and evaluates their clinical relevance. Research was historically focused on cell intrinsic mechanisms. More recently it was expanded to include immune microenvironmental components, with a focus on how these dependencies could be leveraged to derive new treatment strategies based on a novel concept called 'synthetic immunity'. The team has also developed a new program regarding drug resistance and treatment innovation in multiple myeloma. The team continues to study acute myeloid leukemia in the context of translation biomarker / molecular classifier discovery initiatives.

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team's research is focused on the mechanisms of persistence of leukemia cells, and evaluating their clinical relevance. The research was historically focused on cell intrinsic mechanisms. More recently the research scope was expanded to include consideration of immune microenvironmental component with focus on how these dependencies could be leveraged to derive new treatment strategies based on a novel concept called 'synthetic immunity'. The team has also developed a new program regarding drug resistance and treatment innovation in multiple myeloma. The team continues to study acute myeloid leukemia in the context of translation research with biomarker / molecular classifier discovery initiatives.

Catégories de personnel	Effectifs
Professeurs et assimilés	7
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	13
Sous-total personnels permanents en activité	26
Enseignants-chercheurs et chercheurs non permanents et assimilés	3
Personnels d'appui non permanents	4
Post-doctorants	0
Doctorants	14
Sous-total personnels non permanents en activité	21
Total personnels	47

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

# **EVALUATION**



# Overall assessment of the team

The team's scientific production is excellent to outstanding, with 62 original articles in the field of oncology/onco-haematology published in leading positions in generalist and specialised journals such as Science Immunology, Blood, Blood Advances, J Clin Oncol, Cell Reports, Nat Comm, Elife. The attractiveness is excellent as attested by success in one European Interreg grant and competitive calls at the national level (1 ARC Programme Labellisé, ANR JCJC Switchkine, 1 ARC-Sign'it, 5 ARC program grants with team members as PI). The interaction with the non-academic sector is outstanding: eight filled patents and two startups (Switchkine and Lattice Medical). The team has been active in training, with eleven PhD students defending their work in the evaluation period and five members achieving promotion at the university or Inserm during the evaluation period.

### Strengths and possibilities linked to the context

The team's major strength is its ability to perform high impact research across basic, translation and clinical aspects of disease resistance in AML and MM. The team has positioned itself to perform this within the context national groups (Alfa groups). of French study in these diseases and IFM The team is continuing in its niche concepts focused on the basic and translational biology of residual/ persistent cancer cells in two study models AML and MM, in particular in relation to highly original synthetic immunity strategies and concepts. The team published 62 original articles in the field of oncology/onco-haematology published in leading positions in generalist and specialised journals such as Science Immunology, Blood, Blood Advances, J Clin Oncol, Cell Reports, Nat Comm, Elife. Funding included one European Interreg grant and one ARC Programme Labellisé, one ANR JCJC, one ARC-Sign'it, five ARC program grants with team members as PI. The team has developed state of the art/or beyond state-of-the art 'multi-omics' and functional/ phenotypic approaches for their work in synthetic immunity (as shown in the recent Science Immunology paper, for example). The team is centralising ambitious ancillary biology programs in the context of phase II/III clinical trials in MM (phase III IFM 2017-03 clinical trial; NCT03993912 and the phase 2 IFM2021-01 trial). The team's most novel findings for patient treatment are transitioned to start up for clinical development by the team (SwitchKline therapeutics). The team has identified the need for new recruitment and is applying to host a Chair Junior Professorship. A young investigator candidate has been identified for recruitment to Inserm.

### Weaknesses and risks linked to the context

The team has relatively few permanent engineers.

The team could assess its strategy for recruiting additional MD to PhD programs and international post-docs. Members did not succeed in International/ EU grants.

### Analysis of the team's trajectory

The team's trajectory is a solid if ambitious programme focusing on the historic themes of the team, while adding a new area of investigation regarding 'synthetic immunity'. There are two main objectives: 1/ studying the role of molecular plasticity (genomic, metabolic, phenotypic) in cancer cell persistence and 2/ dissecting the tumour/microenvironment interactions for enhanced synthetic immune responses. The focus is on two study models - multiple myeloma and AML. Funding has been achieved and preliminary data is convincing and abundant. The rationale and added value of an emerging paediatric onco-haematology team, under the leadership of a DR Inserm from the team, was not sufficiently clear to be fully convincing, at this stage.

# RECOMMENDATIONS TO THE TEAM

The committee recommends that this dynamic team continue to prioritise excellence in research in order to increase overall attractiveness and to raise its international reputation. A key aim will be to raise the number of very high impact papers. In fine, this will accelerate transfer of innovations to the patient. The new team leaders who have already demonstrated their effectiveness by getting the new research programme launched with funding and published data, are strongly encouraged to focus together on the strongest projects, and to pay careful attention to the balance between translational and basic science findings, combining both into joint, high impact papers when possible. The proposed new direction with a clinician and basic scientist -is highly commendable.

The team could consider applying for ERC funding or other grants at the EU level. The team could consider hosting / co-hosting a Marie Curie training programme.



# CHARACTERISATION OF THE UNIT

- Name: Laser Assisted Therapies and Immunotherapies for Oncology
- Acronym: OncoThAl Label and number: U 1189
- Composition of the executive team: Mrs. Nadira Delhem, Mrs. Anne-Sophie Vignion

# SCIENTIFIC PANELS OF THE UNIT

SVE4: Immunity, Infection and Immunotherapy

ST1: Mathematics

ST2: Physics

SVE7: Prevention, Diagnosis and Treatment of Human Diseases

### THEMES OF THE UNIT

Research within the OncoThai unit aims to develop oncological applications of photo-dynamic therapy (PDT), an innovative assisted laser therapy, and to evaluate its biological impact on immune responses. The unit is comprised of two research teams dedicated to developing basic, translational and clinical projects using a multidisciplinary approach.

# HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The current OncoThai unit "Assisted laser therapies and immunotherapies for oncology" emerged from the unit U703 "Interventional therapies assisted by image and simulation", which was set up in 2005 and renewed twice. In 2015, the single-team unit was called OncoThai and focused on the treatment of certain types of cancer using photo-dynamic therapy (PDT). The unit has historically been based at the Lille University Hospital (CHU of Lille), with financial and material support from Inserm, the University of Lille 2 and the CHU. During the last mandate, the unit became a two-team unit with the integration in 2020 of the immunology and cancer immunotherapies team "immunoPDT". The 2 teams share their specific skills and work together to develop new therapeutic solutions for the treatment of cancers and better understand the role of PDT in immune regulation. The two teams were located at different sites until September 2022, when they moved into the new OncoLille building on the Lille CHU campus. Shortly after its re-creation in 2020, the departures of several physicists affected the functioning of the unit. In September 2020, the PhysicoPDT team leader resigned to become CEO of the startup Hemerion, and in February 2021, the unit director and new PhysicoPDT team leader also stepped down. The ImmunoPDT team leader, who had been deputy director, took over as director of the OncoThai unit.

### RESEARCH ENVIRONMENT OF THE UNIT

The unit is a member of the federative research structures of the site SFR "Health Technologies" and the SFR "Cancer" and has developed close links with the LRGP (Laboratoire Réactions et Génie des Procédés) laboratory in Nancy on the chemistry and pharmacology aspects associated with their research activities. The two OncoThai teams have strong collaborations with five clinical units and five hospital laboratories of the Lille CHU Hospital, for which Cancer and immunotherapy strategies are major activities. This strong integration also provides medical students for internships. Around twenty medical doctors are integrated in the OncoThai research unit. The unit is well positioned in the international PDT ecosystem, and is integrated to the Clinical Investigation Center of Lille (CIC) that provides the infrastucture for their clinical studies. The OncoThai unit benefits from the logistical and scientific support of the Biomedical research and Public Health Committee (Cors2) of Lille University campus, for which one Oncothai-affiliated physicians of the unit is the President and also the national coordinator of the network of regional expert centers for the management of malignant pleural mesothelioma labeled by INCa in 2020. OncoThai members are members of the French Society of Immunology (SFI) and the international Society of Exosomes and Microvesicles. The unit was also associated to the emergence of start-ups (Immune InsighT and Hemerion Therapeutics), 2 spin-off of the laboratory.



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

Catégories de personnel	Effectifs
Professeurs et assimilés	10
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	]
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	19
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	10
Post-doctorants	0
Doctorants	9
Sous-total personnels non permanents en activité	0
Total personnels	29

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

Nom de l'employeur	EC	С	PAR
U LILLE	4	0	0
Inserm	0	1	4
CHRU LILLE	8	0	0
AUTRE	1	0	1
CNRS	0	0	0
INST PASTEUR LILLE	0	0	0
CLCC LILLE	0	0	0
Total personnels	13	1	5



# **GLOBAL ASSESSMENT**

OncoThAI develops an innovative therapy, Photodynamic Therapy (PDT), essentially for cancers that have reached a therapeutic impasse. The originality of the unit's project lies in the study of the interplay between PDT and the immune system. The scientific objectives align with the unit's expertise and are clinically relevant. The unit's strengths lie in its close integration within the local hospital ecosystem and the interdisciplinary nature of its research activities. Despite the difficulties encountered early in the mandate, including the departure of the unit director and a team leader, the unit performed satisfactorily, as evidenced by the number of publications, the acquisition of research funds to finance clinical studies, new patents and the training of PhD students.

OncoThAI was successful in obtaining local (La Ligue Contre le Cancer, Gefluc) and national (CEA, PCSI ITMO Cancer, CNO, SFR Cancer) contracts, as well as funding from the pharmaceutical industry (BMS, Texinov) and valorisation agencies (SATT), representing a total amount of 2.500 k€.

The attractiveness and leadership are very good to excellent. The director and Oncothai-affiliated physicians are invited to speak at national and international conferences and are coordinators or members of several national and European networks. The unit has trained 24 PhD students, half of whom are/were medical students. However, the unit has lost team members without attracting new researchers. The unit is attractive for the quality of its technological equipment and has developed a biological ancillary study platform in 2020 for immunological exploration of samples from clinical trials.

Scientific output is excellent in terms of quantity (199 international articles, 109 of which the members of the unit are first and/or last authors), and very good in terms of quality, with numerous publications in specialised journals such as British Journal of Dermatology, Frontiers in immunology or Journal of Extracellular Vesicles. More than half publications are medical publications, linked to clinical trial results and multicentre studies (Annals of Oncology, Lancet, New England, etc.) and signed by the unit's clinicians and coordinators of translational axes. Among the team's highlights is the work on the role of galectin-9 in tumour development, which led to two patented monoclonal antibodies for immunotherapy, one of which has been industrially licensed.

Transfer activities and interaction with the non-academic sector are overall outstanding, with six clinical trials for which Oncothai is the scientific sponsor, 4 patents, partnerships with Pharma and Biotech companies (Hemerion Therapeutics, BMS, Texinov, Modulight...), new medical devices, 2 start-ups (spin-offs from Oncothai), and a very good media coverage.

# **DETAILED EVALUATION OF THE UNIT**

# A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

In the 2018-2019 evaluation, the Hcéres recommended that the Oncothai unit (1) strengthen its research program via the recruitment of young researchers (PhD students and postdocs), (2) publish their work in higher ranked journals, (3) reinforce the scientific animation between the teams, and (4) regroup their intellectual property under a single mandate. The unit has followed these recommendations by increasing their number of supervised PhD students from nine during the previous term, to 24 in the current term. The overall publication track record remains very good to excellent, but the quality of target journals has not improved. The two teams have regular meetings and have overlapping projects through which interactions are enforced. The unit has not followed the recommendation to regroup their patents via a single mandate, although this may not have been possible with the coinventors.



# **B - EVALUATION AREAS**

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

# Assessment on the scientific objectives of the unit

The scientific objectives are excellent, in line with the unit's expertise and highly relevant from a clinical point of view.

### Assessment on the unit's resources

The Oncothai unit's ressources are very good to excellent. The unit has had access to the necessary resources to pursue their ambitious research program. This includes biology labs, custom-made illumination devices for cell biology and in vivo research. Furthermore, the unit has access to the microscopy, flow cytometry, histology and animal experimentation platforms located on the medical campus.

# Assessment on the functioning of the unit

The unit has faced difficulties over the past term, including the departure of a team leader and the unit director. Nonetheless, the unit has performed satisfactorily, as indicated by the number of publications, acquisition of research funds to finance clinical studies, new patents, and the training of PhD students. The unit is rated very good to excellent on this criterion.

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

### Strengths and possibilities linked to the context

The OncoThai unit has historical and recognised expertise in photodynamic therapy (PDT) and the design of medical devices that is unique in France. Since 2020, the unit has combined this expertise with that of the immunoPDT team to assess the impact of PDT on immune responses. Understanding the biological and immune mechanisms associated with this innovative therapy is clearly justified by the growing interest in its use in oncology over the last few years. The main objectives of the unit were to develop tools and skills in order to gain a better understanding of the mechanisms of photodynamic therapy, and to set up clinical protocols to treat certain cancers in therapeutic failure, such as glioblastoma, malignant pleural mesothelioma and peritoneal carcinomatosis of ovarian origin. Scientific objectives are structured around five translational research axes, each coordinated by a clinician. Thanks to its integration into the clinical environment of the University Hospital campus and the effective participation of several clinicians from the CHU of Lille, six new clinical protocols have been initiated, some of which are still in progress. The scientific objectives are in line with the unit's expertise, clinically relevant and have been realised through effective fundraising efforts at local and national levels and industrial partnerships. Strengths of the unit are in close integration with the hospital local ecosystem and the interdisciplinary nature of its research activities.

### Weaknesses and risks linked to the context

As mentioned in the self-assessment document, the unit faced major difficulties during the mandate, which had an impact on the unit's dynamism and scientific activities, with the unexpected departure of one clinician (PU-PH) and three scientists, including the unit director, the PhysicoPDT team leader and an engineer, who held most of the expertise in optics and physics.



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

Strengths and possibilities linked to the context

Recurrent funding from institutional bodies (Inserm, Université de Lille and CHU) represents an average of 150 k€/year. These resources are mainly used to purchase common consumables, maintain laboratory equipment and carry out missions. Over the evaluated period, OncoThAI was able to secure several local and national contracts, as well as funding from the pharmaceutical industry and valorisation agencies, representing a total of 2,500 k€ in own resources.

The unit comprises 26 permanent staff members including nine MD-Professors (PU-PH), two MD-Associate Professors (MCU-PH), one PU, one MCU, one Inserm DR, six hospital praticians (PH), two research engineers, two technical engineers, one lab manager and one administration assistant, and fourteen non-permanent members including nine PhD students, two post-docs and three non-permanent fixed-term contracts engineers. This represents a total of 20.5 full-time equivalent positions, and twelve scientists/clinicians have an HDR. Members of the unit are located in the same building, over one floor and shared working spaces and technical platforms. The unit has readily access to the different technological core facilities of the OncoLille building.

# Weaknesses and risks linked to the context

There is a clear imbalance between scientific researchers and hospital researchers/clinicians with the lack of full-time researchers (CRCN or DR) in the unit. No young researchers were recruited during the last evaluation. More than half of the unit's members work part time in the hospital, which may be beneficial for pursuing clinical aspects of research projects, but is not optimal for basic academic research. Considering the current workforce, the number of research projects seems somewhat excessive.

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

The OncothAl unit, which comprises two teams, is headed by a director and a deputy director, assisted by a management and financial secretary. Meetings to discuss science and the general running of the laboratory are organised every week with the members of the unit. A unit committee made up of the management team, all the unit's permanent researchers, team leaders, Pls, a health and safety representative, the laboratory director, a research engineer representative, a student representative and a post-doctoral student representative meets three times a year. The unit actually hosts one visiting MCU from abroad (Algeria). Each new recruit receives a 'welcome booklet' describing the laboratory's organisational, safety and intellectual property rules and policies, and signs a confidentiality agreement setting out the rights and obligations in terms of confidentiality, intellectual property and publications. The scientific, social and supervisory quality of placements is assessed anonymously by Masters and Bachelor students. The unit takes into account the results, which have been very positive to date, in order to improve them further if necessary. Authorisations and agreements are obtained for the use of biological resources (blood bags) and for animal experimentation protocols on mice, rats and mini-pigs. A document allows to answer the administrative questions that arise from PhD students and post-doctoral fellows (paid leave, insurance reimbursement, social benefits, useful contacts such as a psychologist, handicap service, psycho-social risks, equality and diversity service). Up to 2022, the unit had implemented various systems for protecting and backing-up its computer data (RAID, secure storage servers, archiving of data with an approved hosting provider, private cloud). Since their arrival at the OncoLille Institute, they are using the computer park of the University of Lille for computer security and data backup. The unit is in an eco-responsible approach (setting rules for recycling, exchange, donation of old equipment setting recycling rules, donation and recycling exchanges).

### Weaknesses and risks linked to the context

Although the two teams and the unit are headed by women, overall women only represent 24% of permanent staff. The electronic laboratory notebook will not be in use until September 2024.

# Assessment on the attractiveness of the unit

The attractiveness of the unit is very good to excellent as attested by invitations of the PI to national and international conferences, active participation in scientific and medical networks, regular funding from national and charity grants (CEA, PCSI/ITMO, INCA PHRCK, Ligue contre le cancer), and also via valorisation of its work (SATT, BMS). This is all the more notable as PhysicoPDT lost team members early in the mandate. The unit has trained 24 PhD students and has been attractive for the quality of its technological equipment.

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

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

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

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

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

The attractiveness and leadership of the director and OncothAl-affiliated physicians is demonstrated by their participation in structuring activities as coordinator or chairman (SFR health technology, European Network of Rare Skin Cancers (Euracan), Biomedical research and Public Health Committee (CORS2) of Lille University campus, French College of Biophysics and Nuclear Medicine, National network of regional expert centers for the management of malignant pleural mesothelioma, National College of Pneumology Teachers and French Society of Radiology). A member of the immunoPDT team is the scientific Director of the Cancéropôle Nord Ouest (CNO). The unit develops the technologies and tools necessary for the implementation of PDT in human clinics and has a recognised expertise in the design of medical devices, mathematical modelling of photodynamic mechanisms, treatment planning and simulation and dosimetry estimation during treatment. Members of the unit are affiliated to national or international networks or societies such as the international Photodynamic Association (IPA), the French Society of immunology (SFI) or the international Society of Exosomes and Microvesicles (ISEV). During this mandate, Oncothai's members have organised local and national meetings (Journées d'Immuno-Oncologie du Nord-Ouest, 14es Assises de Gynécologie Obstétrique) and two international conferences (15th congress of the European-African Hepato-Pancreato-Biliary Association, Lyon, 2023; Conférence internationale de l'international Mesothelioma interest group-iMig-à Lille).

The unit is committed to the quality of its staff hosting policy, which has led to seven promotions, one MCU-PH and one PU-PH positions, and to ensuring that staff have the necessary resources, such as training and mentoring, to carry out their work effectively. The unit encourages its research engineers to obtain a HDR and co-supervise thesis students. Clinical project investigators, team's leaders, the director and the deputy director work in coordination to define unit's priorities and research strategy. All unit members contribute to the general unit functioning and discussions concerning scientific and social issues. Since its relocation to the OncoLille building in 2022, staff has benefited from a highly favorable and attractive scientific and technological environment.

The two OncoThAI teams have been successful in several national grant applications (CNO, SFR Cancer, INCa, PCSI). Most of their funding (total of 2,000 k€) was obtained from industry and valorisation agencies (SATT Nord, BMS, Texinov, I Latex, Galderma). In particular, the immunoPDT team obtained around 600 k€ from the SATT Nord for the maturation of their projects and the valorisation of new patented drugs. The funds raised led to the recruitment of three engineers, two post post-docs and two PhD students. In addition, thanks to the licensing of the Gal-9 patent with Fibrogen, the OncoThAI unit has obtained around 200 k€ from patent royalties. The unit hosted two international researchers from Japan and Algeria, and students from European and non-European countries. The unit has trained 24 PhD students, half of whom are/were medical students and has welcomed around 5 Master's students each year. All of them have found a position, either as a PhD student or as an engineering assistant within the unit or outside. However, the unit has lost team members (researchers and engineers) without attracting new researchers. PhD students are recruited through grants from charities (La Ligue Nationale contre le cancer), industrial partnerships (2 Cifre) and ministerial grants from the Ecole Doctorale. One



former PhD student from the PhysicoPDT team was behind the creation in 2020 of the startup Hemerion Therapeutics.

The unit has made notable effort in the development and acquisition from its own resources of several technological instruments, equipments, and an IT infrastructure. The quality of the developed tools and medical devices for the implantation of PDT in human clinics is excellent. Oncothai has recently developed a state-of-the-art platform for immunomonitoring and immunophenotyping clinical samples from ancillary studies that is supported by a qualified staff. The unit has implemented a quality control policy to develop quality research projects.

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

Although the unit has excellent funding resources, it does not have European or international grants. There was no recruitment of researchers/staff with biophysics expertise and experience.

# EVALUATION AREA 3: SCIENTIFIC PRODUCTION

### Assessment on the scientific production of the unit

Although the level of journal publications is very good, both in terms of number (199 articles total, 109 with members of the unit in leading position) and quality (specialty journals such as British Journal of Dermatology, Frontiers in immunology, Lasers in Surgery and Medicine), more than half of all publications concern medical multicenter studies on subjects that are far from the unit's core research. The scientific output is fairly balanced between articles in scientific journals and clinical trials described in medical journals. Nonetheless, the PhysicoPDT team's recent drop in the number of publications is a cause for concern.

- 1/ The scientific production of the unit meets quality criteria.
- 2/ The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.
- 3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.

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

The scientific output is divided between articles in medical journals (generally published by university-hospital medical staff) and more scientific or technological journals (generally published by researchers and/or teacherresearchers). 199 articles were published, of which 109 with members of the unit as first and/or last authors) in specialty journals (e.g., British Journal of Dermatology, Frontiers in immunology, Journal of Extracellular Vesicles, Lasers in Surgery and Medicine, PLOS one, International Journal of Molecular Sciences...). The number of publications is well distributed between the two teams, with many publications including members of both teams (41%). 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. Only a few of the papers are in predator journals such as MDPI. All of the papers are available at Hal open science deposit. Communications at international or national conferences was mainly driven by a PU-PH and the director of the IPIC team (e.g., 5th Annual World Congress of Digestive Disease 2022, 14th International Conference on Lasers, Optics & Photonics Chicago 2022 or Global Summit of Biopharma 2023). The rule of thesis students signing as first authors and senior researchers towards the end is well respected.

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

More than half of all publications (52%) are medical publications linked to multicentre studies that are far removed from the unit's scientific themes, but they are related to the specialties of the hospital-academics. These publications generally involve a large number of authors (>10), with only one or two authors from the unit. This large number of publications is mainly signed by three PU-PH. The evolution of scientific publications over



time is fairly revealing of the trajectory of the teams within the unit. At the start of the reference period, the level of publications by the two teams was fairly balanced, with a fairly equal number of single-team publications between the two teams (although the number of publications signed by members of the PhysicoPDT team was slightly higher) and a good level of collaborative publications between the two teams. However, from 2022 onwards, there was a fairly drastic drop in the number of publications co-authored by members of the PhysicoPDT team, more precisely the PhysicoPDT team director, the unit director and a research engineer. The relatively small number and often middle position in the list of authors of the future PhysicoPDT team leader is quite logical in view of her status as a research engineer.

# EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The interaction with the non-academic sector is outstanding, with six clinical trials, four patents, commercial partners, two startups (Immune InsighT & Hemerion Therapeutics), new light and dosimetry instrumentations and notable media attention (France 3, radio, Youtube).

- 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

OncoThAI's research was very technology-driven (4 new patent families over the reference period). It has spun off into a start-up (Hemerion Therapeutic, created by physicoPDT alumni) and had strong collaborations with industry (Texinov in heated textiles, one of physicoPDT's key research areas). ImmunoPDT team has stron ties with national and international pharmaceutical industries (BMS, ModulighT, Immune insighT). As result of these emerging technologies, combined with the clinicians that are associated with OncoThAI's teams, OncoThAI is now globally recognised and valued for its ability to translate PDT to the clinic for hard-to-treat cancers (e.g., glioblastoma) via the Hemerion Therapeutics spin-off company.

The staff is also actively involved in international and national scientific communities. They are involved in various networks and learned societies, again at both international (3) and national (6) levels. Over the period, four conferences were organised by doctors affiliated to OncoThAI. Team members (Oncothai-affiliated physicians) occupy important strategic positions: Presidencies (Biomedical Research Committee of Lille University Campus; European Network of Rare Skin Tumours; National College of Pneumology Teachers), Scientific Director of the Canceopole Nord Ouest, and National coordinator of the network of regional expert centers for the management of malignant pleural mesothelioma. Several doctors and hospital-professors regularly appear on radio and television or in mainstream medical journals on subjects related to their medical and scientific expertise. Doctoral students are actively involved in public events (2 participations in MT180, Fete de la Science, etc.).

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

The unit's strong links with the economic sector seems to be diminishing (at least for the PhysicoPDT team). Scientific activities mainly concern networks or learned societies linked to the pathologies treated by doctors associated with OncoThAI. They seem to be much more limited when specifically considering the scientific fields covered by OncoThAI.



# **ANALYSIS OF THE UNIT'S TRAJECTORY**

The two teams will merge into one as part of the OncoLille unit. The contribution and integration of the work in a single team will provide real added value to the joint projects. For the next contract, several new projects will thus be initiated with a very original translational and transdisciplinary approach. Its aim will be not only to demonstrate that PDT is an effective therapy that can be applied in the treatment of cancer, but also that it allows to modulate the immune system, and thus play the role of a true anti-cancer vaccine adjuvant. The same oncological pathologies as in the previous contract will be studied.

# **RECOMMENDATIONS TO THE UNIT**

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

The committee encourages the new team to maintain its transdisciplinary and translational approach, and supports its integration into the OncoLille project.

The committee recommends that the team implement a policy to attract and recruit young researchers, in particularly in physics or engineering science. The team should secure long term fundings and attract more international PhD and postdoctoral fellows. Opportunities for EU funding should be increased. This may help to obtain more post-doctoral positions that may be critically needed to reach all the goals of the project. The committee recommends that the OncoThAI team better integrate into the new OncoLille unit, to benefit

from the state-of-the-art methods, platforms and scientific expertise that the institute has to offer. Considering the current workforce, the number of research projects seems somewhat excessive. It would be advisable to refocus the activity of the unit on the most promising axes.

# Recommendations regarding the Evaluation Area 2: Attractiveness

Despite its excellent ability to finance its projects and its expertise in the field of PDT and immunotherapies, this unit has not fully capitalised on its research activity and network. The unit should leverage its scientific expertise to increase its participation to European programs and networks. The recruitment of new scientific staff would enhance the unit's competitiveness. The addition of more competitive academic grants (European or French) would help improve the unit's current level. The unit should fully exploit the momentum sparked by the creation of the unit to achieve these goals.

# Recommendations regarding Evaluation Area 3: Scientific Production

The committee recommends that the unit avoid dispersion by focusing on a few cancer pathologies, and that deeper mechanistic investigations should be carried out. This would allow publications in more prestigious journals. The committee recommends that the new team continue to expand its research activities into basic, translational and clinical projects. The committee recommends that the team expands on its experimental studies with state-of-the art methodologies (transcriptomics, proteomics, metabolomics) to uncover the mechanisms of PDT and combination therapies in a more comprehensive manner.

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

No specific recommendations



# **TEAM BY TEAM ASSESSMENT**

Team 1: ImmunoPDT: Laser Assisted Therapies and Immunotherapies for Oncology

Name of the supervisor: Mrs. Nadira Delhem

# THEMES OF THE TEAM

The team ImmunoPDT aims to offer an innovative therapy essentially for cancers in therapeutic impasse. Indeed, the use of PDT in oncology has been increasing during recent years, in particular due to its impact on the activation of the immune response and the emergence of immune-therapies. Based on this rationale, ImmunoPDT is dedicated to the development of basic, translational, and clinical projects, in order to characterize the effects of PDT (alone, or in combination with conventional treatments) on the regulation of the immune response.

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous Hcéres committee recommended that the team (1) apply a more ambitious methodology within their biological research to increase the originality and impact of their work, (2) improve communication strategies with team PhysicoPDT, and (3) focus research efforts on the interaction between PDT and immune responses. The team has followed most of these recommendations, as communications with team PhysicoPDT have indeed been achieved through frequent unit meetings. New projects on immunotherapies have emerged, albeit not always in conjunction with PDT. Moreover, the teams will now merge for the coming mandate. However, the implementation of state-of-the-art methodologies such as RNAseq, proteomics, and advanced flow cytometry remains largely unexplored.

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	11
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	4
Post-doctorants	0
Doctorants	8
Sous-total personnels non permanents en activité	12
Total personnels	23

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

# EVALUATION



### Overall assessment of the team

The publication track record is very good, with 74 clinical articles of which 34 signed as first, last or corresponding author and 45 original research articles with 33 signed as first, last or corresponding author. Some articles are in reputable journals such J. Extracellular Vesicles and Br J Dermatol. The attractiveness of the team is very good. The team has excellent funding with a total of 1390 K€, mostly

from industry and valorisation activities (932 K€ from SATT NORD, BMS). 258 K€ were secured from national calls or associations and foundations (CNO, SFR Cancer, CEA, PHRC, ITMO Aviesan) as partner, and 1 Inserm Ariane as coordinator.

The interaction with the non-academic sector is outstanding with six clinical trials, two startups (Immune InsighT & Hemerion Therapeutics), two patents and notable media attention (France 3, radio, Youtube).

### Strengths and possibilities linked to the context

The size of the team is coherent with its research activity and scientific objectives and is composed of five professor-clinicians, one lecturer-clinicians, one Inserm researcher (DR1), one researcher-engineer (IGR1), three technicians/engineers including two permanent (IE students (10 defended). During the last period, the team trained eighteen PhD students (10 defended). The team has excellent funding with a total of 1390 K€, mostly from industry and valorisation activities (932 K€ from SATT NORD, BMS); 258 K€ were secured from national calls or associations and foundations (CNO, SFR Cancer, CEA, PHRC, ITMO Aviesan) as partner, and one Inserm Ariane as coordinator. Since 2018, the team has produced 45 articles in leading position (33 original research articles, 4 reviews and 8 meeting publications) and 74 clinical article (34 in leading position). Among the team's highlights is the work on the role of galectin-9 in tumour development, which led to two patented monoclonal antibodies for immunotherapy, one of which has been industrially licensed. The team has also filed three declarations of invention and has been involved in the creation of two start-ups (Immune InsighT and Hemerion Therapeutics), spin-offs of the laboratory based on the team's expertise, both bio-incubated by the Eurasante pole of excellence. The team is nationally and internationally well recognised and several members of the team are involved in various international and national scientific and medical societies (International Society of Exosomes and Microvesicles, Society of Gynecology, SFI). The team has also been involved in four clinical trials and in a large number of clinical translational research published in high prestigious journals (Lancet, Lancet Oncology, New England Journal, ...). All PI of the team are involved in teaching at the Faculty of medicine. Several PI have participated to interviews or YouTube podcasts (France 3, youtube).

### Weaknesses and risks linked to the context

There is an imbalance between scientific researchers and hospital researchers/clinicians. Specifically, no young researchers were recruited during the last evaluation period. Although the team has excellent funding, it does not have European and international grants. The projects developed by the team are numerous and concern different oncological pathologies. Most of the team's most impactful research papers are not related to the topic of Oncothai.

### Analysis of the team's trajectory

At the time of the previous Hcéres evaluation, the main objectives of the OncoThAl unit were to develop its tools and skills in order to gain a better understanding of the mechanisms of photodynamic therapy, and to initiate several clinical protocols to treat certain cancers that had reached a therapeutic impasse, such as glioblastoma, malignant pleural mesothelioma and peritoneal carcinomatosis of ovarian origin. Above all, the extremely successful integration of the onco-immunologist team (ImmunoPDT), has made it possible to evaluate at the biological level the efficacy of PDT on tumour cells and the impact of PDT on the modulation of the immune system.

Furthermore, at the beginning of the previous evaluation, the two teams constituting the unit aimed to initiate a new research program focused on the therapeutic valorisation of PDT in the era of combined therapies. Thus, the expertise of the two teams, together with the team of clinicians associated with the OncoThAl unit and the contribution of the pharmaceutical industry (Novartis, BMS), made it possible to initiate new projects combining immunotherapy and PDT.

For the next contract, in pursuit of this dynamic, several new projects will thus be initiated with a very original translational and transdisciplinary approach aiming not only to demonstrate that PDT is an effective therapy that can be targeted in the treatment of cancer but also that it allows to modulate the immune system and



thus play the role of a true anti-cancer vaccine adjuvant. The same oncological pathologies as in the previous contract will be studied.

# RECOMMENDATIONS TO THE TEAM

The committee recommends that the team implement a policy to attract and recruit young researchers The team should avoid dispersion by focusing on a few cancer pathologies. Deeper mechanistic investigations should be carried out, which would allow publishing in more prestigious journals.

The committee recommends that the team continue to expand its research activities into basic, translational and clinical projects.

The committee recommends that the team expands on its experimental studies with state-of-the art methodologies (transcriptomics, proteomics, metabolomics) to uncover the mechanisms of PDT and combination therapies in a more comprehensive manner.

Team 2



Immunotherapies for Oncology

Name of the supervisor:

Mrs. Anne-Sophie Vignion

# THEMES OF THE TEAM

The PhysicoPDT team develops the technologies needed to implement photodynamic therapy (PDT) in the human clinic. Their research involves mathematical modelling of photodynamic mechanisms (in-silico studies), treatment planning and simulation, dosimetry estimation during treatment, and the design of medical devices.

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

It was previously recommended that the team (1) maintain a high level of valorisation, publications, and biological/immunological collaborations, and (2) avoid engaging in trials for too many applications.

Together with team ImmunoPDT, the first recommendation was followed. However, the second recommendation was not followed, as more projects have emerged within the novel thematic of combined therapeutic approaches. Taking into account the departure of the unit director, the deputy director, a postdoc, and research engineer, these new projects may jeopardize the progress and completion of previously started projects in a timely and impactful manner.

Interactions with the immunology team ImmunoPDT, recommended in the previous Hcéres evaluation, have been successful, facilitated by their regrouping in the same center in 2022. The recruitment of physicists (postdocs and PhDs) was recommended to strengthen the PhysicoPDT team. Over the past assessment period, the team was instead faced with the departure of a medical physicist (MCU-PH and deputy director of the unit), a postdoc, a physicist Inserm IE and the unit director (Inserm DR). Overall, the number of permanent staff was reduced from twenty in 2020 to thirteen in 2022. Concerning the recruitment of non-permanent staff, as of 31/12/2022 only one part time thesis student and one engineer on work-study contracts are part of the team. It was also recommended that the PhysicoPDT team avoid spreading its work by multiplying test for too many different applications. While the total number of applications has fallen, five (initiated by the PhysicoPDT team) are still mentioned. These however, are in the context of a growing collaboration with imunoPDT team.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	6
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	7
Sous-total personnels permanents en activité	14
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	3
Total personnels	17





# Overall assessment of the team

The scientific production is very good to excellent, with 85 publications from the team, 43 from clinical team members. Some work was published in respected journals (Br J Dermatol and J Eur Acad Dermat Venereol). The attractiveness is good: although research funds with team ImmunoPDT have been obtained, PhysicoPDT has lost team members without attracting new researchers. Funding was from regional and national agencies (CNO, SFR Cancer, INCA, Inserm Ariane, SATT Nord, Cancéropôle Nord Ouest...).

The interaction with the non-academic sector is outstanding, with 6 clinical trials, four patents, commercial partners, and new light and dosimetry instrumentations.

### Strengths and possibilities linked to the context

The PhysicoPDT team has a history and expertise in photodynamic therapy that is unique in France. This expertise covers most of the aspects of these therapies, from numerical simulation, device design and implementation of new therapeutic protocols, validation on ex- and in-vivo models, scheduling, intraoperative therapy guidance, to the creation of simulators for device validation. The team was at the origin of the creation of the Inserm U703 and then U1189 (OncoThAI) laser therapy unit. This expertise has been extended since the ImmunoPDT team was integrated into the Inserm OncoThAI unit following its restructuration in 2020. Most of PhysicoPDT's thermotherapy research axes now include aspects of immunotherapy, this association is a real strength, reinforcing the effect of the therapies.

The team has a very strong clinical base in the various therapeutic departments of Lille University Hospital. All PhysicoPDT research projects have a PU-PH or MCU-PH as principal investigator. The team has been remarkably successful in developing and conducting clinical pilot studies on several innovative approaches or medical devices. Funding was from regional and national agencies (CNO, SFR Cancer, INCA, Inserm Ariane, SATT Nord, Canceropole Nord Ouest...) for a total of 693 k €. Clinicians were strongly involved in research projects. The team also has a strong capacity for industrial developments, with the emergence of a start-up, Hemerion Therapeutics, headed by senior physicists from PhysicoPDT and supported by the SATT Lille. The team also has numerous collaborations with industrialists in France (Hemerion Therapeutic, Texinov) and abroad (Modulight, Finland). The level of scientific production is very good to excellent: 86 publications from the lab ad 43 from the team's clinicians, of these, over 70 are first or last authors. Most works are in respected specialty journals, and some works are in highly respected journals in their field (e.g., Br J Dermatol). All graduated PhD students have been authors on at least one scientific publication in peer-reviewed journals. It should be noted that methodological articles were mainly published in the first part of the reference period. One patent, one software application and one invention statement were registered. Some of the medical staff members attached to the team have a very high international profile and are often invited to conferences, or sit on editorial committees, but more in their medical specialty than on the team's themes. The unit's former director was also highly visible in the field directly related to the team.

### Weaknesses and risks linked to the context

The imbalance between researchers from physics or engineering sciences and hospital researchers, already noted in the previous evaluation, was accentuated during the current assessment period through the departure of key personnel. The absence of newly attracted researchers in this team is a substantial weakness that brings several risks. First, not renewing personnel can lead to the stasis of the scientific projects by failing to bring new ideas and dynamics to the group. Secondly, new projects may be stalled due an absence of manpower and existing projects may be delayed. This decrease in the workforce is also resulting in a decline of attractiveness and a drop in the number of PhD and post-doctoral fellows.

Another risk is the absence of representation of a health technology expert in the direction/codirection of the team, which may not lead to the optimal diffusion of PhysicoPDT's research findings towards the scientific community and public audiences.

### Analysis of the team's trajectory

As described above, the team is maintaining these clinical aspects, but is faced with a loss in strength in health technology due to the departure of key scientists from the unit. The contribution and integration of the work of the Immuno PDT team provides real added value to the PhysicoPDT team's projects. There is a continued need



for innovative illumination devices, dosimetry research, and implementation protocols that team PhysicoPDT will develop upon merging with ImmunoPDT.

# RECOMMENDATIONS TO THE TEAM

Recruiting researchers in physics or engineering science is critical to maintaining research activity over the long term. A real policy of recruiting full-time researchers or teacher-researchers in these fields should be pursued by the team, the unit and even at the highest level of OncoLille. This recruitment is also necessary to attract PhD students and post-docs. The technological advances and innovations should be more prominently developed, and these advances should be better presented by the team leader and deputy, who are not experts on these topics. The structure of the merged team brings together biologists, clinicians, and physicists, which allows for highly interdisciplinary research. The merged team should benefit from this attractive mix to pursue multidisciplinary research that is highly impactful, attractive, and has enormous potential for elevating the quality of future publications.



# CHARACTERISATION OF THE UNIT

- Name: Laboratory of Cell Physiology
- Acronym: PhyCell
- Label and number: UMR1003
- Composition of the executive team: Mrs. Natalia Prevarskaya

# SCIENTIFIC PANELS OF THE UNIT

SVE6 : Physiologie et physiopathologie humaine, vieillissement

SVE4 : Immunité, infection et immunothérapie

# THEMES OF THE UNIT

Research within the Phycell unit aims to explore the role of ion channels and inflammasomes in tumour initiation and progression, with a particular focus on prostate cancer and intestinal inflammation. The two teams of Phycell conduct research with a strong translational component, covering the development of new therapeutic approaches to improve responses to anti-cancer drugs and mitigate their adverse toxicities.

# HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The Phycell laboratory was created in 1997 on the Sciences and Technologies Campus of the University of Lille, and has been headed by the current director from the start. Phycell became a single-team research unit supported by the University and Inserm in 2006, and a multi-team structure in 2020 (Inserm U1003) with the arrival of a new team (team 2). The two teams are located on different sites. Team 1 is still located at the Sciences and Technologies Campus, while team 2 has been housed in the OncoLille building on the University/Hospital campus since October 2022.

# RESEARCH ENVIRONMENT OF THE UNIT

The unit belongs to the biology department of the Faculty of sciences and Technologies (FST) of Lille University since its creation and has been actively involved in the administration of the department and in the 2 federative research structures of the site (FRA Bio and SFR Cancer). Whithin the framework of FST's actions, the unit is leading a project on the role of ion channels in pathologies, including cancer. The Unit also contributes to the direction committee of the PLBS platform (Plateformes Lilloises en Biologie et Santé, UAR2014 CNRS-US41 Inserm). This service unit gathers all the platforms dedicated to biological studies including animal housing, genomics, imaging and flow cytometry platforms. Phycell hosts part of the BICel imaging platform, and has been involved in the implementation of advanced approachs of single-cell RNA sequencing and single-cell proteomics.

The unit is part of the OncoLille cancer research institute and was an active member of its structuration. Team 2 moved to the OncoLille building in October 2022, while Team 1 has remained located to the FST Campus. This integration fosters interactions and collaborations with other research units, teams and members of the OncoLille Institute working on cancer biology, technologies for health, microtechnologies, Mathematics and Human and Social Sciences providing an Interdisciplinary approach. The location of the OncoLille institute on the university hospital campus encourages interactions with clinicians from Lille hospital and from the anti-cancer centre Oscar Lambret (CLCC COL), and the transfert of the research findings to the clinic.

Both Phycell teams are also involved in the regional cancer research cluster Cancéropole Nord-Ouest. The unit is affiliated with the EDBSL doctoral school of the University of Lille.

Phycell is a co-founder and member of the Labex ICST, a national scientific network of excellence on the topic of channelopaties. The Labex ICST has been renewed in 2020 in the frame of the government's Programmes National d'Investissement (PIA).



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

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maîtres de conférences et assimilés	5
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	11
Sous-total personnels permanents en activité	24
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	6
Post-doctorants	2
Doctorants	7
Sous-total personnels non permanents en activité	17
Total personnels	41

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

Nom de l'employeur	EC	С	PAR
U LILLE	9	0	7
Inserm	0	4	4
CHRU LILLE	0	0	0
AUTRES	2	0	0
CNRS	0	1	0
INST PASTEUR LILLE	0	0	0
CLCC LILLE	0	0	0
Total personnels	11	5	11

# **GLOBAL ASSESSMENT**

Phycell's unit project covers the fundamental aspects of ion channel biology and inflammasomes, with a particular focus on the cellular mechanisms and the consequences of their dysregulation during epithelial carcinogenesis and associated inflammatory diseases. The unit is a pioneer in the study of the role of ion channels in cancer, and has gained clear international recognition in this field.

Research findings have been patented and published in scientific articles, with several contributions in top-tier journals. The presence of top-level team leaders with international recognition makes Phycell a leading unit in the field of ion channels and cancer biology.

The unit's overall attractiveness is remarkable, with numerous invitations to international meetings (20 including 13 in Europe), participation in three European networks, expert committees and very high success rates in competitive grants, as investigators: two INCa-PLBio, seven ANR (4 as PI), three Inserm/ITMO cancer, 1Labex, Feder, European MSCA, and one "team label" from the FRM, thirteen fundings from the Ligue Nationale/Régionale contre le Cancer. This is also evidenced by the awards received (EMBO Women in Science, Junior Member of IUF, member of the European Academy of Sciences). In addition, the unit has developed state-of-the-art electrophysiology and single cell platforms to support their research. In terms of human resources, the unit is also very attractive. The unit has trained nineteen PhD students, including fifteen foreign



students, hosted ten post-docs, and recruited two new research scientists. The unit's scientific output is excellent, with 60 scientific articles signed as first and/or last author and/or corresponding author by members of the unit (including high-level journals such as Nat. Commun, Embo J, Gut, Gut microbes and Physiological reviews). National and international collaborations have also led to the publication of excellent articles in widely read journals (Nat Commun, Cell, Science, Nat Med). The unit pioneered original research concerning the role of ion channels in oncogenesis and inflammatory diseases and has contributed to the notion of "oncochannelopathies" in the field (Physiol Rev 2018). The unit addressed relevant questions concerning the role of intracellular calcium in the control of the pro-tumoural behavior of senescent cells (Nat Comm 2022), the identification of a specific Na+ /Ca2+ signature required for persistent invasion of metastatic prostate cancer cells (Embo J. 2023) and the link between inflammation and pathogen infection (Nat. Comm 2018). The overall work environment is described as excellent.

In terms of valorisation and technology transfer, the unit is also considered as excellent with 6 patents, one of which has been licensed to a private company and another has led to an incubation phase prior to the creation of a startup, as well as very good public outreach activities.

The unit is classified as remarkable for the innovative character of the research conducted and attractiveness (participation in European networks, invitations to prestigious international conferences, awards).

# **DETAILED EVALUATION OF THE UNIT**

# A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The unit followed the recommendations made in the previous evaluation. Notably, the number of patents was increased and its participation in European projects and networks improved over the period through one MSCA-ITN, one COST actions/Era-Net, two Feder and a Joint Program Initiative-funded network. Improvements have been also made in increasing the training of PhD students and their scientific production, as well as in the recruitment of post-doctoral fellows. Communication among members of the unit has been improved by promoting weekly meetings in both teams and scientific retreats. The unit has implemented a better balance of tasks for the technical staff between the two teams.

# B - EVALUATION AREAS

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

### Assessment on the scientific objectives of the unit

The scientific objectives of the unit are excellent. The unit has established a competitive and cutting-edge research program in the field of cancer, focusing on the role of calcium-transporting channels and inflammasome in epithelial carcinogenesis. The aim is to understand how alterations in calcium/inflammasome signature influence tumourigenesis, in order to identify novel biomarkers or targets for improved cancer therapy. The scientific objectives are coherent and clinically relevant.

### Assessment on the unit's resources

The unit has secured funding, technical and human resources required for its research during the reporting period. The unit has succeeded in attracting funding and acquiring novel state-of-the-art equipments. The unit is rated excellent on this criterion.



# Assessment on the functioning of the unit

The functioning of the unit is excellent, thanks to efficient and stable direction. The unit complies with its institutional requirements regarding working conditions, safety, scientific procedures and reduction of environmental footprint. Communications between unit members has improved during the mandate.

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

### Strengths and possibilities linked to the context

The unit pioneered original research concerning the role of ion channels in oncogenesis and inflammatory diseases and has contributed to the notion of "oncochannelopathies" in the field (Physiol Rev 2018). The unit addressed relevant questions concerning the role of intracellular calcium in the control of the pro-tumoural behavior of senescent cells (Nat Comm 2022), the identification of a specific Na+ /Ca2+ signature required for persistent invasion of metastatic prostate cancer cells (Embo J. 2023) and the link between inflammation and pathogen infection (Nat. Comm 2018). The innovative nature and coherence of this research may have clinical utility to treat these diseases. The unit has a clear vision and knowledge of its research environment and its players, and since 1997 has contributed to two federative research structures on the Lille site (FRABio and SFR Cancer) and has been an active partner in the Siric OncoLille, which led to the creation of the OncoLille research center. The unit is also actively involved in the strategic committee of the local PLBS technology structure. Scientific objectives take into account the policies and priorities of the Inserm strategic plan in terms of standard procedures and operating methods, ethics, open-science and FAIR practices. The unit implicates all their staff members to develop their research strategy.

### Weaknesses and risks linked to the context

How the five clinicians of the unit integrate into the research strategy involving interaction with the hospital (UCL) and the anti-cancer centre (Centre Oscar Lambret) is not clear.

The "Ion channel" team remains at a different site away from the OncoLille building at the CHU. This poses a risk regarding direct interactions with the other teams.

# 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

Phycell's funding resources from Inserm and University of Lille prove around 160 k€/year and external sources contribute to 700 k€ to 1500 k€ annually. The unit was very successful in securing competitive grants (charities, INCa, ANR, Labex, Feder, European-funded networks ...) and acquiring new equipment (Inserm, CPER). The funding resources of the unit from regional, national, international and industrial grants have increased about 2fold over the assessment period. The unit has sufficient human resources to carry out its research activities. It hosts 45 people including five permanent researchers (2 DR and 3 CRCN), three Professors and five Associate Professors from the University of Lille, one PH, two MCU-PH, three clinicians, three invited Professors, four postdoctoral researchers, seven PhD students, and twelve PAR (10 permanent and 2 non-permanent fixed-term contracts on own ressources). The unit has access to the different technological core facilities of the FSP and OncoLille campus.

### Weaknesses and risks linked to the context

None



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

Phycell unit is made up of two teams and headed by a director assisted by two deputy directors and two administrative managers. The unit works to promote work-life balance (parental leave, flexible working hours for colleagues with children, support for enrolment in childcare facilities) and gender equality. It organizes weekly laboratory meetings and an annual retreat to encourage interaction between staff.

The issue of psychosocial risks is integrated into the Duerp (document unique), a working group made up of volunteers and led by the prevention assistant allows with the support of the management committee of the research and the laboratory council to improve the quality of life at work.

The unit assesses its GES (gaz à effets de serre) emissions and takes measures to reduce its environmental footprint (grouped orders for consumables, teleconferencing instead of delocalised meetings, management of chemical, biological, electronic, paper and cardboard waste, stopping the discharge of bleach into the sewer system). Computer data is backed up on five systems (the researcher's computer hard drive, an external hard drive, Network Attached Storage with VPN access, a data centre (https://hpc.univ-lille.fr/stockagescientifique/stockage-granulaire) and a secure cloud provided by the University of Lille (https://nextcloud.univ-lille.fr). In addition, experimental data is recorded in the "electronic laboratory notebook" set up by Inserm. The unit has implemented a business continuity plan.

### Weaknesses and risks linked to the context

Women only account for only 16% of permanent scientific staff. The unit did not emphasize staff career development and staff training.

# EVALUATION AREA 2: ATTRACTIVENESS

### Assessment on the attractiveness of the unit

The attractiveness of the unit is outstanding, as attested by invitations to prestigious international conferences (Gordon Conference, EMBO workshops, ECC or Faseb), scientific prizes and awards (e.g., EMBO Women in Science, Junior Member of IUF, member of the European Academy of Sciences) and success in competitive European and national calls for projects (including two Feder Plan Etat-Région). The unit has hosted around 30 junior scientists (PhD and post-docs) and recruited two new research scientists, demonstrating its competitive position. The unit has been attractive for the quality of its equipment, which is supervised by qualified staff.

- 1/ The unit has an attractive scientific reputation and is part of the European research area.
- 2/ The unit is attractive because for the quality of its staff support policy.
- 3/ The unit is attractive through its success in competitive calls for projects.
- 4/ The unit is attractive for the quality of its major equipment and technical skills.

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



The number of invitations at national and international meetings has increased since the previous mandate (20 outside France, including 13 in Europe), including in some prestigious ones (Gordon Conference, EMBO workshops, ECC or Faseb). Unit members have also been invited in France to around fifteen meetings and symposia. During this last mandate, the two teams have organised national and local workshops and two international meetings. Unit members hold editorial responsibilities (Frontiers in immunology, immunology section of Scientific Report) and participate in scientific expertise committees (ANR, Foundation ARC, LNCC, CNU, Anses, FNRS).

Phycell researchers have been awarded by scientific prizes and awards during this contract (e.g., EMBO Women in Science, Junior Member of IUF, member of the European Academy of Sciences), including one PEDR.

The unit is involved in the quality of its staff hosting policy, which enabled it to improve the status of two of its members (one DR2 and one assistant engineer promotions) and ensures that personnel have the necessary resources, such as training and mentorship, to perform their jobs effectively. Phycell has attracted two junior researchers, one on a "young team leader" position and the other was recruited as a CRCN Inserm. During the mandate, a new team, currently Team 2, joined the unit, in order to develop a new subject on "ion channels and inflammation. The unit has trained a significant number of students (21 Master 2 students and 19 PhD students, including 15 foreign students) and hosted ten Postdocs. During this last mandate, it also welcomed four visiting scientists from Italy, Germany, USA and Ukraine). Both teams have obtained European funding: a total of six grants, including two Feder, a joint program initiative network (JPI HDHL), a COST action and the renewal of a Marie Sklodowska-Curie ITN program (pHioniC). The unit has developed many partnerships with European teams including the creation of an International Associated Lab (LIA) with two Europeans partners in Italy and Germany, resulting in collaborative works and co-supervision of twol PhD students. The level of scientific recognition is also corroborated by an exceptional level of competitive funding during the mandate: three Team labels awarded by LNCC and FRM, six ANR grants (2 as coordinator and 4 as partner), three INCa PLBio grants (2 as coordinator and one as partner), one LNCC "Pain and Cancer" program as coordinator, and two Inserm programs (Grand Programme Transversal Microbiote and Programme HTE Plan Cancer) as coordinator as well as other grants from charities (Fondation ARC) or the SATT Nord. The unit is also involved within the French framework of the « programmes d'investissements d'avenir (PIA) » through the ICST Labex for Team 1 and the Equipex Imaginex Biomed accreditations for Team 1 and 2.

The unit has successfully responded to calls from the CPER and Inserm to set up new scientific equipment that are shared within the research community. The unit is equipped with conventional cell and molecular biology tools and hosts a "single cell analysis" technical platform with state-of-the-art equipment for analysing ion channel activities at the single cell level. Recently, the unit has developed a new technology called OMD (Organelle Membrane derived) patch clamp, allowing to study ion channels behaviour at single molecule level. Each of the unit's equipment is supervised by qualified scientific and technical staff and access is managed via an online reservation system.

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

The international visibility of the unit relies mainly on its two team leaders. The team "Inflammasome and ionic channels" only recruited few PhD students.

# EVALUATION AREA 3: SCIENTIFIC PRODUCTION

# Assessment on the scientific production of the unit

The scientific production is excellent. Phycell published 60 scientific articles in leading position, including prestigious international journals (Nat Comm, Embo J, Gut, Physiological reviews), 38 as collaborations, and three clinical publications. The quality of the scientific publication reflects the interest and conceptual originality of oncochannelopathies established by the research unit and the use and develoment of advanced techniques in single cell and ion channels analyses.

- 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

Sixty scientific articles are signed with first/last and/or corresponding authorship by the members of the unit. 4 articles are published in prestigious journals that target a large audience. These articles are highlighted in the portfolio (Physiological Reviews journal 2018, Nat Commun 2018, Nat Commun 2022, and Embo J 2023). The unit also published in leading specialist journals as Gut, Gut Microbes, Autophagy, Cell Death Dis, Front Immunol or PloS Pathog. The unit also produced 38 scientific articles from national or international collaborations published in high profile journals some with a broad audience (Nat Commun 2021, Cell 2018, Science 2023, elife 2020, Gut 2018 and 2023, Nat Med 2020 etc.), and 3 clinical publications. The quality of the scientific production reflects the innovative character of the research conducted on the role of ion channels and inflammasome in carcinogenesis, and the development of electrophysiological molecular methodological approach for the study of ion channels involved in cancer. The average scientific production per team is well balanced and proportionate to the size of the unit. PhD students published their work in proportion to their participation. Most of them signed as first author in articles from their main research project. The practice of including research support staff as co-authors on publications to acknowledge their contributions is noteworthy. Another positive sign is the fact that junior researchers and post-doctoral fellows are strongly encouraged to publish in leading positions, and even as last authors.

The unit has identified a clear strategy for long-term storage management of produced data. The scientific production complies with the principles of research integrity, ethics and open science with all publications available on HAL.

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

The teaching load and administrative tasks of some university lecturers may severely challenge their time dedicated to research and scientific production.

Although the unit teams have published in prestigious journals, there is still room for further improvement.

# EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The interaction with the non-academic sector is also excellent. The unit filed six patents with one licenced and another which should lead to the creation of a start-up. Unit members granted newspapers interviews for BFMTV, France Culture).

- 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

Since its last evaluation, Phycell unit has been active in the transfer of its research toward the economic world. Thanks to the financial support of Inserm Transfert and SATT Nord, the unit has published four declarations of invention and the filing of six patents, one of them has been licensed (MabQi). Team 1 is working in close collaborations with MAbQi to develop a monoclonal antibody that could help treating patients with late-stage cancers, and thus could represent a new curative treatment for patients at a therapeutic dead-end. Team 1 is also to the initiative to create a startup (Immunomems, currently incubated by the bioincubator Eurasanté with the support of a BFT Lab funding from Bpifrance). The microfluidic tools developed by the Immunomems project



represent a new technology with multiple applications including diagnosis, personalised medicine, drug screening, CAR cell development and evaluation, etc...

The unit's policy includes the valorisation of the Laboratory's research through very close collaboration with pharmaceutical companies. As a result, a number of contracts have been signed with pharmaceutical companies in recent years: Miyarisan Pharmaceuticals Ltd., «Johnson & Johnson» (USA), Servier (France), Bayer, Nanion. Two PhD students were funded by Johnson & Johnson USA), one partially by Miyarisan Pharmaceuticals Ltd. and one post-doctoral fellow by Servier.

The unit developed unique approaches to molecular electrophysiology, which were then strengthened by implementing organelle membrane derived patch and confocal microscopy combined with patch clamp. These new approaches are an important means of technology transfer allowing the establishment of collaborations with academic but also private laboratories such as Miyarisan Pharmaceutical Co Ltd. and Servier, France.

The members of the laboratory are in charge of several courses and modules at the University of Lille (from first year to Master 2 level) and are also involved in the supervision of undergraduate students (BSc, IUT or BTS). The members of the laboratory are responsible for two course modules ("Integration of physiological signals: from molecule to organism" and "Cell calcium homeostasis and pathophysiology"). The unit is also involved in public discourse while maintaining scientific integrity and ethics. Team members have had the opportunity to present their research to the general public (Movember: general presentation to the public of prostate cancer in order to raise general awareness; presentation to donators from La Ligue Nationale Contre le Cancer; participation to the "Journée jeunes chercheurs en cancérologie" of ARC foundation in the presence of their donators...). Head of Team 1 participates in the presentation of cancer cell biology (prostate cancer) for patients and their families (organised by the Ligue again Cancer). In addition, the main published results of the unit have been disseminated to the lay public through both podcasts (eg. BFMTV, France Culture, and BeIRTL) and magazines, such as Notre Temps, Médecine/Sciences et Science&Santé (published by Inserm), and Envie de Savoir (published by the Institut Pasteur de Lille).

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

No weaknesses were detected.

# **ANALYSIS OF THE UNIT'S TRAJECTORY**

The Phycell unit will close and the two current teams will integrate the new proposed OncoLille unit. The projects of the two Phycell teams will be a continuation of their studies on ion channels in cancers, with a specific emphasis on tumour inflamasome, microenvironmental regulation and therapeutic resistance. Each team has proposed a solid scientific research program with a clear strategy for the next five-years.

The teams' projects are innovative and have a high potential in terms of generating ground-breaking findings in the field of therapeutic resistance, as well as in terms of development and exploitation. The two projects are well-designed, fully credible and well supported by the current manpower and secured funding. The Phycell unit should be well integrated in OncoLille Institute since its members have participate from the very beginning (2012) to the long process of cancer research structuration in Lille (e.g., Siric OncoLille). The loniC PhyCell team will add its expertise to the OncoLille unit and help constitute a niche on ion channels as therapeutic targets and markers to fight cancer resistance and persistence. In addition, Phycell's excellence and experience in European networks and partnerships will bring considerable added value to the new OncoLille unit.

# **RECOMMENDATIONS TO THE UNIT**

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

The committee recommends that the unit develop the transversal topic of ion channels within the OncoLille Unit. The unit is encouraged to facilitate the visibility of other PIs in addition to that of the Laboratory leader.

# Recommendations regarding the Evaluation Area 2: Attractiveness

The unit should continue its contribution to the construction of the European research area by increasing the application and participation to European research projects and networks. Team 2 should implement a policy to attract and recruit PhD students on a more regular basis.



Recommendations regarding Evaluation Area 3: Scientific Production

The committee encourages the teams to continue their excellent and original research activities and projects with their current staff.

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

No specific recommendations

# **TEAM BY TEAM ASSESSMENT**

Team 1	lonic: Ion Channels and Cancer
Name of the supervisor:	Mrs. Natacha Prevarskaya/Lemonnier

# THEMES OF THE TEAM

Research carried out by the team "Ion channels and Cancer" stems from the original observation of a functional role for ion channel signalling in cancer biology developed by the unit Director, who is a pioneer researcher in the field. Since then, the team has been studying the involvement of ion channels in tumour initiation and the establishment of the metastatic niche as well as in therapeutic resistance. With the arrival in 2020 of a new team, the team has developed a new project on the inflammasome and ion channels.

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team followed most of the recommendations from the previous evaluation. These included an increase in number of patents, application to international grants, an increase in the number of PhD students and their scientific production. Over the current assessment period the team increased the number of patents. It also increased the number of PhD students thanks to collaborations and student co-supervision. The team also increased the number of national and international grants, and recruited post-doctoral fellows.



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

Catégories de personnel	Effectifs
Professeurs et assimilés	4
Maîtres de conférences et assimilés	5
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	11
Sous-total personnels permanents en activité	23
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	7
Sous-total personnels non permanents en activité	9
Total personnels	32

# EVALUATION

# Overall assessment of the team

The scientific production of the team is excellent with two publications as PI in highly reputed journals (Embo J. 2023, Nat Comm, 2022). The team's attractiveness is outstanding with invitations to international conferences e.g., EMBO workshops, Gordon Conference, European Calcium Society, Faseb; participation as coordinator to a European network; success in grant funding (PLBio INCa (2 as PI), ANR (3 as PI), Ligue Nationale contre le Cancer (3 as PI), Europe MSCA as partner and recruitment of two new research scientists and twelve post-doctoral fellows. The contribution to the society is excellent (6 patents + 1 licensed)

### Strengths and possibilities linked to the context

The team consists of three Inserm researchers and nine faculties, three clinicians, and eleven engineers/technicians, and has recruited twelve postdocs and eighteen PhD students, maintaining a balanced mix of senior and junior scientists. Locally, they engage in the Biology Department and committees of PLBS platform and are part of the OncoLille research group since 2022.

The team has pioneered research in channels in prostate cancer, establishing the oncochannelopathy concept. Key findings include TRPC3's role in calcium transfer between the ER and mitochondria and in senescence (Nature Comm. 2022) and NALCN's role in prostate cancer metastasis and invadopodia formation (Embo J. 2023). They also explored other TRP family channels, such as TRPM8 in prostate cancer and TRPV6 in pancreatic ductal adenocarcinoma and conduct studies on Orail channels in leukaemia and resistance to treatments. The team was very successful in securing local and regional grants (e.g., Cancéropôle Nord Ouest) and acquiring new equipements (Inserm, CPER). It also secured competitive national and European funding such as grants from PLBio INCa, ANR, Ligue Nationale Contre le Cancer as coordinator, or from LabEX ICST, and European MSCA network as partners for a total of 3800k€ during the period. The team has published extensively: 44 articles with 40 papers as PI: twenty research articles, including articles in high-impact journals like Nature Comm. and Embo J. and twenty reviews (1 invited review in Physiological Reviews journal). Internationally recognised, the team is frequently invited to speak at major conferences (EMBO workshops, Gordon Conference, Faseb). They organised the "Ion Channels in Cancer Meeting" in 2022. Nationally, they renewed their partnership with the Ligue Nationale Contre le Cancer and participate in the Labex ICST network. They are also involved in the European Marie Curie project "pHioniC," studying ion channels in pancreatic cancer and in a LAI (International Associated laboratory) that was accredited in 2018 by University of Lille with the teams from Germany and Italy.



Several staff members of the team are participating in research steering bodies (Swiss National Science foundation, ANR, Ligue Nationale Contre le Cancer) and are referee for recognised scientific journals (e.g Cell, Nature, Cancer Res., Oncogene...). The team actively translates its research into economic applications, proposing therapeutic strategies such as a patent for monoclonal TRPV6 channels to target prostate cancer metastasis. Collaborations with SATT Nord and Inserm Transfert support this work, leading to patents and licenses. They have developed with the SMMiL-E team microfluidic devices to monitor calcium responses in leukemic and immune cells, securing additional patents and support from SATT Nord and Eurasanté incubator.

### Weaknesses and risks linked to the context

Although the team developed clinical research collaborations, the integration of the 3 clinicians in the team is not clear. Visibility of the team is very dependent on the international visibility of the laboratory leader, and less on other PI notoriety.

### Analysis of the team's trajectory

The team project is a continuation of the study of ion channels in cancers, with a specific emphasis on tumour inflammasome and microenvironment and resistance of cancers to traditional therapies. This will be conducted in the context of the new project of OncoLille institute. In this dynamic context built around cancer research, team 1 will bring its expertise to the niche of ion channels as therapeutic targets and markers to fight cancer resistance and persistence.

The team projects are innovative and highly relevant to clinical research, potentially leading to new therapies. The overall project is well-designed, fully credible and well supported by the current manpower and secured funding. See also comments concerning the unit's trajectory above.

# RECOMMENDATIONS TO THE TEAM

The committee recommends that the team continue their excellent and original research activity and projects with their current staff, and further develop the transversal topic of ion channels within OncoLille Unit. See also recommendations to the unit above.



Team 2

Inflammasome; Inflammasome and Ionic Channels

Name of the supervisor:

Mr; Mathias Chamaillard

# THEMES OF THE TEAM

Team 2 of Phycell is interested in defining how the mucosal immune response to microbiota contributes to microbial tolerance, host defense and antitumour immunity, and how deregulation of these processes breaks down in Crohn's disease and colitis-associated colorectal cancer. Using a variety of techniques and complex genetic models, the team has made significant contributions to the understanding of mucosal immunology. They have identified novel dendritic cell subsets and several pathways underlying inflammation-driven carcinogenesis and have studied the impact of gut microbiota dysbiosis in colorectal cancer patients.

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

One of the main recommendations of the previous report was to valorise the team's research. During the reporting period, the team published two invention disclosures and three patents. It was also previously noted that the number of PhD students was low and this remains the case.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	7
Sous-total personnels permanents en activité	9
Enseignants-chercheurs et chercheurs non permanents et assimilés	3
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	0
Sous-total personnels non permanents en activité	4
Total personnels	13

# EVALUATION

### Overall assessment of the team

The research activity and scientific production of the team is excellent, as attested by publications in leading position in highly visible generalist journal (Nat Comm.) or excellent journals in their speciality (Gut, Gut Microbes), as well as excellent collaborative publications in generalist journals (e.g., Science, Nat Med). The attractiveness is also excellent for the size of the team, as attested by the grants obtained: 2 European grants (1 Feder as coordinator and 1 Joint Programming Initiative as partner), four national grants (including Plan relance, Programme transversal Inserm and InCa as PI), and 4 charity grants including the prestigious "team FRM" label). The interaction with the non-academic sector is very good to excellent (e.g., 3 patents with one license and another which should lead to the creation of a start-up. Team members are involved in public outreach (BFMTV, France Culture...).



### Strengths and possibilities linked to the context

Team 2 is a small team composed of two scientists (1DR Inserm and 1 DR CNRS), three clinicians, five PAR, three of whom are permanent (1 IR, 1AI (50%) and 1 TN (50%) from the University of Lille) and two IR engineers on contract) and 1 post-doc.

Team 2 is a pioneer in the study of the role of the inflammasome in inflammatory diseases and cancer, and is currently investigating the role of microbiota dysbiosis in colorectal cancer (CRC).

The team has been very successful in securing competitive funding for a total of 2.7 M €: two European grants (1 Feder as coordinator and one Joint Programming Initiative - A Healthy Diet for a Healthy Life as partner), four national grants (3 as PI Plan relance, Programme transversal Inserm, InCa and one ANR as partner). It also obtained funding from charities, including one prestigious label: "Team Fondation pour la Recherche Médicale" (3-year contract in 2022) and three Ligue contre le cancer contracts (2 as PI and 1 as partner).

During the contract period, the team produced seventeen scientific articles as first/last/corresponding author and eighteen others in collaboration with other laboratories, published in prestigious international journals (Nature communications, Gut...). Highlights include the finding that loss of Nod2 signalling in myeloid cells aids tissue repair of the inflamed colon through lysozyme secretion by myeloid cells (Front Immunol 2023), which may pave the way to design new therapeutics to limit the inflammatory and tumourigenic functions of NOD2. The team also showed that the proteasomal degradation of NOD2 by NLRP12 in monocytes promotes bacterial tolerance and colonisation by enteropathogens (Nat Comm 2018) and that the loss of either RIPK2 or the Ctype lectin REG3b impairs the ability of intestinal phagocytes to trigger IL-17A-mediated neutrophil influx by innate lymphoid cells for efficiently limiting pathogen colonisation and tissue damage at the early phase of the infection (Gut 2020).

The team is internationally recognised in the field of ion channels/cancer and dysbiosis/cancer (particularly in CRC), as shown by invitations of team members to international conferences (e.g., Workshop of the European Helicobacter and Microbiota Study Group, EMBO, COST Action Presto, ECCO, etc...) and the organisation of national meetings (35<sup>ème</sup> journées Institut Cochin-JC Dreyfus, OncoLille days). Members of the team are also involved in expert committees (Hcéres, ANR, ANRS, Ligue Nationale Contre le Cancer) and have won several prizes (Plan Cancer - Programme HTE, Laureate of the Grand Programme Transversal Microbiote). All the principal investigators are referees for several prestigious journals (Journal of Experimental Medicine, Nature immunology, Nature Communications, Nature Medicine, Cell reports, Embo J, EJI, Gut, Gastroenterology etc...). The team has published 2 declarations of invention and 3 patents, one of which is currently licensed to a private company and another has led to an incubation phase prior to the creation of a startup. The team's main published results have been released to the lay public through both podcasts (e.g. BFMTV, France Culture, and BelRTL) and magazines, including Notre Temps, Médecine/Sciences et Science&Santé (published by Inserm), and Envie de Savoir (published by the Institut Pasteur de Lille).

### Weaknesses and risks linked to the context

Only one PhD student was trained and defended his thesis during the contract.

### Analysis of the team's trajectory

The knowledge on mucosal immunology and the pathophysiology of inflammatory bowel diseases accumulated by the team over the past two decades has begun to be applied to the study of the disequilibrium in the gut microbiota of colorectal cancer patients in general, and the cancer-potentiating effect of toxin-producing bacteria in particular since 2020. This involvement in colorectal cancer pathology, as well as the PI's expertise in mucosal immunity and gut microbiota, make the team's project in full adequacy with OncoLille's priorities.

# RECOMMENDATIONS TO THE TEAM

The committee recommends that the team should implement a policy to attract and recruit PhD students. The committee encourages the team to continue its excellent research activities.



# CHARACTERISATION OF THE UNIT

- Name: Laboratory of Cellular and Molecular Physiology
- Acronym: LPCM
- Label and number: UR UPJV 4667
- Composition of the executive team: DU Halima Ouadid-Ahidouch, DU Adjoint Mathieu Gautier

# SCIENTIFIC PANELS OF THE UNIT

Scientific panels of the unit SVE6, SVE 3, SVE 7, SVE 1

### THEMES OF THE UNIT

The single team unit is dedicated to basic and translational research in the field of cancer. It investigates the role of ion channels and the microenvironment in the pathophysiological mechanisms of cancer cells. The team has a recognised expertise in electrophysiology techniques. Three cancers with poor prognosis are studied: pancreatic ductal adenocarcinoma, invasive mammary ductal adenocarcinoma, and non-small cell lung cancer.

### HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The laboratory was created in January 2003, and reorganised the local research forces in the field of ion signalling in cancer biology. This new research project was first developed in the Physiology laboratory, which has since been renamed the 'Cellular and Molecular Physiology Laboratory (LPCM)'. Having previously been part of the "Mechanisms of bone marrow Resorption" Unit (UMRO), the team obtained a young team status (JE 2530) from 2008 to 2011. From 2011 to 2016, the Unit (with the status of EA), entered into collaboration with the Amiens University Hospital, which enabled members of the CHU's departments to join the laboratory. Since 2018, LPCM has the status of University Research Unit (UR-UPJV4667). The LPCM is located in the Science Department of the UFR des Sciences in Amiens.

### RESEARCH ENVIRONMENT OF THE UNIT

LPCM developed close collaborations with the Amiens University Hospital, in particular with the Anatomy and Pathological Cytology Department and the Obstetrics and Gynaecology Centre. The Department of Pathological Anatomy and Cytology, some of whose staff are members of the LPCM, is located nearby at the CHU Nord. This environment has allowed the development of projects that combine the expertise of cell biologists, physiologists and clinicians. LPCM has access to local University platforms, in particular the Centre de Ressources Régionales en Biologie Moléculaire (CRRBM).



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

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maîtres de conférences et assimilés	5
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	12
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	6
Total personnels	18

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

Nom de l'employeur	EC	С	PAR
UPJV	7	0	2
CHU AMIENS	0	0	2
AUTRES	1	0	0
Total personnels	8	0	4

# **GLOBAL ASSESSMENT**

The scientific production of the unit is good to very good, with publications in specialised journals (Cancers, Cell Calcium, Frontiers in Physiology). Attractiveness is very good. The team was partner in a European Network (MSCA network) and was successful in grant funding (Ademe, Anses) for organizing a national consortium in the field of "pollution and cancer".

Contribution to society is very good. The team is involved in public outreach activities, and in teaching and student training at Jules Verne University. It has few interactions with socio-economic field.

# **DETAILED EVALUATION OF THE UNIT**

# A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The single team unit followed some of the previous recommendations. The previous Hcéres committee recommended that "The organisation chart should be consolidated and the potential for supervising theses extended"; accordingly, the team organised the defence of two HDR during the reference period.



# **B - EVALUATION AREAS**

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

### Assessment on the scientific objectives of the unit

The single-team unit has very good scientific objectives. Its research is focused on the role of ion channels and the microenvironment in the pathophysiological mechanisms of cancer cells. The unit has strong expertise in electrophysiology techniques.

### Assessment on the unit's resources

The unit's resources are very good, as illustrated by its access to local University platforms, in particular the Centre de Ressources Régionales en Biologie Moléculaire (CRRBM). four permanent technicians/engineers are part of the unit.

# Assessment on the functioning of the unit

The functioning of the unit was esteemed to be very good. Its relatively small size hindered an optimal organisation, for instance, in terms of prevention and pychosocial risks policy.

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

Strengths and possibilities linked to the context

The team has a recognised expertise in electrophysiology techniques. Using these techniques, several ion channels of interest have been studied, including the TRPC1, ORAI1 and ORAI3 calcium, the IP3R3 endoplasmic reticulum calcium channel, TRPM7 chanzyme and the Kv10.1 potassium channel.

Weaknesses and risks linked to the context

There appear to be many different projects given the size of the single-team unit.

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

### Strengths and possibilities linked to the context

The single-team unit was organised around four main areas of research recruited by the Faculty of Sciences of the University of Picardie Jules Verne (2 PU and 5 MCU), with four permanent PAR, one contract engineers, one ATER and three PhD students. The team has no permanent researchers (DR and CR). Over the course of the contract, the team trained ten PhD students (all defended), and two HDR were defended. Self-funding from research grants was 108 k€/year. For the future contract, the team will be strengthened by a PU-PH from Amiens Hospital.

### Weaknesses and risks linked to the context

As indicated above regarding scientific objectives, the imbalance between the volume of projects and the unit's strengths can be a risk.



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

LPCM is organised as a single team led by a director assisted by a deputy director and an administrative manager. Parity is respected, with 57% of staff being women.

Staff have access to training courses offered by the university, but not all of these are covered by the unit's budget. The building is old, but work has been carried out to improve working conditions (replacement of windows, installation of air conditioning, covering of the outside staircase).

Computer data is stored on the university's cloud and on hard drives supplied by the laboratory.

### Weaknesses and risks linked to the context

Annual staff interviews are not systematically organised and a laboratory council does not seem to have been set up. Prevention assistant and contact person for RPS do not seem to have been appointed. The fact that the team is spread over two floors despite its relatively small size does not encourage interactions between staff. No measures have been put in place to sort non-biological or chemical waste (paper, cardboard, plastic, glass) to protect the environment.

# EVALUATION AREA 2: ATTRACTIVENESS

# Assessment on the attractiveness of the unit

The attractivenss of the unit is very good. The unit notably participated in a European network (Marie Skłodowska-Curie Innovative Training Network) and established a national consortium ( supported by Ademe, Anses and CNO). However the unit did not succeed in securing competitive funding (ANR, INCa or other).

The team recruited twelve PhDs: seven started during the period and nine defended their PhD

- 1/ The unit has an attractive scientific reputation and is part of the European research area.
- 2/ The unit is attractive because for the quality of its staff support policy.
- 3/ The unit is attractive through its success in competitive calls for projects.
- 4/ The unit is attractive for the quality of its major equipment and technical skills.

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

The unit participated in a European network (Marie Skłodowska-Curie Innovative Training Network) on the role of membrane transporters in the adaptation of cancer cells to pH variations in the pancreatic tumour microenvironment, "pH and IonTransport in Pancreatic Cancer - pHioniC". The team is responsible for the task "Expression profiling of the pH-regulatory and -sensitive transportome: epigenetic analysis and correlation with clinical parameters". The team established a national consortium on the role of the TRPM7 channel in the activation of pancreatic stellate cells induced by cadmium exposure supported by Ademe (1 thesis subvention), Anses ( $22K \in$ ) and CNO. Additional regional grants include CPER Région (112, 22,5 and 41 K $\in$ ). The team is regularly supported by regional Ligue Contre le Cancer. The team did not secure ANR or INCa grants. The team is strongly involved in teaching at Jules Verne University. Team members presented their work in oral communications at national scientific meeting and in one international specialised meeting (XVI International Magnesium Symposium, Glasgow UK). Some team members sat on regional scientific committees (e.g., CNO



Scientific Steering Committee). The team recruited twelve PhDs. Among them, seven started during the period and nine defended their PhD. The team did not recruit postdocs.

The laboratory manages the UFR des Sciences animal facility, and has responsibility for the Animal Facility Pharmacy school. Members of the laboratory also sit on the Scientific Advisory Board of the Platann platform (Animal Facility - at the University of Picardie Jules Verne) and on the Regional Ethics Committee for Animal Experiments in Picardie (Cremeap). Being located in the Science Department of the UFR des Sciences in Amiens, members of the LPCM are strongly involved in student training and in hosting many Master's and Bachelor's students for internships in the laboratory

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

The team did not secure competitive national fundings, and did not attract permanent researchers The unit does not have sufficient visibility at local and national levels.

# EVALUATION AREA 3: SCIENTIFIC PRODUCTION

### Assessment on the scientific production of the unit

The scientific production of the unit was good to very good: 28 publications including sixteen original research articles in leading position in specialised journals in the field of cancer basic research (Am. J. Cancer Res., Cancers), Cell biology (Int. J. Mol. Sciences, Cells) and Cell Physiology (Cell calcium, Frontiers in Physiol.). Twelve publications (40% of total) were reviews.

- 1/ The scientific production of the unit meets quality criteria.
- 2/ The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.
- 3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.

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

The team has published 28 publications as PI principally in the field of ion channels and cancer: sixteen original research articles and twelve reviews. Articles were published in specialised journals in the field of cancer basic research (Am. J. Cancer Res., Cancers), Cell biology (Int. J. Mol. Sciences, Cells) and Cell Physiology (Cell calcium, Frontiers in Physiol.). The members or the team also signed 52 collaborative publications. All LPCM members published and PhD students had at least one publication during the period.

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

Until 2022 a number of manuscripts (11) were published in journal of the "grey zone". The team has only one review article in 2023

# EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The interaction with the non-academic sector is very good: one project with SATT Nord involving the screening of small molecules targeting the kinase domain of TRPM7. The team has very little visibility with the general public research



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

Research on the role of the TRPM7 chanzyme in cancer following exposure to pollutants led to an Anses "Environment-Health-Work" National Research Plan and Ademe (Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail) support in the form of a doctoral grant.

The unit also structured teams from the Cancéropôle Nord-Ouest (CNO) around a project with patentability potential (SATT Nord) involving the screening of small molecules targeting the kinase domain of TRPM7 (2022-2025). The laboratory has presented its work to local committees of the Ligue Nationale Contre le Cancer, but has very little visibility with the general public research: one article in the Courrier Picard (December 2021), a presentation to members of the "Ligue Contre le Cancer" Somme committee, and a publication in Cahiers de la Recherche N°22, Anses (October 2023).

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

Despite the translational potential of some of their research topics such as the role of TRMP7 kinase domain in pancreatic cancer for pharmaceutical companies, LPCM's interactions with non-academic institutions was not developed to conduct this project. LPCM has already been collaborating with Phycell and Canther for several years, with common grants and networks, and co-supervision of doctoral students. The team will contribute to the topic with its expertise on ion channels, which is relevant to clinical research, and which may lead to the identification of new targets and novel therapies. Joining the OncoLille project should help the team to develop its project by increasing manpower, providing access to other platforms, and improving success in obtaining national and international grants.

# **RECOMMENDATIONS TO THE UNIT**

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

The committee recommends that the team continue projects on ion channels and TRPM7 chanzyme and to capitalise on this nationally recognised expertise in the contest of PancRest team.

# Recommendations regarding the Evaluation Area 2: Attractiveness

Despite its national recognition in the field ion channels and cancer, the team should improve its research activity with competitive national grants and continue to participate to network through national consortium and European research projects.

# Recommendations regarding Evaluation Area 3: Scientific Production

Publication of the current researches should be done as soon as possible. We strongly recommend to avoid predatory or pseudo-predatory journals.



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

The translational potential of the research activity could be translated into patent applications or industrial contracts. The team should elaborate a clear communication strategy.



# CONDUCT OF THE INTERVIEWS

# Dates

**Start:** 04 novembre 2024 à 09h00

**End:** 05 novembre 2024 à 17h30

Interview conducted: on-site

# INTERVIEW SCHEDULE

### 4 NOV Day 1: arrival of committee members

8h00-8h30 Closed door meeting of committee.

8h30-8h45 Presentation of the committee to the Unit

8h45-8h50 Isabelle VAN SEUNINGEN, Director of OncoLille: Presentation of the structuring of cancer research in
Lille: The OncoLille Cancer Research Institute, 5 min
Presentation by the 4 unit directors, open to all
8h50-9h15 Canther; Isabelle VAN SEUNINGEN
15 minutes overview of past activities, 10 min questions
9h15-9h35 PhyCell; Natalia PREVARSKAYA
10 minutes overview of past activities, 10 min questions
9h35-9h55 OncoThAl; Nadira DELHEM
10 minutes overview of past activities, 10 min questions
9h55-10h10 LPCM; Mathieu GAUTIER
5 minutes overview past activities, 10 min questions
10h10-10h30 OncoLille Unit Project
10 min presentation (Isabelle VAN SEUNINGEN), 10 min questions (in the presence of Natalia PREVARSKAYA, Nadira DELHEM, Alexis CORTOT)

# 10h30-11h00 committee debrief Individual team presentations:

11h00-11h10 team Mucin, Isabelle VAN SEUNINGEN 5 min presentation (past activities), 5 min questions 11h10-11h30 team PancRest, Nicolas JONCKHEERE (emergent) 10 min presentation (project), 10 min questions 11h30-11h50 team EpiCARe, Audrey VINCENT (emergent) 10 min presentation (project), 10 min questions 11h50-12h15 team Target, David TULASNE 15 min presentation (past+project), 10 min questions

12h15-14h00 lunch (boxed lunch), committee debrief

14h00-14h20 team NMD, Fabrice LEJEUNE (emergent) 10 min presentation (project), 10 min questions 14h20-14h45 team Plasticity Chann LAGADEC 15 min presentation (past+project), 10 min questions 14h45-15h05 team Disco, Mohamed ELATI (emergent) 10 min presentation (project), 10 min questions

15h05-15h40 committee debrief

15h40-16h05 team SenFib, Christelle CAUFFIEZ
15 min presentation (past+project), 10 min questions
16h05-16h15 team Leukemia, Salomon MANIER
5 min presentation (past activities), 5 min questions
16h15-16h35 team Perstim, Salomon MANIER, Suman MITRA (emergent)
10 min presentation (project), 10 min questions
16h35-16h55 team PROTECT-L, Meyling CHEOK (emergent)
10 min presentation (project), 10 min questions
16h55-17h55 individual meeting of PIs (current and future) with committee (closed door)



17h55-19h30 end of day committee debrief

dinner **5 NOV Day 2: 8h00-8h45 morning debrief** 8h45-9h10 team OncoThai, Laurent MORTIER 15 min presentation (past+project), 10 min questions 9h10-9h35 team Ion Channels, future IoniC, Loic LEMONNIER 15 min presentation (past+project), 10 min questions

9h35-10h00 team Inflammasome/ future MIMIC, Mathias CHAMAILLARD 15 min presentation (past+project), 10 min questions

10h00-10h30 individual meeting of PIs with committee (closed doors)

10h30-11h00 committee debrief

11h00-11h30 Committee splits in 3 groups for discussion with: 1/students/postdocs 2/permanent researchers 3/administrative personnel, supporting staff (IE, IR)

11h-30-12h15 committee debrief to discuss above meetings

12h15-14h00 Boxed lunch, committee debrief

14h00-14h30 Meeting with managing bodies InsermIT Cancer : Alain EYCHENE Déléguée régionale Inserm : Bénédicte SAMYN-PETIT CNRS INSB : Patrick BLADER Université Lille : Régis BORDET (Président UL), Olivier COLOT (VP Recherche UL), Karine FAURE pour l'UFR3S (Santé) ; Yan PENNEC pour la FST (Sciences, Biologie) CHU Lille : Fréderic BOIRON, Brigitte COURTOIS, Fréderic GOTTRAND Université Picardie Jules Verne : Denis POSTEL

14h30-14h45 Meeting with managing bodies (secondary) Centre Oscar Lambret; Philippe PEUGNY (directeur adjoint) Institut Pasteur de Lille ; Fréderic BATTEUX (directeur)

14h45-15h15 Meeting with the director and deputy directors

15h15-18h00 Final debriefing of the committee

### PARTICULAR POINT TO BE MENTIONED

NA

# GENERAL OBSERVATIONS OF THE SUPERVISORS



Université de Lille

Les vice-présidents recherche de l'Université de Lille

valorisation

- Département d'Evaluation de la Recherche

Objet : Courrier d'observation de portée générale Université Lille DER PUR 260025102

Direction générale déléguée Recherche et valorisation Direction d'Appui à la Recherche

Affaire suivie par :

Directeur jean-francois.delcroix@univ-lille.fr dar-structurespartenariats@univlille.fr T. +33 (0)3 62 26 91 35 Chère, Cher collègue

L'université de Lille tient tout d'abord à remercier le comité de visite HCERES pour l'attention qu'il a portée au travail mené par l'unité CANTHER – Hérérogénéité, plasticité et résistance aux thérapies des cancers - et pour la qualité de l'évaluation qu'il a produite.

Le comité de visite a été l'occasion, pour les membres de l'Unité de Recherche et pour l'Université, d'approfondir certaines questions et de répondre aux interrogations des experts, dans un esprit constructif dont il faut se féliciter.

Les recommandations émises dans le rapport d'évaluation seront précieuses pour l'unité pour le déploiement de son projet lors du prochain contrat.

Vous trouverez ci-joint un relevé des erreurs factuelles à corriger en vue du rapport définitif.

Nous vous prions de croire, chère collègue, cher collègue, à l'expression de notre considération distinguée.

Pour le Président et par délégation, Les Vice-Présidents Recherche de l'Université de Lille

Olivier Colot

Sandrine Chassagnard

Université de Lille Cité scientifique 59650 Villeneuve d'Ascq The Hcéres' evaluation reports are available online: www.hceres.fr

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