Research evaluation

EVALUATION REPORT OF THE UNIT

INFINITE - Institute for translational research in inflammation

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université de Lille – U Lille

Centre Hospitalier Universitaire de Lille - CHU Lille

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

EVALUATION CAMPAIGN 2024-2025

GROUP E

Report published on February, 18 2025

High Council for evaluation of research and hgher education

In the name of the expert committee :

Bernard Pirotte, chairman of the committee

For the Hcéres :

Stéphane Le Bouler, acting president

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

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

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

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:	Mr Bernard Pirotte, Université de Liège, Belgique
Experts:	Ms Gaelle Boudry, Inrae, Saint-Gilles Mr Yves Delneste, Inserm, Angers (representative of the CSS3) Mr Vincent Leroy, Université Paris-Est Créteil (representative of the CNU) Mr Niclas Setterblad, Sorbonne Paris-Cité (representative of the research support personnel)

HCÉRES REPRESENTATIVE

Mr Kamel Benlagha

REPRESENTATIVE(S) OF SUPERVISING INSTITUTIONS AND BODIES

Ms. Bénédicte Samyn, Inserm

Mr. Raymond Bazin, Institut thématique Physiopathologie, métabolisme, nutrition - IT PMN

Mr. Olivier Colot, Université de Lille

Ms. Karine Faure, UFR3S, Université de Lille

Ms. Camille Gladieux, CHU Lille

CHARACTERISATION OF THE UNIT

- Name: Institute for translational research in inflammation
- Acronym: Infinite
- Label and number: U1286
- Number of themes: 4
- Composition of the executive team: Mr Laurent Dubuquoy (director), Mr David Launay (deputy director, clinical expertise) and Ms Virginie Chameroy (deputy director, research support).

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement
SVE6 Physiologie et physiopathologie humaine, vieillissement

THEMES OF THE UNIT

Infinite aims to decipher the origins, mechanisms and consequences of chronic inflammation and to discover new treatments and biomarkers for chronic inflammatory diseases. The research unit chose to focus on digestive, liver and systemic inflammatory diseases for which no curative treatments are available notably due to the observation of resistance to treatments. In order to respond to this situation, Infinite has built a scientific program organized into 4 interconnected work-packages (WP).
Theme 1: Environmental contributions to mucosal homeostasis and IBD susceptibility.
Theme 2: Epithelium integrity: from pathogenic regeneration to homeostasis.
Theme 3: From chronic inflammation to fibrosis: role of immune cells.
Theme 4: Therapeutic innovation targeting inflammation.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The Institute for Translation Research in Inflammation (called Infinite), previously known as the Lille Inflammation Research International Center (Liric), was founded by Pierre Desreumaux in 2001. The research facility is mainly located in the Lille Faculty of Medicine's "Pôle Recherche" research wing, close to the clinical departments of the University Hospital of Lille. Some projects are performed at the Institute of Immunology at the Centre de Biologie-Pathololgie Génétique (CHU-Lille). The drug discovery activities and microbiology units are located in the Department of Pharmacy of ULille.

RESEARCH ENVIRONMENT OF THE UNIT

Infinite is under the supervision of the University of Lille, Inserm, and the Lille University Hospital. The unit benefits from a well-structured milieu, encompassing clinical departments, a European non-profit research foundation (DigestScience), 3 biotech companies, and the federative research structure SFR2I: Infection & Inflammation. The translational strength of the unit lies in the involvement of university hospital researchers and proximity to clinical departments.
The strategic geographical position of the University of Lille promotes beneficial collaborations with cross-border entities, enhancing its European and international impact. The University gathers 64 research units, inclusive of 11 Inserm-accredited (including Infinite), 29 CNRS-accredited, 2 Inrae-accredited units, and 2 Inria partnership units. This ecosystem comprises four thematic hubs: (1) Precision health; (2) Science for a changing planet; (3) Digital transition serving humankind; (4) Evolving cultures, societies, and practices. In this ecosystem, Infinite is a core component of the HUB Precision Health and is connected to the doctoral School of Biology and Health.
Infinite collaborates closely with some regional Units, such as: Prism U1192 (Proteomics Inflammatory Response Mass Spectrometry Unit); MSAP UAR3290 (Miniaturization for Synthesis, Analysis, and Proteomics); Canther U1277-UMR9020 (Cancer Heterogeneity, Plasticity and Resistance to Therapies); Advanced Drug Delivery Systems U1008; Nuclear receptors in the gastrointestinal tract U1011; Functional (Epi)Genomics and Mechanisms of Type 2 Diabetes and related diseases U1283-UMR8199.
Infinite has access to the Biology and Health Platforms of Lille (PLBS, UAR2014-US41), comprising seven transversal platforms offering 35 technical facilities across various themes, including genomics, proteomics and cell imaging. The link with the economic and social sectors is strengthened through partnerships with Intestinal Biotech Development and the European non-profit research foundation DigestScience. The connection of the unit with the economic sector is also exemplified by several industrial contracts (Aliri, Astra-Zeneca, Biopredic, Cousin Biotech, CSL Behring, Danone, GSK, Lactalis, Lesaffre, Myltenyi Biotec, NutriEarth, Nutricia, Octapharma, Pfizer, Therakos, Revertech, Roquette, Sanofi, Servier). Infinite is also involved in technology transfer and start-up creation, in collaborating with technology transfer entities such as Satt Nord, Inserm Transfert, Eurasanté.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	21 + 6 PH
Maîtres de conférences et assimilés	18
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	20
Sous-total personnels permanents en activité	**70**
Enseignants-chercheurs et chercheurs non permanents et assimilés	8
Personnels d'appui non permanents	20
Post-doctorants	10
Doctorants	23
Sous-total personnels non permanents en activité	**61**
Total personnels	**131**

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

Nom de l'employeur	EC	C	PAR
U Lille	39	0	15
CHU Lille	6	0	3
Inserm	0	5	2
Total personnels	**45**	**5**	**20**

GLOBAL ASSESSMENT

Infinite is a single team focusing on inflammation, from its origins to its consequences, and on the identification of new biomarkers and innovative therapeutics. Mainly, on severe chronic inflammatory diseases (IBD), chronic liver disease and systemic sclerosis, which share common pathophysiological features (exogenous and endogenous environmental factors, fibrosis/altered tissue regeneration and unmet medical needs). Infinite is scientifically organized into 4 interconnected themes.

Infinite benefits from a strong international visibility thanks to its excellent publications (1,639 articles), including 1,489 original articles and 150 reviews: eighty percent are clinical research (1,189 articles) and thirty percent (447) are basic/translational research articles, of which 1/3 are signed as PDC. The proportion of clinical/basic/translational research articles is homogeneous on the 4 themes. Some publications have appeared in the top 1 or top 10 of general peer-reviewed journals (Jama, Sci Rep, Faseb J) or specialized journals (Gut, J Hepatol, Gut Microbes, . …) and collaborative studies (Nat Commun).

One of Infinite's strengths is the excellent quality of its translational research, thanks to the excellent integration of clinicians in the implementation of research projects, and its location in the local scientific and medical environment (Université de Lille, CHU). Infinite is a leader in the creation of unique patient datasets and biobanks that feed into research projects. The unit obtained its funding through various calls: 4 European contracts (2 as PI, IMI2 C4C connect4chilldren €50k; EU4Health ERN ReConnect, €100k); national grants (1 ANRS-Mie Monitocov-Ageing, €269k as PI; 14 ANR (including 9 in PI), etc.; 18 regional contracts: such as 2 AAP Stimule and 1 Feder in PI (€136k, €180k and €375k respectively); from charitable associations (1 FRM-labeled team, etc.). Infinite has also obtained numerous contracts with industrials (3 Servier €250k, Therakos €56k, Astra-Zeneca €350k, GSK €300k, etc.) or with smaller companies (e.g. Biopredic €15k, IBD Biotech, €158k). All of these industrial collaborations represent a total of €2,660k between 2018 and 2023. Training is very good, as Infinite hosted 10 post-doctoral fellows and 28 PhD student defended their thesis (39 HDR). Attractiveness is also guaranteed by access to technical facilities with state-of-the-art equipment and the development of in-house facilities supported by Infinite members. Attractiveness is also illustrated by the appointment of three permanent positions ((2MCF et 1 CPJ).

The unit is committed to promoting a human resources policy aimed at creating a stimulating environment and attentive to working conditions, with particular attention to gender equality and the prevention of psychosocial risks (health and safety committee). Ethical issues, scientific integrity and carbon footprint are taken into account. The unit's governance is clearly defined, with thematic supervisors, cross-functional steering committees and a laboratory council. Particular attention has been paid to the scientific supervision of young researchers, to encourage scientific interaction.

The holistic approach of the project (devoted to all aspects of inflammation in different contexts, from mouse models to humans in different physiological and pathological conditions) carries a potential risk of lack of coherence and dispersion of themes and sub-themes, which may lead to a lack of efficiency and competitiveness. Despite an excellent recruitment policy and the attractiveness of local institutions, no young Inserm CRCN was appointed during the period. Technical facilities rely mainly on non-permanent staff, with a significant risk of losing expertise and technical skills. Members publish in the best specialist journals; however, particular attention should be paid to publication in generalist journals (with a leading position) and excessive non-publication in journals with a permissive editorial policy. The global assessment is excellent.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous report of 2019 identified four recommendations to which the unit responded appropriately.
1) *To continue to publish at high level, but with more articles in high impact generalist scientific journals*
During the last years, the members of the unit have in fact published in journals with high visibility as key authors (Jama, Nat. Commun (in collaboration) or as co-authors (Lancet, Nat. Med., Nature, NEJM …), as well as key authors in the best journals of specialty.
2) *To create a MSc in Immunology and Inflammation under the direct control of the unit*
Members of the unit, have piloted the structuring of an educational path in the MSc biology and health dedicated to infection, immunity and inflammation.
3) *To increase the number of non-clinical postdocs and to improve the attractiveness of talented scientists*
The unit created a website as an international showcase for laboratory news and successes. It dedicated part of its funds to emergence and attractiveness.
This effort was successful by welcoming 7 non-clinical postdocs and talented scientists.
4) *To identify theme leaders*

The unit designated theme coordinators to ensure scientific animation and encourage interaction between researchers in the themes.

B - EVALUATION AREAS

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

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

Assessment on the scientific objectives of the unit

The unit has set an integrated scientific project with several interfaces between themes and scientific questions that require an interdisciplinary approach. The unit developed successfully this project thanks to researcher expertise, the favourable local environment with access to multiple expertises and facilities, the strong connections with university clinicians with unique access to patient data set, biobanks and clinical trial expertise, and the number of potential academic and industrial partners. The assessment on the scientific objectives is excellent.

Assessment on the unit's resources

Human resources include 131 members (69 permanent from inserm, university and hospital and 62 non-permanent staff). The average annual budget of the unit has been 3 392 kE/year since 2020, with 14% of the budget coming from authorities (Inserm, University, CHU Lille) and 86% coming from local, regional, national and international public grants and industrial collaborations. The assessment on the unit's resources is excellent.

Assessment on the functioning of the unit

The unit is committed to promote a human resource policy aiming at building a stimulating environment attentive to the working conditions of the staff. The unit governance is clearly defined, including themes responsibilities and transversal steering committee and laboratory board. The assessment of the functioning of the unit is outstanding.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The Infinite unit is a single team focusing on all aspects on inflammation from its origins to its consequences. More specifically, its general scientific objective is to better understand the origins, mechanisms, and consequences of chronic inflammation in order to develop biomarkers and innovative treatment. The unit that historically focused on inflammatory bowel disease has extended its research field to a wide spectrum of chronic inflammatory diseases including IBD, chronic liver diseases and systemic sclerosis. While heterogeneous, these different models share common patophysiological process including the interactions of the immune system with the environment, fibrosis and regeneration, and unmet medical needs in terms of targeted therapies. These general objectives are supported by a well-defined organisation in 4 themes, from the environmental contributors to inflammation, regeneration, fibrosis to therapeutic innovation targeting inflammation. This organisation, with each theme exploring different areas and different approaches from basic to clinical that are connected to each other, is highly convincing.

The unit has set an integrated scientific project with several interfaces between themes and scientific questions that require an interdisciplinary approach. The topics that are addressed include all the aspects of chronic inflammation involved in a wide spectrum of chronic diseases that share high unmet medical needs from epidemiology to personalized cares and social impact. The relevance of the topic and the potentially strong impact of research results offers a unique opportunity. The combination of researcher expertise, the favorable local environment with access to multiple expertise and facilities, the strong connections with university clinicians with unique access to patient data set, biobanks and clinical trial expertise, and the number of potential academic and industrial partners is another strength and offer an opportunity to pursue the development of the project in this competitive field at an international level.

Weaknesses and risks linked to the context

The holistic approach of the research program dedicated to all the aspects of inflammation in different settings from mouse models to humans in different physiological and pathological conditions carries a potential risk of lack of consistency of the global project with a dispersion of themes and subthemes and a lack of efficiency and competitivity

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

Human resources include 131 members (69 permanent from Inserm, university and hospital and 62 non-permanent staff) representing 80.5 full-time equivalent, with a wide diversity of profiles (5 full-time researchers, 26 clinical full and assistant professors, 12 full and assistant professors, 6 clinicians, 40 support staff, 18 post-doc and 24 PhD students. Concerning financial resources, the mean annual budget of the unit has been 3 392 kE/year since 2020, with 14% of the budget coming from authorities (Inserm, University, CHU Lille) and 86% coming from local, regional, national and international public grants and industrial collaborations. Scientific resources include access to various facilities and platforms (Lille University, Pasteur Institute of Lille) and access to unique patient data sets and biobanks facilitated by a strong connection with the Precise FHU).Implentation of the unit in the local scientific and medical environement (Lille University, University Hospital) appears to be particularly successfull with a majority of the team members being full or associate professors, easy access to all the local facilities, technical platforms and associated expertise, and strong connection with patient datasets and collections favouring translational approaches.

Weaknesses and risks linked to the context

The main weaknesses identified are related to the high number of non-permanent staff members especially involved in facilities support and technical expertise that is crucial to maintain high standard experiments and expertise dissemination (especially to support facilities). Moreover, while many applications to call for proposals were successful with a high number of funded projects there is a lack of big funding especially from EU.

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 unit is committed to promote a human resource policy aiming at building a stimulating environment attentive to the working conditions of the staff, including a specific attention to gender equality and prevention of psycho-social risks with the creation of an health and safety committee. Ethical issues, scientific integrity and footprint carbon are taken into account. The unit governance is clearly defined, including themes responsibilities and transversal steering committee and laboratory board. Attention has been paid to the scientific animation that benefits from a scientific animation group gathering junior and senior researchers from all themes to favour scientific interactions through specific events and meetings (journal club, Infinite Scientific Coffee Break).

Weaknesses and risks linked to the context

No weakness identified

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

INFINITE has a solid international reputation due to 1) its outstanding publication track record (1639 articles), 2) number of research and structuring grants and prizes obtained by the INFINITE PIs (>150, including 2 European projects as leader, 17 national projects as leader, 41 contracts with industrial partners and 16 individual prizes); 3) the active participation of many Infinite members to expert groups and committees (>160). The attractiveness of the unit is also warranted by the access to technical facilities with cutting-edge technology equipment and by the excellent staff hosting policy with many processes and tools implemented to support staff members in their work. Hence, Infinite has attracted 10 post-doc fellows / scientists during the contract. The overall assesment is excellent.

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

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

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

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

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

Infinite fulfills all the standards requested for attractiveness, as demonstrated by the presence of 25 foreign post-doc fellows or PhD students within the past 5 years and the appointment of 3 tenure-track assistant (2MCF) or full professor (1 CPJ). PIs of Infinite have earned awards and research prizes (ex: IUF label, Esophageal atresia World Award, CSL foundation), were invited to or chaired sessions in international conferences (Espen, Espghan, ASH, etc.), were involved in national or international conference organization on their specialties (fibrosis, esophageal atresia, Car-T cells, etc), reviewed articles for international journals (ex: J Hepatol, Part & Fiber Tox, Clin Nutr, Gastroenterology, Sci Rep, CMGH), or grant proposals for national (ANR, Anses, Inca, etc.) or international (ex: ERC grants, Irish Research Council, Israel Science Fondation, Univ of Wisconsin Aquatic Research Center, etc.) funding bodies. Many PIs are involved in expert groups, juries or committees at both the local, national and international levels (ex: CNU 64, 55 & 47, Inserm CSS3, scientific committee of Lille University, secretary of GFHGNP, member of Afef council, secretary of Société Française de Transplantation, Chair Esophageal atresia Special Interest Group, Espghan, etc.). Moreover, Infinite has set-up various internal tools and processes that ensure excellent and attractive staff hosting: material and financial resources for new PI joining the unit, support for staff advancement, charters, actions and support from either internal or external referents for ethics and deontology and open science to assist members of the unit.

Infinite PIs have applied to local, national or international competitive calls such as ANR, Inca, Iresp, CPER, Marie Curie, FRM…) and are leaders of 2 European grants, 17 national grants, 41 contracts with industrial partners, 21 contracts with local funding bodies, 30 grants from charities. On average on the last 5 years, >85% of the total budget of Infinite originated from external funding (with an average 2, 7 M€ per year of external fundings). PIs are particularly active to find funding for PhD students, with different types of funding (Univ of Lille, Cifre, Region Council Haut de France, etc.). Likewise, they earned many grants to acquire cutting edge technology equipment (polysome profiling, spatial transcriptomics, confocal microscopy). Noteworthy, Infinite implemented 13 technical facilities (cell culture, molecular biology, histology, biochemistry, western blots, chemistry, etc.) with well identified referents (technical and health and safety referents) for each of them. This ensures equal access to equipment to all members of the unit and technological developments within these platforms.

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

Despite excellent staff hosting policy and attractiveness of both the unit and the Lille university environment, no young Inserm CRCN was appointed during the last 5-years. The organization of the unit in technical facilities relies on a low number of permanent staff and mainly on non-permanent staff. There is a huge risk of expertise and technical loss.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

During the current period, the unit published a total of 1,639 articles (1,489 original articles and 150 reviews), among which 447 are related to basic/translational research. One third are signed as first, last and/or corresponding author. Articles have been published in top 1-10 peer reviewed generalist and speciality journals. The scientific production is proportionate to the research potential and follows the ICMJE authorship criteria. Publications are deposited in LillOA/HAL. The overall assessment is very good to excellent.

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

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

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

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

During the current period, the unit published a total of 1,639 articles, including 1,489 original articles and 150 reviews: 70% are clinical research articles and 30% are basic/translational research articles. One third are signed as first, last and/or corresponding author. The ratio of clinical research/fundamental-translational research articles is homogeneous between the 4 themes. The mean scientific production is 8.5 articles/scientist over the period. Some publications have been published in top 1 or top 10 peer reviewed generalist journals (Jama, Nat Commun (in collaboration), Sci Rep, Faseb J) or specialty journals (Gut, J Hepatol, Gut Microbes, Am J Gastroenterol, Front Immunol, Jama Dermatol, Arthritis Rheumatol). Median publication numbers are 3 and 3.5 by PhD students and junior/post-doc scientists, respectively. Scientists are encouraged to deposit their full text to HAL or local database (26% in HAL database). The ratio of clinical research/basic-translational research articles is consistent across the 4 themes. Each theme led to the publication top generalist and specialty journals.

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

The unit's members publish in the best specialist journals; particular attention should be paid to publishing in generalist journals (with a prominent position in the list of authors). Scientists should take care not to over publish in journals with permissive editorial policy (MDPI). Some projects are not as productive as others in terms of scientific production, in addition to a relative heterogeneity between disciplines and individuals. This issue needs to be addressed. Members have to increase the number of articles deposited in LillOA/HAL.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The unit stands out by the quality and quantity of its non-academic interactions (partnership with Big Pharma (Servier, Therakos, Astra-Zeneca, GSK…) or with smaller companies (Biopredic, IBD Biotech; total grants of 2 660 k€ between 2018 and 2023). The unit develops products for the cultural, economic and social world (4 patents in the period 2018-2023; one GNU license [CC-BY-NC-ND 4.0.]; a software Tool for molecular dynamics simulations). Members share their knowledge with the public and takes part in debates in society (participation to the annual "Fête de la Science", to general public conferences and television shows, on social media, PhD students participation to "My thesis in 180 seconds", use of the youtube channel of FHU PRECISE @fhuprecise3765). The overall an assessment is very good to excellent.

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

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

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

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

Infinite has developed different types of partnership with the economic world (Big Pharma or small biotech). In particular, Infinite obtained numerous contracts with industrials (Servier, Therakos, Astra-Zeneca, GSK…) or with smaller companies (e.g. Biopredic, IBD Biotech). All these industrial collaborations represent a total of 2 660 k€ between 2018 and 2023. The contracts with valorization actors like the Satt represent a total of almost 836 k€. The researchers of the drug discovery group file 4 patents in the period [2018-2023], resulting of their research in interaction with biologists and clinicians. A GNU license (CC-BY-NC-ND 4.0.) Software Tool for Analysis and Visualization of Interaction Networks of Molecular Dynamics Simulations (Sinaps) was also developed. To open the science to the public, Infinite participated to the annual "Fête de la Science", to general public conferences, in appearing in television shows, on social media in publishing articles in mainstream newspapers, in writing articles in some parliamentary journals. Some members of Infinite intervened specifically with young public (project "Apprentis chercheurs"), or in front of pupils of a primary school. PhD students participated to "My thesis in 180 seconds". Infinite also used the youtube channel of FHU Precise @fhuprecise3765 to disseminate the research activity of the unit. It also has strong interaction with patient association.

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

Infinite recognizes that the unit doesn't have a professional community manager who could boost its communication.

ANALYSIS OF THE UNIT'S TRAJECTORY

For the next few years, Infinite decided to consolidate its trajectory around the same 4 WPs with overall similar contours but completed by new challenges, new actors and new projects. The unit wants to keep the organization as a single-theme and single-team unit focused on inflammation from its origins to its consequences. Infinite will continue to utilize registers, cohorts, and biobanks, which provide relevant insights into clinical and pathophysiological questions arising from the collaboration between clinicians and scientists. Compared to the current contract, the development of original diagnosis and prognostic markers will be fully integrated to WP1 to 3 and not isolated in the WP4. The arrival of new members will remove certain blockages to develop new cutting-edge projects. More details about the trajectory of each theme are given below. Strengths, weaknesses and recommendations are also reported for each theme. The Expert Committee notices that the trajectory proposed for each WP is in line with the expertise of the members of the unit and that appropriate supports will be implemented in terms of staff commitment, equipment and financial resources (for more details, see below for each WP).

RECOMMENDATIONS TO THE UNIT

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

- Politic/selection of new research projects to maintain scientific consistency.
- to strengthen human resources to maintain know-how (permanent position)

Recommendations regarding the Evaluation Area 2: Attractiveness

- More EU funding
- attract and prepare junior scientists

Recommendations regarding Evaluation Area 3: Scientific Production

- Aim to publish in generalist journals
- Continue to publish in the best specialty journals

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

- No specific recommendations

THEME ASSESSMENT

Theme 1:	Environmental contributions to mucosal homeostasis and IBD susceptibility
Name of the supervisor:	Cécile Vignal and Frédéric Gottrand

THEMES OF THE THEME

Theme 1 aimed at assessing the origin of inflammation through the evaluation of the contribution of environmental factors to mucosal homeostasis and susceptibility to inflammatory bowel disease (IBD), with a particular focus 1) on the impact of nutrition on intestinal barrier maturation or in graft-vs-host disease, 2) on function of gel-forming mucins in mucus permeability and mucosal susceptibility to inflammation, 3) on exploration of IBD origin and evolution through epidemiological and experimental approaches and 4) on the role of pathobionts and microbiota in inflammation.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No specific recommendations were made.

WORKFORCE OF THE THEME: IN PHYSICAL PERSONS ON 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	5 + 1PH
Maîtres de conférences et assimilés	11
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	8
Sous-total personnels permanents en activité	**28**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	7
Post-doctorants	1
Doctorants	7
Sous-total personnels non permanents en activité	**16**
Total personnels	**44**

EVALUATION

Overall assessment of the theme

This theme was very productive in term of publications and grant applications. The multitude of complementary approaches is a great asset. Yet, the number of collaborations between the different axis appears quite low.
The overall assessment is very good to excellent.

Strengths and possibilities linked to the context

The main strength of this theme is the use of different levels of approaches, from microbiology to cell and animal models, including GMO ones to cohorts (ex Pensine) and epidemiological approaches (ex Epimad registry). Noteworthy, original animal models have been set-up (transgenic models for mucus studies, graft-vs-host disease models). Likewise, the establishment of the Pensine cohort is a great achievement to the theme. This cohort will undoubtedly produce many relevant data that will foster original translational research projects.
The sub-theme on the impact of milk technological process is very original. Similarly, the continuum from epidemiology to experimental approach in the sub-theme environmental factor risks for IBD is a great example of translational research. The theme has a very good publication track record: the theme produced 428 article (171 in PDC), 391 originals/37 reviews and a good balance between clinical and fundamental research (210 clinical research/218 fundamental research. The PhDs are involved in 70 articles (33 in PDC). The theme obtained many grants from different origins (ANR and other national calls: 10 as leader, 2 as partners, European call (1 as leader, conect4children, Collaborative Network for European Clinical Trials For Children), 7 contracts with industry as leader, 9 local funding bodies as leader and 2 as partner, 8 fundings by charities as leader.

Weaknesses and risks linked to the context

The different sub-themes seem to live independently from each other and only few collaborations between PIs of the different subthemes are mentioned. Although very relevant and productive in terms of publications, the subtheme on the environmental factors (air pollution, microplastics, aluminium) involved in alteration of gut homeostasis is very competitive at the international level.

Analysis of the theme's trajectory

Theme 1 trajectory is built on similar objectives and add oesophageal atresia as an origin of mucosal inflammation. The future project integrates or consolidates new approaches such a multi-omics analysis of microbiota-host interaction and the increased use of organoids and organotypic models and will rely on facilitated access to cohorts and their associated biobanks to enhance the 'translational-ness' of their research.

Many animal models and technologies are available in the unit. Funding and staff (post-doc, PhD) are secured for each sub-theme. Cohorts and biobanks have been implemented and are ready-to-use. The interactions between sub-themes are scarce and it sounds like each sub-theme stands on its own and does not beneficiate from the others. Many projects rely on omics data (microbiota, metabolomics) and data integration but no such expertise (microbiota analysis, data integration) seems present in the unit. International competition on early life microbiota development and human milk oligosaccharide (HMO) is high. Likewise, the impact of environmental factors and gut homeostasis is a hot topic with high international competition.

RECOMMENDATIONS TO THE THEME

Collaborations between PIs should be increased. In particular, studies on gel-forming mucins in early life and the link with HMO and microbiota could be very original. Similarly, phage biology could be studied in the other sub-theme and would be very innovative. Consolidate expertise on microbiota analysis and data integration through hiring of expert in this field.

Theme 2 Epithelium integrity: from pathologic regeneration to homeostasis

Name of the supervisor: Silvia Speca and Cyril Sobolewski

THEMES OF THE THEME

The Theme 2 main objective is to decipher the cellular mechanism linking inflammation and the regenerative response as well as the balance between the homeostatic tissue repair and the pathological fibrosis in some physio pathogenic situations including inflammatory bowel disease and alcoholic liver diseases. Global assessment includes mechanistic explorations and complementary academic clinical research and biomathematical approaches that have been implemented to improve the continuum between basic and translational research findings and patient management.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

NA

WORKFORCE OF THE THEME: IN PHYSICAL PERSONS ON 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	6 + 2 PH
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**16**
Enseignants-chercheurs et chercheurs non permanents et assimilés	4
Personnels d'appui non permanents	5
Post-doctorants	5
Doctorants	6
Sous-total personnels non permanents en activité	**20**
Total personnels	**36**

EVALUATION

Overall assessment of the theme

Theme 2 contains 4 subthemes including clinical, translational and basic approaches aiming at 1) evaluate the mechanisms of post-operative recurrence in Crohn's disease in mouse models and to test therapeutic strategies 2) elucidate the importance of epithelial tissue integrity in the liver cellular microenvironment in alcoholic associated liver-diseases 3) develop biomathematical approaches to improve risk stratification and patient management and 4) decipher post-transcriptional dynamic in chronic liver diseases and its potential role in promoting liver cancer. Projects are funded and have led to scientific publications in top-ranked specialty journals. Overall assessment is very good to excellent

Strengths and possibilities linked to the context

Theme 2 appears to be well organized and involve clinicians and basic researchers as well as doctoral students and technical staff. It benefits from technical facilities including animal models. One of the major achievements was the understanding of the hepatocyte regeneration blockade occurring in alcoholic hepatitis due to a markedly alterated Hippo/YAP pathway, leading to a progressive shift from hepatocytes to biliary cells (J Hepatol 2021, 75, 912-923). This translational project was funded (ANR) and offers important therapeutic perspectives. The theme is globally very productive, with 302 original articles published. The quality of the clinical research should be highlighted. Among other important achievements during the last years, the unit developed a model of postoperative recurrence in HLA-B27 transgenic rats, a model of spontaneous spondyloarthritis. This model demonstrated the crucial role of the AIEC LF82 strain in lesions associated with postoperative recurrence and, for the first time, the preventive efficacy of the probiotic Saccharomyces cerevisiae (Valibouze et al. World J Gastroenterol. 2023, 29, 851-866). The hepatology group designed and conducted a large multicenter clinical trial (NCT02281929: AntibioCor) to evaluate the potential of prophylactic antibiotic treatment on mortality in alcoholic hepatitis. This randomized academic study, involving 24 centers in France and Belgium. The unit showed for the first time that the loss of tristetraprolin (post-transcriptional regulator) in mice significantly reduces the development of steatosis, but also of fibrosis and hepatic carcinogenesis. This study illustrates the importance of mRNA regulatory proteins in MASLD (Metabolic dysfunction–Associated Liver Disease) and its progression to hepatocellular carcinoma (Dolicka et al. Cell Mol Gastroenterol Hepatol 2021, 11, 597-621). Quantitatively the theme is productive with 328 articles (82 in PDC), 302 originals/26 reviews and 229 clinical research/99 fundamental research. The PhDs are involved in 51 articles (17 in PDC).

Weaknesses and risks linked to the context

The theme 2 is organized into 4 sub-themes that are independent from each other, with no obvious transversal approach. The Crohn's disease sub-theme 1 is not associated to a clinical validation counterpart while identification of biomarkers of recurrence is an objective. The sub-theme 2 is very productive but the connections between the translational and the clinical part seem to be limited. The sub-theme 4 seems to be disconnected while scientific questions are related to sub-theme 2.

Analysis of the theme's trajectory

Subtheme1 will switch to the understanding of the interplay among the loss of epithelial homeostasis, regeneration defects, and IBD-associated intestinal fibrosis by using the same mouse models and human samples. Subtheme 2 will aim at a deep evaluation of the YAP pathway already describe by the team along to the fine characterization of the intra-hepatic micro-environment in order to identify potential specific targets. The clinical part of this subtheme is not mentioned. Subtheme 3 will focus on public health and the evaluation of innovative strategies to help public health decision-makers to combat chronic liver diseases.

RECOMMENDATIONS TO THE THEME

We encourage the theme to reinforce the interactions between clinicians and basic researcher with a more visible bedside to bench to bedside strategy, as all human resources and facilities are available on site. The subtheme 2 would benefit for a reinforcement of basic researchers and pathologists, with clinician main task to provide well phenotyped patients, serum and liver samples, statistics and clinical research expertise to test/validate innovative biomarkers/therapeutic approaches.

Theme 3: From chronic inflammation to fibrosis: role of immune cells

Name of the supervisor: Myriam Labalette and Bertrand Meresse

THEMES OF THE THEME

Theme 3 develops translational research focused on the complex interaction between chronic inflammation and fibrosis. More precisely, the objectives of this theme are to (i) decipher the role of immune cells, and especially B and T lymphocytes and eosinophils, in chronic inflammatory diseases (systemic sclerosis, IBD) and their role in fibrosis and (ii) identify novel diagnostic and prognostic/follow-up biomarkers in systemic sclerosis.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report emphasised that this theme is conducted by a translational research team incorporating talented clinicians and clinical biologists (university hospital researchers) and academic researchers. They have developed very successful projects, thanks to an integrated and comprehensive approach relying on patient's databases and biocollections, epidemiology and innovative in vitro and in vivo models of chronic inflammation and fibrosis (some of which have been developed and validated during the current period). The theme has succeeded in developing an integrated, interdisciplinary research program organized into 4 sub-tasks aiming to address fundamental and translational questions: origin of inflammation, mechanisms of impaired tissue regeneration, mechanisms involved in the switch from chronic inflammation to fibrosis, innovative therapeutic and diagnostic approaches).
Overall, they have succeeded in achieving their objectives, with a good balance in terms of scientific output between the 4 themes (although there is some heterogeneity in the quality of journals between the four subtasks).
The previous report emphasised that funding was mainly from clinical and industrial grants. This point has been addressed during the current period, with funds originating from the FRM (Equipe labellisée) and grants from regional (CPER Resist-Omics) and national institutions (Inserm (Messidore project), Precise FHU, ANR). We should also mention funding from technology transfer office and national agencies (Satt, BPI) and industrial contracts (Therakos, Miltenyi biotec).

WORKFORCE OF THE THEME: IN PHYSICAL PERSONS ON 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	10 + 3 PH
Maîtres de conférences et assimilés	4
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**22**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	12
Post-doctorants	4
Doctorants	9
Sous-total personnels non permanents en activité	**27**
Total personnels	**49**

EVALUATION

Overall assessment of the theme

Theme 3 is organised into 3 subthemes aiming to study the role of B cells in systemic sclerosis, intestinal epithelial T cells (IEL) in chronic IBD, and eosinophils in chronic inflammation. Each subtheme is (i) led by senior scientists (HU, EC, Engineer) and integrates a number of PhD students and postdoc scientists and (ii) addresses fundamental and translational questions. Subthemes are funded and have led to scientific publications in top-ranked specialty journals. The overall assessment is very good to excellent.

Strengths and possibilities linked to the context

The three subthemes include fundamental and translational research programs.

Subtheme 1 is dedicated to the analysis of B cell homeostasis and function in systemic sclerosis (SSc) and inflammatory diseases (Imid;) it is based on integrated multi-omics analysis and data integration and has led to the identification and validation of fibrosis signatures and biomarkers. These projects are supported by integrated Inserm (Messidore) and Inserm-Inria (Endomic) programs, and rely on original biobanks (FHU Precise, IMID). The projects have generated original models of reconstructed skin in vitro. Subtheme 1 led to the publication of 13 major articles in specialized journals (Front Immunol, Proteomics, Arthritis Rheumatol, Ann Rheum Dis, Jama Dermatol). Of note, subtheme 1 has conducted collaborative studies with biotechnology and pharmaceutical companies (valorisation of technical expertise); one of these collaborations has led to a publication in the journal Nat Commun, in which members of subtheme 1 are co-authors.

The subtheme 2 is devoted to the study of IEL in chronic inflammatory bowel disease. The project is based on data obtained during the previous contract, which led to the identification of an IEL subpopulation that is protective against the chronic inflammation associated with C. parvum infection. Subtheme 2 has developed an in vitro model of IEL incorporating infection by C. parvum. To date, only one major article has been published during the current contract (Front Immunol). Subtheme 3 aims to characterise the phenotypic, molecular and functional properties of circulating and tissue-resident eosinophils in inflammatory skin diseases such as DRESS syndrome and mastocytosis. The theme also generated original methods for assessing the heterogeneity of tissue eosinophils, thanks to access to national (COHesion) and international biobanks and collaboration with an internationnally recognized expert (UWisconsin). This subtheme led to the publication of 5 major articles in journals of speciality (Jaci, Clin Exp Allergy, Jaci Immunol Practic). Quantitatively the theme produced 822 article (232 in PDC), 741 originals/81 reviews and 739 clinical research/83 fundamental research. The doctorants are involved in 97 articles (26 in PDC). Funds originating from the FRM (Equipe labellisée) and grants from regional (CPER Resist-Omics) and national institutions (Inserm (Messidore project), Precise FHU, ANR). Funding are also from technology transfer office and national agencies (Satt, BPI) and industrial contracts (Therakos, Miltenyi biotec). Collectively, theme 3 is well organised, with a good balance of supervision for each subtheme between clinicians and biologists; each subtheme includes doctoral students and technical staff. Scientists benefit from their integration in strong research networks and have established productive collaboration with international experts (UStanford).

Weaknesses and risks linked to the context

The theme 3 is organized into 3 subthemes which appear relatively independent from each other. There is not obvious transversal intra-Theme 3 project, underlining a risk of under-exploiting the original tools which have been implemented. The subthemes are also fairly heterogeneous in terms of numbers of tasks, especially in subtheme 1, with the risk of dispersion and consequently a delay in the publication of data (because of the increase in the number of models to be developed or used). Collaborative projects with industries/biotechs are a good source of funding and of recognition of expertise, but accentuate the risk of dispersion.
Subtheme 2 is not very productive despite a very focused topic. The project appears to be poorly integrated into the general theme of Theme 3. The lack of publications is particularly damaging to the visibility and legibility of the scientists integrated in this theme. Subtheme 3 is presented as an emerging project and is based on the specific expertise in the biology of eosinophils. The project, which addresses clear and relevant questions through an integrated approach based on biobanks, integrates an associate senior scientist who is a world well-known expert in the biology of eosinophils. His forthcoming retirement has been anticipated in terms of scientific and technological integration. This subtheme does not present any particular risk.

Analysis of the theme's trajectory

The trajectory of theme 3 is a continuation of the projects conducted during the previous period and is based on the unique expertise of the team in the field of Imids, and in particular SSc and ulcerative colitis (which could be extended to certain severe type-2 mediated diseases, such as atopic dermatitis and asthma).

The project is organized into 2 main subthemes. Subtheme 1 is an integrated program which aims to decipher the role of adaptive cells in chronic inflammation and fibrosis. Task 1 aims to (i) evaluate the role of autoantibodies and B cells in the pathophysiological process of SSc (use of unique biocollections and original preclinical models) and to decipher the dialog established between B cells with environmental cells, i.e. epithelial cells and endothelial cells, fibroblasts) ; these subtasks will allow to identify new diagnostic and prognostic markers and validate new therapeutic approaches (such as the Jak/Stat pathway), (ii) characterise the heterogeneity of SSc in order to identify endotypes (FHU Precise) and (iii) evaluate new therapeutic approaches (through industrial contracts and collaboration with theme 4). The objective of Task 2 is to evaluate the role of B and T cells in chronic inflammation, fibrosis and colitis-associated colorectal cancer by (i) exploring the role of humoral responses in the development of inflammation and fibrosis (using ex vivo and in vivo models) and (ii) clarify the role of CD103+ intraepithelial lymphocytes (IEL) in tissue protection. Task 3 aims to (i) characterize the status of therapeutic Car-T during the generation process before injection into patients and (ii) develop 2nd generation Car-T (collab. CHU Rouen). The second subtheme focuses on the role of eosinophils in chronic inflammation and fibrosis. It benefits from the implementation of original models from the University of Wisconsin, thanks to the integration of Dr Esnault (part-time research associate), a world-renowned specialist in the biology of eosinophils. The main focus of this axis is to conduct an exhaustive phenotypic, transcriptional, and functional characterisation of circulating and tissue eosinophils in various eosinophilic and type 2 diseases (Neos project). Theme 3 is benefiting from a thematic focusing, which will improve the visibility and coherence of the scientific project and its scientific production. The team has secured funding that will enable it to carry out the projects. The robustness and the feasibility of the project are guaranteed by the clinical-research continuum, based on a strong network of local, national and international collaborations. The use of biobanks and clinico-biological databases is an obvious asset to the project.

RECOMMENDATIONS TO THE THEME

To maintain a high level of scientific publications in top-level specialised journals. Scientists of Theme 3 are encouraged to publish in generalist journals.

To diversify its sources of funding, particularly by obtaining grants from national agencies (ANR).

There is some imbalance in the human resources (PhD students, supporting staff) allocated to each subtheme/task. Special attention is required to get specific financial support for each subtheme.

Scientists should be cautious not to include programs of research that do not fall within the general theme of the project or that are more specifically relevant to clinical research.

Strengthen internal collaboration and the sharing of experience/expertise within theme 3 and with the other themes of the unit.

Theme 4: Therapeutic innovation targeting inflammation

Name of the supervisor: Régis Millet and Natascha Leleu-Chavain

THEMES OF THE THEME

This theme aims to develop innovative therapeutic strategies targeting inflammation using an already established workflow of drug discovery. This theme benefits from the discovery of novel biological targets identified in collaboration with the other themes.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The unit designed two Theme leaders for theme 4, as recommended in the previous report.
The number of postdocs, but also PhD students, remains low despite the recommendation made in the previous report. Many publications of the team were made in the best specialist journals, but rarely in high-level generalist journals.

WORKFORCE OF THE THEME: IN PHYSICAL PERSONS ON 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	6
Sous-total personnels permanents en activité	**12**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	2
Post-doctorants	2
Doctorants	2
Sous-total personnels non permanents en activité	**8**
Total personnels	**20**

EVALUATION

Overall assessment of the theme

The theme develops a diversity of therapeutic approaches to treat inflammatory diseases (classical small molecules, nanoparticles for vaccines, cell therapy). The theme is also known to possess a strong expertise in in silico approaches and is therefore involved in a large panel of drug discovery projects. The recent research projects developed in this theme conducted to concrete achievements (lead compounds and innovative treatments selected for preclinical and clinical trials). Secured grants and scientific staff seem to be sufficient for the future. The overall assessment of theme 4 is very good to excellent.

Strengths and possibilities linked to the context

This theme considers five separate parts: drug discovery, in silico approaches, advanced methods of structural bioinformatics, development of nanoparticle-assisted vaccines and chimeric antigen receptor (Car)-T cell therapy.
The drug discovery approach follows a classical process comprising in silico analysis, chemical synthesis and biological evaluation. Through rational design and appropriate chemoinformatics, the research unit identified three promising lead compounds (small molecules) selected as candidates for preclinical in vivo trials to treat inflammatory diseases.

Considering P2RX7 as a potential therapeutic target in inflammation, the unit identified a positive P2RX7 modulator named HEI3090 effective against lung cancer by promoting anti-tumoral immune responses. A license with the company Domain Therapeutics has been established. Nat. Commun. 2021, 12, 653) (in collaboration). The theme also developed an orally administered compound able to prevent the PD-1/PD-L1 interaction resulting in the restoration of the cytotoxic activity of T lymphocytes directed against tumour cells (EP/2023/306103.5).

A first selective Nod1-RIPK2 inhibitor active in the nanomolar range was studied as a promising therapeutic agent for inflammatory diseases i.e. ulcerative colitis (J Med Chem, 2023, 2023, 2024). A patent application covering this new class of selective inhibitors is in preparation. The theme develops strong expertise in in silico approaches (structural bioinformatics) and is therefore involved in a large panel of drug discovery projects (J. Chem. Inf. Model. 2022).

Infinite also developed nanoparticles from cationic starch hydrogel used in the composition of vaccines (WO2023/036814). The unit participated to a filed patent covering an anti-Sars-CoV2 vaccine that has been licensed to LoValTech start-up with the perspective of a phase 1 clinical trial in 2024.

Lastly, the Lille University Hospital associated to Infinite studied an innovative chimeric antigen receptor (Car)-T cell therapy on patients.

Quantitatively the unit produced 77 article (31 in PDC), 68 originals/9 reviews and 20 clinical research/57 fundamental research. The doctorants are involved in 19 articles (14 in PDC).

Secured grants are 795 k€ [including CPER Resist-omics 400 k€; other (Satt, Region, University, FMR….) 395 k€]

Weaknesses and risks linked to the context

The number of international collaborations established by the theme seems to be relatively low (University of Sussex, Univ Medical Freiburg, GE, Univ Gothenburg, SW)), therefore, an international recognition of expertise in drug discovery is not clearly demonstrated.

Analysis of the theme's trajectory

For the next five years, the team dedicated to theme 4 planned to pursue 2 drug discovery projects developed during the period 2018-2023 and to extend expertise in *in silico* approaches.

Nod1-RIPK2 inhibitors: the development of selective Nod1-RIPK2 inhibitors would be highly beneficial in targeting inflammatory and metabolic diseases. In this project, the team will perform the synthesis of potent selective Nod1-RIPK2 inhibitors by developing three different drug design strategies: 1. by occupying the ATP binding pocket of RIPK2 with new selective inhibitors of Nod1 (patent expected in 2025); 2. by degrading RIPK2 exploring the concept of targeted Protein Degradation (TDP), an emerging new drug design strategy ; 3. by disrupting RIPK2 interaction with its specific partner XIAP, playing an essential role in the activation of RIPK2 inflammatory pathways.

Financial support of this project: Satt Nord de France, FRM and CPER ResistOmics.

New staff on this project: one post-doctoral researcher in chemistry and one assistant engineer in biology.

P2RX7 modulators: The team wants to decipher the mechanisms of action of P2RX7 modulators at the molecular and cellular levels (positive and negative allosteric modulators). Key amino acids for the binding and ligand-induced conformation changes will be validated by site-directed mutagenesis and biological assays. This study will provide guidelines for the design and synthesis of a series of optimized ligands displaying high efficiency.

This study will be supported by a grant from CPER Resist-omics.

A project engineer in chemistry and project engineer in biology will be recruited to work on this project.

In silico approaches: To pursue the in silico approaches in drug discovery, the team will recruit a new professor assistant in 2024 in order to maintain the expertise of the unit in structural bioinformatics (protein modelling, molecular simulations) and chemoinformatics (virtual screening, chemomining, machine learning), and to develop a new bioinformatics axis dedicated to the analysis of the growing omics data from RNA sequencing experiments (single-cell, whole-transcriptome).

RECOMMENDATIONS TO THE THEME

We recommend the theme to concretize the recruitment of young investigators and assistant engineers. Moreover, we strongly recommend the members of the team to attract new Ph.D. students dedicated to the drug discovery projects. Indeed, doctoral and post-doctoral researchers being predominantly devoted to experimental tasks, they will ensure the production of new scientific results.

As a suggestion for the Infinite unit, we also recommend that the theme continues the organization of scientific meetings at least once a year (the "Infinite day"?) during which the young researchers (Ph.D. students and post-doctoral researchers) from the different work packages are invited to present their research (posters and/or short oral communications). The aim is to create/improve the contacts between the young researchers of the unit and to favour the establishment of new intern collaborations.

CONDUCT OF THE INTERVIEWS

Date

Start: 21 novembre 2024 à 09h00

End: 21 novembre 2024 à 17h00

Interview conducted: online

INTERVIEW SCHEDULE

08h30 Présentation du comité
08h45-09h15 Présentation globale de l'unité organisation et trajectoire (15 mn) (15mn de questions)

9h15-10h15 Présentation des faits scientifiques marquants et trajectoire du WP1 (10 mn)
Titre et présentateur : Contributions environnementales à l'homéostasie des muqueuses, santé et maladie. Cécile Vignal.

Présentation des faits scientifiques marquants et trajectoire du WP2 (10 mn)
Titre et présentateur : Intégrité épithéliale : de la régénération pathologique à l'homéostasie. Laurent Dubuquoy.

Présentation des faits scientifiques marquants et trajectoire du WP3 (10 mn)
Titre et présentateur : De l'inflammation chronique à la fibrose : rôle des cellules immunitaires. Bertrand Meresse.

Présentation des faits scientifiques marquants et trajectoire du WP4 (10 mn)
Titre et présentateur : Innovation thérapeutique ciblant l'inflammation. Natascha Leleu.

Questions (15 mn)
Pause - café : 15 min

10h30-11h00 Rencontre du comité avec les chercheurs + post-docs (huis clos)
Représentant chercheurs/post-doctorants : Cécile Vignal
11h00-11h30 Rencontre du comité avec les étudiants (huis clos)
Représentant étudiants : Laure Dubernat
11h30-12h00 Rencontre du comité avec les PAR (huis clos)
Représentant PAR : Marie Delbeke et Arnaud Dendooven

Pause - café : 15min
12h15-12h45. Réunion du comité en huis clos
12h45-13h45. Pause déjeuner

14h00-14h30 Rencontre du comité avec les tutelles (huis clos)
Inserm : Bénédicte Samyn, Déléguée régionale
IT PMN : Raymond Bazin, Chargé de Mission
Univ. Lille : Olivier Colot, Vice-Président Recherche
UFR3S : Karine Faure, Vice-Doyenne Recherche
CHU Lille : Camille Gladieux, Directrice Adjointe Recherche et Innovation

14h30-15h00 Réunion du comité à huis clos
15h00-15h30 Rencontre avec le directeur (L Dubuquoy, D Launay, V Chameroy)
Pause - café : 15min
15h45-17h45 Réunion du comité (huis clos)

GENERAL OBSERVATIONS OF THE SUPERVISORS

RÉPUBLIQUE FRANÇAISE
Liberté Égalité Fraternité

Université de Lille

—
Direction générale déléguée
Recherche et valorisation

Les vice-présidents recherche de l'Université de Lille

à

HCERES - Département d'Evaluation de la Recherche

Lille, 27/01/2025

Objet : Courrier d'observation de portée générale Université Lille DER PUR 260024851

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

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—

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 INFINITE – Institute for translational research in infflamation - 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.

Cependant, nous nous interrogeons – comme l'unité dans son document d'observations de portée générale joint – de l'avis global ("The global assessment is very good to excellent"), qui apparaît peu cohérent avec les avis émis dans la *Detailled Evaluatio*n qui comportent 4 avis 'oustanding' ou 'excellent' et seulement 2 avis 'very good to excellent'.

Vous trouverez également 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

—
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Fichier d'observations de portée générale
DER-PUR260024851 - INFINITE - Institute for translational research in inflammation

L'analyse faite est positive mais ne reflète pas les discussions que nous avions eues avec le comité le 21 novembre 2024.

Le point critique concerne l'avis global : "The global assessment is very good to excellent", qui apparaît peu cohérent avec les avis émis dans la Detailled Evaluation qui comportent 4 avis 'oustanding' ou 'excellent' et seulement 2 avis 'very good to excellent' :

Evaluation Area 1 : Profile, resources and organisation unit
- Assessment on the scientific objectives of the unit : The assessment on the scientific objectives is **excellent**.
- Assessment on the unit's resources : The assessment on the unit's resources is **excellent**
- Assessment on the functioning of the unit : The assessment of the functioning of the unit is **outstanding**.

Evaluation Area 2 : Attractiveness
- Assessment on the attractiveness of the unit : The overall assesment is **excellent**.

Evaluation Area 3 : Scientific production
- Assessment on the scientific production of the unit : The overall assessment is **very good to excellent**.

Evaluation Area 4 : Contribution of reseach activities to society
- Assessment on the inclusion of the unit's research in society : The overall an assessment is **very good to excellent**.

Avez-vous connaissance d'une pondération qui s'applique entre les items pour expliquer que c'est l'avis minoritaire qui a été retenu comme avis global ?
Cet avis global nous apparaît d'autant moins compréhensible que nous n'avons eu que très peu de recommandations émises (qui sont d'ailleurs plutôt d'ordre général ou global, plus que spécifiques à INFINITE).

Parmi les recommandations de 'Evaluation Area 3: Scientific Production', il est proposé : '- Better specialty journals'. Nous constatons une discordance entre cette recommandation et les commentaires et évaluations émises tout au long du rapport soulignant à plusieurs reprises qu'INFINITE publie dans les meilleurs journaux de spécialités.

Le 20 janvier 2025
Laurent Dubuquoy, David Launay, Virginie Chameroy

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