Evaluation of Research

EVALUATION REPORT ON THE UNIT:

CIRI - Centre international de recherche en infectiologie

UNDER THE SUPERVISION OF INSTITUTIONS AND RESEARCH BODIES:

Université Claude Bernard Lyon-I - UCBL
Hospices Civils de Lyon - CHU LYON HCL
École normale supérieure de Lyon – ENS Lyon
Institut national de la santé et de la recherche médicale - Inserm
Centre national de la recherche scientifique - Cnrs
Université Jean Monnet - UJM

EVALUATION CAMPAIGN 2025-2026
GROUP A

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High Council for the evaluation of research and higher education

On behalf of the committee of experts:

Julien Diana, Chairperson of the committee

For Hcéres:

Coralie Chevallier, President

In accordance with articles R. 114-15 and R. 114-10 8° of the Research Code, evaluation reports drawn up by the committees of experts are signed by the chairpersons of these committees and countersigned by the president of Hcéres.

To facilitate the reading of the document, the terms used in this report to designate functions, occupations or responsibilities (expert, researcher, teacher researcher, professor, lecturer, engineer, technician, director, doctoral student, etc.) are generic and gender neutral.

This report is the outcome of an evaluation by a committee of experts the composition of which is specified below. The assessments it contains are an expression of the independent and collegial deliberation of the committee. The data within it are the certified accurate data extracted from the application forms submitted by the supervising bodies on behalf of the unit.

This version of the report is public under Article R. 114-23 of the Research Code. Sections of the report considered confidential, and responses to points of attention from supervisors are not included in it.

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UNIT CHARACTERISATION

- Name: Centre international de recherche en infectiologie
- Acronym: CIRI
- Label and number: CNRS UMR 5308, Inserm U1111
- Number of teams: 27
- Composition of the executive team: Mr Thierry Walzer (interim director)

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement
SVE4 Immunité, infection et immunothérapie

THEMES OF THE UNIT

The Centre International de Recherche en Infectiologie (CIRI) is a joint research unit primarily based in Lyon Gerland, France, dedicated to understanding infectious diseases and immune defenses. Its overarching mission is to play a major role in academic research and to be a centre widely open to therapeutic innovation in medical prevention and treatment of infectious and immunological diseases. CIRI achieves this through an integrated approach combining fundamental research, clinical research, and epidemiology, while maintaining a strong socio-economic interface. It brings together human and financial resources from primary managing bodies (Université Lyon 1, ENS de Lyon, Inserm, CNRS) and secondary ones (Hospices Civils de Lyon and Université Jean Monnet de St Etienne), along with partners like Institut Pasteur, Etablissement Français du Sang (EFS), and VetagroSup. CIRI relies on 517 people with 150 permanent researchers working in twenty-one teams, three CIRI groups and one emerging theme.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The CIRI was created in 2013 by federating local academic and clinical research strengths in infectiology and immunology in Lyon. From this new structure, CIRI has grown from seventeen teams to twenty-seven after recruiting teams from Lyon Sud and Saint-Etienne and offering the opportunity and resources to particularly bright young researchers from within or outside the Center to set up their own teams or CIRI-groups. The CIRI occupies 8,600 m², mainly in the Lyon-Gerland Biodistrict. The recent expansion of the CIRI was achieved through a series of real estate developments, including the inauguration of the new Rosalind Franklin Building. This new facility consolidates all administration and management services, houses eight research teams and one CIRI group, and includes state-of-the-art BSL-2 and BSL-3 laboratories. In addition to this site, CIRI is located in the Inserm Cervi Tower, the ENS Monod site, the Lyon Sud Hospital, and the Université Jean Monnet and CHU of St Etienne. Additionally, the BSL4 Jean Mérieux Laboratory is an independent but closely collaborating partner with CIRI, supporting advanced research in vaccines and antiviral. CIRI shares cutting-edge equipment with SFR Biosciences, particularly in cytometry, imaging, vectorology and protein sciences. There is therefore an obvious opportunity for exchanges between research teams, hospital services and private life science companies in the Lyon-Gerland Biodistrict. A new CIRI/CHU Saint-Étienne building is under construction for Controlled Human Infection Model studies.

UNIT RESEARCH ENVIRONMENT

The CIRI is part of a rich basic research, medical, and biomedical environment within the Lyon-Gerland Biodistrict. CIRI maintains close links with clinical practice, as illustrated by the management of several National Reference Centers (e.g. Staphylococcus, Legionella, Hemorrhagic Fevers, Respiratory Viruses) by its researchers, offering privileged access to patient cohorts and biobanks. The centre is also involved in the Programme d'Investissements d'Avenir (PIA), participating in RHU projects (ID-Bioriv), Biocluster BCF21, SHAPE-Med@Lyon, EquipEx+ InfectioTron, IHU Everest, EID@Lyon, PEPR MIE. CIRI collaborates with the technology transfer offices of its supervisory bodies and SATT Pulsalys for technology transfer.
The SFR Biosciences is a research support unit that operates state-of-the-art technological core facilities for the biological sciences on the Lyon Gerland campus and at the Lyon Sud University Hospital. SFR Biosciences is financed and managed by Inserm (US8), CNRS (UAR3444), ENS de Lyon and University Claude Bernard Lyon 1.
CIRI is affiliated with four doctoral schools, and is involved in teaching programs. Many CIRI members direct or co-direct major teaching programs, such as the Erasmus Mundus LIVE (Leading International Vaccinology Education) Master's program.
Members of CIRI teams are active in creating and supporting start-ups (6 during the past mandate), underlining their commitment to translating scientific discoveries into practical applications and technological innovations.

UNIT WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	47
Maitres de conférences et assimilés	48
Directeurs de recherche et assimilés	18
Chargés de recherche et assimilés	35
Personnels d'appui à la recherche	101
Praticien hospitalier	23
Sous-total personnels permanents en activité	**272**
Enseignants-chercheurs et chercheurs non permanents et assimilés	36
Personnels non permanents d'appui à la recherche	51
Post-doctorants	25
Doctorants	133
Sous-total personnels non permanents en activité	**345**
Total personnels	**517**

BREAKDOWN OF THE UNIT'S PERMANENT STAFF BY EMPLOYER: IN PHYSICAL PEOPLE AS OF 31/12/2024. NON-SUPERVISING EMPLOYERS ARE GROUPED ON THE HEADING "OTHERS".

Nom de l'employeur	EC	C	PAR
CHU LYON HCL	53	1	37
CNRS	0	22	7
ENS LYON	6	0	5
INSERM	0	26	30
UCBL	19	0	21
UJM	18	0	3
Autres	17	4	21
Total personnels	95	53	124

GLOBAL ASSESSMENT

The Centre international de recherche en infectiologie (CIRI) has received an excellent overall assessment across key evaluation areas, positioning it as a leading centre dedicated to understanding infectious diseases and immune defenses.
The CIRI's scientific objectives, organization, and resources were deemed excellent. Its primary mission is to play a major role in academic research and serve as a centre for therapeutic innovation in infectious and immunological diseases. This is achieved through an integrated approach combining expertise in microbiology, immunology, cell biology, clinical research, and epidemiology. Strategically located in the Lyon-Gerland Biodistrict, CIRI leverages new facilities, including the Rosalind Franklin Building, which houses state-of-the-art BSL-2 and BSL-3 laboratories. Between 2019 and 2024, CIRI secured over €50 million in funding and is strategically structured into three speciality poles: immunology, bacteriology, and virology, to encourage collaboration.

The unit's scientific output, impact, and attractiveness are excellent. During the evaluation period, CIRI researchers published 2,360 articles, with 400 appearing in high-profile journals. The unit demonstrated high visibility during the COVID-19 pandemic, and its translational research has directly influenced clinical practice and policy, such as the study on heterologous vaccination which impacted national policy.
CIRI's inclusion of research activities in society is outstanding. Researchers hold prominent national and international positions, managing National Reference Centers and advising major bodies like the French COVID-19 Scientific Council. The unit excels in innovation and technology transfer, having filed 124 patents, granted seven licenses, and created 6 start-ups based on its findings. Furthermore, CIRI is strongly involved in training, having trained over 600 students across all levels.
Despite its high performance, the CIRI faces a few challenges. It must increase applications for international grants and improve gender balance, particularly in senior and leadership positions. There is also a recognized difficulty in consistently recruiting international doctoral and post-doctoral students. The CIRI needs to restore and enhance the unit's public image through the transformation of governance and mentality within the institute. The overall trajectory of CIRI, however, is one of expansion, aiming to consolidate its position as a world leader in infection and immunity research through a focus on scientific excellence, translational research, and strengthened governance.

DETAILS OF THE EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

CIRI integrates the recommendations of previous evaluation reports into its overall strategy, demonstrating an ongoing commitment to improving its scientific performance, organization and societal impact.
1. Recommendations on scientific production and activities:
- Compliance with publication signature rules (authors): CIRI has drawn up internal regulations and circulated them to teams to ensure compliance with these rules.
- Supporting young researchers for international training courses and conferences: Efforts are being made at team and doctoral school level to encourage and support the participation of young doctoral students in at least one international event during their thesis.
- Increasing European funding: CIRI strongly encourages its researchers to apply for competitive programs such as ERC grants and other European programs, in line with the policies of its supervisory bodies. This contributes to the broader objective of increasing European subsidies and raising CIRI's international profile.
- Increase the unit's visibility by inviting a wide range of international scientists: CIRI has recruited a new director, Dimitri Lavillette, who is committed to strengthening international collaborations, particularly with developing countries.
2. Recommendations on the organization and life of the unit:
- Improved well-being, transparency and inclusiveness: CIRI has recently put in place measures such as alert and assistance channels, training of resource persons, anonymous annual staff well-being surveys, and a QVT (Quality of Life at Work) committee. Independent administrative investigations have been carried out.
- Revision of technical staff resource allocation, mobility, professional training and internal communication: A mobility campaign is planned, and internal communication has been strengthened with meeting minutes available on the intranet, CoDir agendas and a newsletter.
- Recruitment of foreign students and post-docs: Although limited by administrative constraints, CIRI aims to develop its own international networks to facilitate such recruitment.
3. Recommendations on scientific strategy and projects:
- International calls for applications to recruit top-level researchers: The selection process for the new director was transparent, and welcome packages were offered to new team leaders, reinforcing CIRI's international profile.
- Market research to identify industrial partners and support researchers' engagement with industry: CIRI is well identified by networks such as Lyon Biopôle and has numerous industrial collaborations. It pursues a proactive technology transfer policy with organizations such as SATT Pulsalys, Inserm-Transfert and CNRS Innovation.
- Increased internal funding to strengthen collaboration between teams: CIRI offers welcome packages to new team leaders and an intra-CIRI projects program that has invested €408,100 and funded 15 projects, some of which have motivated the creation of new scientific teams.
- Strengthening clinical links: CIRI's university hospital staff are very active, notably via the ARTEMIS biomanufacturing platform for innovative therapies and the coordination of hospital research themes. Clinicians have joined teams previously made up solely of basic researchers.
- Implementation of a peer review process for grant proposals: Informal support is already in place, supplemented by training and assistance with the submission of applications offered by sponsoring institutions, with CIRI working to improve communication of these opportunities.

B - EVALUATION AREAS

EVALUATION AREA 1: THE UNIT'S SCIENTIFIC OBJECTIVES, ORGANIZATION AND RESOURCES

Assessment of the unit's scientific objectives, organization and resources

Overall, the CIRI's scientific objectives, organization and resources are excellent. CIRI shows a clear and effective scientific strategy, bringing together expertise in microbiology, immunology, and virology to improve understanding and treatment of infectious and inflammatory diseases. Its multidisciplinary structure encourages collaboration and supports translational research on major public health issues, with teams actively developing innovative projects and building strong partnerships. Recent improvements in buildings and technological facilities have strengthened research capacity and working conditions. To further enhance its impact, the CIRI should continue its effort to ensure optimal interaction among the three departments, increase efforts for European funding and improve gender balance in leadership.

Context-related strengths and opportunities

The primary mission of the CIRI is to gain deeper insights into infectious diseases by investigating host-pathogen (virus and bacteria) interactions, while also addressing inflammatory pathologies to better understand the mechanisms that trigger and regulate inflammation. These complementary approaches aim to drive therapeutic innovation and contribute significantly to the prevention and treatment of both infectious and inflammatory diseases. To this end, the centre adopts an integrative approach, combining expertise in microbiology, immunology, cell biology, clinical research, and epidemiology to advance both basic and applied research.

The CIRI's organization into three poles (immunology, bacteriology, and virology) is well suited for advancing research. It brings together strong expertise across disciplines, with a structure designed to encourage collaboration in addressing key challenges in infectious and inflammatory disease research, through ambitious and highly relevant projects tackling today's major public health issues. This multidisciplinary approach is also made possible by the composition of the centre, which includes not only academic researchers (53 CR/DR and 28 EC) but also HU members (89), fostering strong translational research.

Between 2019 and 2024, the CIRI research teams led or contributed to over 350 large-scale projects at the international, European, and national levels, securing more than €50 million in funding. In this context, the teams were highly active in applying for PIA calls and obtaining support from socio-economic partners and charitable foundations.
Recurrent funding is partly allocated to shared resources, emerging teams, and internal calls for proposals. The remainder is distributed to teams based on their size. This is in line with the policy of a major research centre.

Strategically located in the Lyon-Gerland biodistrict, the CIRI is well placed to foster communication and build collaborations with a wide range of scientific, academic, and industrial partners. Several researchers head national reference centers, while clinicians and immunologists are actively involved in clinical research. The CIRI also have at their disposition patients' cohorts (coordinated by the clinicians). These developments have reinforced translational and clinical research. Their strategic localization also helps the CIRI stay proactive in innovation and technology transfer.

During the period, the CIRI benefited from the completion of the construction of the R. Franklin building that now hosts eight teams, administrative staff and the SFR Biosciences Support Unit, which provides cutting-edge technological platforms (flow cytometry, animal facilities, imaging...) and fosters collaboration and research valorization. The acquisition of BSL-3 and A3 containment areas equipped with cutting-edge technologies has been a major asset for the centre. Renovations to existing buildings have also improved members' quality of life and working conditions.
The CIRI hosts several internal platforms, including a histology platform and the Bioinformatic and BioStat (BIBS) core facility. In addition, the acquisition of a cryo-EM platform within a BSL-2 environment represents a significant advancement, enhancing research capabilities in both cell biology and structural biology.

It is also important to highlight that a new building is currently under construction to support the development of Controlled Human Infection Model studies, and will include 20 beds dedicated to human infection research.

The CIRI has implemented a governance model that aligns well with its overall structure. This approach ensures cohesion across teams while preserving a unified decision-making process. The governance includes a Directory Board, a Team leaders Board, a Laboratory Board and a General Assembly. The CIRI also possess a Scientific Advisory Board (SAB), its role being crucial in the creation of CIRI's groups. There are also various supporting services including the Finances and Administration team, the BIBS, Health and Safety team.

Human resources policy of the CIRI is also aligned with that of the supervisory bodies. A transparent system was introduced for allocating bonuses and promotions, with criteria shared with ITA through their representatives.

Ensuring staff quality of life and preventing psychosocial risks were a CIRI priority during the last years. A Quality of work life (QWL) committee was created and equality/egality referents were nominated. A system was put in place to help staff, report problems, and monitor well-being through regular surveys (e.g. QWL barometer sent twice a year). This proved effective during the previous term. There is also online training courses set up (psychological risks, harassment prevention….), in addition to the training offered by the supervising bodies. Regarding health and safety, a prevention officer was recruited to implement with its team (BSL2/3, assistant, radioprotection referents...) actions and training in collaboration with supervisory bodies. Ongoing support to research teams on safety-related matters is also provided.

Context-related weaknesses and risks for the four references above

Given the CIRI's complex structure with diverse specialities and cross-disciplinary axes, continuing to encourage teams to actively collaborate and apply jointly for national, and possibly European, grants, in addition to internal grants, will be crucial to avoid siloing and foster stronger integration. Maintaining open communication and flexibility will support these collaborative efforts and the development of new research topics.
At the CIRI level, there is potential to increase applications for European grants.

Gender balance remains a significant challenge, particularly in senior and leadership positions, including the CoDir, with positive initiatives such as the promotion of gender-balanced co-leadership, set to be effective during the next period.

A point of concern is the access to and costs associated with using the BSL-4 facility, which could affect certain research activities.

EVALUATION AREA 2: THE UNIT'S SCIENTIFIC RESULTS, IMPACT AND ATTRACTIVENESS

Assessment of the unit's scientific results, impact and attractiveness

The CIRI's scientific output is excellent with 400 peer-reviewed articles published in high-profile journals, contributing to its excellent international visibility in the fields of Immunology, Virology, and Bacteriology. CIRI's impact was especially visible during the COVID-19 pandemic. CIRI is attractive, demonstrating strength in recruiting top talent, securing competitive funding, developing innovative infrastructure, fostering strong industrial connections, and maintaining a robust training environment. In order to increase the international attractiveness of the institute, the CIRI's reputation should be improved.

Context-related strengths and opportunities

CIRI researchers are recognized for their expertise by holding prominent positions in national and international scientific steering and evaluation bodies: member of French COVID-19 Scientific Council (2020–2022) and Co-Chair of COVARS (Committee for the Monitoring and Anticipation of Health Risks), leaders of National Reference Centers (e.g. Staphylococci, Legionella, Hemorrhagic Fevers, and Respiratory Viruses), experts for major national and international funding agencies, including ERC, Wellcome Trust, ANR, ANRS, and the Swiss National Science Foundation.

CIRI researchers published 2,360 articles during the evaluation period. Notably, 400 publications appeared in journals recognized as belonging to very high-profile journals, demonstrating that the unit prioritizes quality alongside productivity. The unit's output includes publications in leading international journals demonstrating CIRI's excellence in fundamental and applied research such as The New England Journal of Medicine, The Lancet, Nature Medicine, Journal of Experimental Medicine, Nature Microbiology, Nature Communications, PNAS among others. Research has led to key discoveries across specialities, such as defining the mechanisms of natural transformation in Acinetobacter baumannii and Legionella species and advancing the understanding

of host immune responses to intracellular S. aureus. In virology, achievements include defining the role of ISG20 and TRIM69 in antiviral defense and identifying the low-density lipoprotein receptor and apoE as mediators of Crimean-Congo hemorrhagic fever virus (CCHFV) entry. In immunology, functional analysis of NLRP3 mutations in CAPS (Cryopyrin-Associated Periodic Syndromes) variants paved the way for functional characterization and suggests a novel approach to diagnosing and treating Familial Mediterranean Fever (FMF).

The quality of CIRI's science is attested by the numerous awards and honours received by its members: Inserm Grand Prize, CNRS Medals and Awards, International Society for Antiviral Research (ISAR) Award, FEBS Excellence Award, Distinguished Honours (Chevalier of the Légion d'Honneur, Officer of the Légion d'Honneur).

The CIRI participates extensively in the coordination and management of its community through a comprehensive governance structure, multiple institutional and specialized committees, dedicated support services, strategic communication initiatives, and active promotion of collective scientific endeavours.
CIRI's coordination rests upon formal structures that ensure representation and collective decision-making involving all levels of personnel: Board of Team Leaders, Board of Directors, Laboratory Council.
The unit is organized into three specialities—Bacteriology, Immunology, and Virology—which aim to enhance scientific and logistical synergies, foster exchanges among principal investigators, and bolster internal and external visibility. Each speciality elects a representative who is a member of the CoDir. CIRI plans to evolve these specialities into formal Departments in the next evaluation period to further structure the centre, provide career development, and anticipate future needs.
The management relies on a dedicated executive team and various understaffed but critical support services that handle the operational aspects of the unit: Executive Team, Financial and Administrative Service, Health and Safety, BioInformatics and Biostatistics Service.
CIRI fosters cohesion and intellectual exchange through mandatory programs and specific committees. Intramural Projects Program launched in 2015, allocates seed grants to encourage collaborative initiatives among at least two CIRI teams. This drives new research dynamics and generates preliminary data for external grants.
CIRI actively organizes external seminars (averaging around twenty per year) and encourages internal weekly seminars, primarily presented by PhD students and post-docs, to facilitate feedback and advice for young researchers. Lunch sessions between invited speakers and students are regularly organized.
Specialities organize dedicated annual scientific days to promote collaboration and exchange. CIRI members are also highly active in initiating and co-organizing numerous major national and international conferences, such as Innasco and IRCI.
CIRI plans to introduce new structures, including a Strategic and Innovation Team to support funding diversification, competitive grant applications (ERC, Gates) and innovation promotion. An AI Think Tank is also planned to explore the use of AI in scientific and administrative tasks.
An Equipment Commission oversees equipment requests, maintenance contracts, and proposals for new acquisitions, collaborating with the team leaders' council and management.

Context-related weaknesses and risks for the four references above

There are acknowledged challenges that could threaten long-term attractiveness, including the difficulty in consistently securing international grants, the limited recruitment of international doctoral and post-doctoral students, and the need to restore and enhance the unit's public image following a recent investigation. Closing the specific BLS4 facility for a year may hinder the research projects of several CIRI teams.

EVALUATION AREA 3: INCLUSION OF RESEARCH ACTIVITIES IN SOCIETY

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

The quality of the CIRI's interactions with society in a national or international context is outstanding. Contact with industrial partnership are strong and materialized by financial contracts, patents, licenses, start-up creation. Members of the unit are engaged in continuing education, in clinical research networks and societies. High expertise of some researchers is recognized as participating in national or international councils. Members of the unit share knowledge with patients' associations, in public exhibitions and participate to scientific mediation through numerous media.

Context-related strengths and opportunities

Most of the CIRI's teams initiate and are involved in partnerships with non-academic world. The valorization of fundamental and translational results is highlighted by 124 patents, seven licenses granted and the creation of

six startups. A notable example is the Nanoscribes VLP-based delivery system for Prime editing (Halegua et al. 2024 Nature Communications), which secured an exclusive license with SANA Biotechnology. Links with companies are concretized by 130 contracts established with 75 companies, regional bodies. Among these industrial partners Pfizer, Novartis, Sanofi, Janssen, Pierre Fabre can be mentioned. These fruitful collaborations allow researchers of the unit to develop vaccine candidates, biological tests, diagnosis tools and clinical trials. Numerous CIRI's members participate in scientific councils or advisory committees to share their expertise with the industrial partners. The unit's external funds are 40 % from contracts concluded with industrial partnerships, foundations and charities. Moreover, PhD students are supported by Cifre industrial agreements from Sanofi, Boehringer, Roche, Genentech, LVMH.
Scientific and medical expertise of the unit's members is recognized by the participation of its members in steering bodies, scientific expertise bodies at national, European and international level. Many members emerge in INSERM, CNRS, ANRS, ANR, CNU, HCERES, ENS, ANSES committees, as well as international research consortium, clinical research networks and societies. They were solicited to give advice in parliamentary and senatorial working groups, High Council of public health, Conseil Scientifique COVID-19 for the President de la République Française, committee for the French government, European organization for economic co-operation and development and to the World Health Organization. CIRI translational research, often conducted by its university hospitalists, directly impacts clinical practice and policy. For example, the study on heterologous vaccination (Nature 2021) influenced national vaccination policy.
CIRI's members participate in continuous training at various levels: PhD levels (136 PhD students), Master of research, teaching in medicine (nephrology, hepato-gastroenterology, organ transplantation for example) or in pharmacy (immunology), veterinary school and high school science educators. They are members of the international committee for students as the Master Erasmus Mundus LIVE, create and coordinate training courses (i.e. the Immunology, Vaccinology and Infectious Disease SFRI IVID). During the evaluated period, more than 600 students (all levels combined) were trained.
Most of the CIRI's team interact with patients' associations to share knowledge (i.e. Eczema day, the MICI AURA days …) and practices (i.e. Training for rapid diagnostic tests in associations of migrants and sex workers). They participate in the general public exhibition: Science festival, Declic program, joint activities with the Musée des Confluences, Ciné Club and organize public conferences.
Researchers spread scientific information and knowledge with numerous media: TV (general channels TF1, France2, Arte, BFMTV…), radio (France culture…), press (Le Monde, Le Figaro, Libération, Tribune de Lyon, Le Progrès…).

Context-related weaknesses and risks for the three references above

No weakness identified.

ANALYSIS OF THE UNIT'S TRAJECTORY

The CIRI and its new director has developed an ambitious strategic vision for its 2027-2031 mandate, aimed at consolidating its position as a world leader in infection and immunity research. This future trajectory is based on an integrated approach covering host-pathogen complexity, immunopathology and translational research.

Strategic Vision and Integrated Priorities (2027-2031)

CIRI's strategy for the next five years is built around several interconnected priorities:

1. Promoting Excellence in Research:
   - CIRI will maintain the highest standards in basic research in bacteriology, epidemiology, immunology and virology, through the support of selected teams and the recruitment of new talent.
   - Technology centers and platforms, belonging to the SFR Biosciences (INSERM, CNRS, ENS, UCBL), will be fully integrated into research workflows. Participation in international networks and institutional partnerships will be expanded to ensure access to emerging technologies and global collaboration opportunities.
2. Anticipating Infectious Threats:
   - CIRI will strengthen its role in anticipating infectious threats, focusing on responsiveness and preparedness. This includes respiratory viruses (influenza, SARS-CoV-2, RSV, hMPV) and will extend to vector-borne diseases (Dengue, yellow fever, West Nile, Chikungunya, CCHF) as well as pathogen evolutionary mechanisms (HIVE, CERP teams).
3. Strengthening of Structural Biology:
   - The planned establishment of Cryo-Tomography facilities at BSL2 level at ENS Lyon (around 2026) will place CIRI at the forefront of structural biology in infectiology. The recruitment of a co-PI of the future MIHVA team and a dedicated engineer underlines this commitment.
4. Talent Attraction and Retention:
   - With several principal investigators approaching retirement, CIRI has the opportunity to recruit new talents and diversify research expertise. Welcome packages are being offered to attract new team leaders.
5. Boosting innovation and added value:
   - Innovation will be actively supported, encouraging disruptive and high-risk projects. The translation of research into the societal impact will be pursued through patents, start-ups and clinical innovations, in close collaboration with local industrial and technological partners.
6. Ensuring a Dynamic and Inclusive Scientific Environment:
   - CIRI will continue to cultivate a vibrant internal scientific community, promoting a culture of inclusion, professional equality and scientific integrity.
7. Increased Financial Autonomy:
   - The centre will aim for greater financial autonomy to support its long-term strategic objectives. A new mixed funding system, including a fixed budget and a levy on external contracts, will be introduced to support teams and strategic initiatives.

Major organizational changes:

- New Director was appointed in April 2025. His mandate includes professionalizing the director's role, enhancing translational research, strengthening internal and external communication, structuring international collaborations, supporting career development, promoting scientific integrity, gender balance and reducing the environmental footprint.
- Strategic and Innovation Team: This team will be set up to diversify funding sources and support researchers in competitive programs. Intramural calls for projects will be integrated as a key tool for this team, with targeted calls based on European or global grant information.
- Think Tank on AI: A reflection on the use of artificial intelligence in science and administrative tasks will be explored.
- Organization into Departments: To enhance visibility and offer career development opportunities, CIRI will move from "specialities" to "departments" of Bacteriology, Immunology and Virology. These departments will encourage in-depth discussions on new technologies and research priorities, while identifying new talent.
  - Bacteriology: Will focus on WHO priorities, including Acinetobacter baumannii and Klebsiella pneumoniae, and strengthen tuberculosis research.
  - Immunology: will maintain basic and translational research, focusing on B and T lymphocytes, innate and adaptive immune responses, autoimmune and inflammatory diseases.
  - Virology: will prioritize basic and translational research on critical public health challenges, anticipation of infectious threats, vector-borne diseases and pathogen evolution. It will focus on diagnostics, the development of broad-spectrum antivirals and vaccine research.

In addition, CIRI has identified five cross-disciplinary research areas to promote synergy between disciplines:

- Risk factors for the development of serious infections.
- Innovative vaccines, immunotherapies and antimicrobials.
- Emergence of zoonotic diseases and mechanisms of high pathogenicity.
- Evolution of pathogens and immune escape or antimicrobial resistance.
- Intrinsic cellular immunity to infection and metabolic stress.

Partnership strategy and evolution of the scientific perimeter:
CIRI will be aligned with the national research strategy and will rely on a number of partners and networks:
- The BSL4 Jean Mérieux Laboratory will support advanced research on vaccines and antivirals, as long as this unique resource remains accessible to all the teams of the institute.
- Programs such as Ecofect LabEx (completed) and InfectioTron EquipEx+ (underway) promote an eco-evolutionary view of infections and establish new platforms, such as a BSL2/3 facility and Cryo-EM infrastructure.
- The Everest IHU (in collaboration with the HepVir, VIRIMI and Imagination teams) will focus on precision medicine for chronic liver diseases.
- CIRI plays a key role in the SHAPE-Med@Lyon initiative and leads the BCF2I Biocluster (2025).
- CIRI will continue to be an active member of the LyonBiopole cluster.

CIRI's scientific perimeter for 2027-2031 will comprise 21 teams and three groups, as well as an emerging theme, with a balanced distribution between departments.
In summary, CIRI's future trajectory is that of a research unit in full expansion and structuring, with a focus on scientific excellence, translational research, innovation, international openness and strengthened governance to meet the complex challenges of infectious diseases and immunity on a global scale. However, this ambitious objective will be achieved through the transformation of governance and mentality within the institute, which is being initiated by the new director.

RECOMMENDATIONS TO THE UNIT

RECOMMENDATIONS REGARDING THE EVALUATION AREA 1: SCIENTIFIC OBJECTIVES, ORGANIZATION AND RESOURCES OF THE UNIT

To further enhance its impact, the CIRI should continue fostering joint grant applications among teams. A significant recommendation is to increase applications for European grants at the CIRI level.
Improving human resource management and institutional culture is also a priority:
• The CIRI needs to improve gender balance in leadership positions.
• Particular attention should be paid to improve communication, especially by making newcomers feel welcome.
• The centre should increase awareness and provide targeted training for team managers to support the career development of postdocs, PhD students, and technical and administrative staff.
Team leaders, associated with the direction of the CIRI, are encouraged to establish a job description for each permanent technical and administrative staff.

RECOMMENDATIONS REGARDING THE EVALUATION AREA 2: THE UNIT'S SCIENTIFIC RESULTS, IMPACT AND ATTRACTIVENESS

To maintain and strengthen its attractiveness and competitiveness:
• The centre should improve the CIRI's reputation to increase the international attractiveness of the institute.
• In the context of highly competitive international grants, collaboration between the new grant office, the direction, senior PIs, and young applicants could be a key to success.
• Regarding core facilities, increasing the number of technicians and engineers could improve innovation, offer better service for CIRI's teams, and facilitate service provision for external companies.

RECOMMENDATIONS REGARDING THE EVALUATION AREA 3: INCLUSION OF RESEARCH ACTIVITIES IN SOCIETY

To maximize the societal inclusion of its research:
• To share scientific knowledge with the general public, PhD students, post-docs, and technical staff (ITAs) could be more implicated.
• Promotion of media training and more delegation of representation could help young Principal Investigators (PIs) to increase their visibility and develop links and benefits with the cultural, economic, and social worlds.

TEAM-BY-TEAM OR THEME ANALYSIS

Team 1: Autophagy infection immunity (APY)

Name of the supervisor: Mr Mathias Faure

THEMES OF THE TEAM

The central theme of the "Autophagy, Infection, Immunity" team is the implication of autophagy in infection and inflammatory bowel disease. It studies the influence of viral infection on autophagy of the host cell, and vice versa, and its consequences for secondary bacterial infection. In inflammatory bowel disease, the team studies the consequences for autophagy of polymorphisms associated with disease.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team was recommended to develop stronger interactions with the international scientific community. The team successfully collaborated with teams in five countries and was involved in four international networks.
The previous evaluation committee recommended reinforcing collaboration with the private sector. The team has signed contracts with the private sector and thus obtained substantial funding.
The team was commended to recruit more PhD students and postdocs. During the last mandate, it hosted six PhD students (for four HDR) and two postdocs.
It was recommended that team members ensure less teaching. This is unfortunately very difficult to achieve in French Universities.
It was recommended that the team increases in size to sustain the ambitious research-plan. It has recruited one part-time researcher clinician and ensured funding allowing the recruitment of PhD students, postdocs, and technicians.
The team was invited to prioritise certain projects the team has published important papers on the two retained projects and obtained substantial funding.
The committee recommended integrating the projects on measles infection and Crohn's disease, reported to be linked. The team convincingly answered that this link was invalidated in the past.
A last recommendation concerned using more physiologically relevant cell types in the study of xenophagy. The team used primary human hepatocytes and dendritic cells and extended its use of reporter cell-lines and bacterial strains.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	5
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	0
Praticien hospitalier	0
Sous-total personnels permanents en activité	**7**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels non permanents d'appui à la recherche	2
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**8**
Total général	**15**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent. This team has been very successful in dissecting mechanisms involved in autophagy and the involvement of this process in viral infections, bacterial secondary infections, and inflammatory bowel disease. It also excels in teaching at the Lyon University. The team steadily grew in size and scientific ambition and successfully developed links with the clinic and with industry.

Context-related strengths and opportunities

The team demonstrated that infection by viruses can subvert autophagy to the latter's advantage and that this can favour or reduce bacterial replication upon secondary infection. It also showed that polymorphisms associated with Crohn's disease can alter autophagy-flux in dendritic cells.
The important findings of the team were published in outstanding journals in the field and beyond (e.g. Autophagy, J Clin Invest). It thus published 11 research articles, 11 clinical papers, 14 reviews/editorials, and five book-chapters on which team members appeared as first, last, and/or corresponding authors. It also published in collaboration 24 more research-papers, 90 clinical papers, and nine reviews/editorials.
The activity of the team has allowed it to obtain a solid (inter-)national reputation illustrated by regular oral presentations at national and, less frequently, at international meetings, including PhD students. Its members are very active in scientific societies, organize (inter-)national meetings, and review manuscripts for prestigious journals (e.g. Science, Nature Cell Biology, Autophagy). Team members are very active in scientific evaluation at the national level, seating on national committees at research institutes (Inserm) and on higher education, and in reviewing grant-applications for several public agencies and associations.
The research of the team was made possible by very successful acquisition of funds. It obtained 13 grants coordinated by team members and four grants as partners for a total of M€2.7. These funds were obtained from public grant agencies (e.g. ANR), associations (e.g. AFA) and the private sector (e.g. Jansen, Sandoz…).
A major mission of most members of the team is teaching. Thus, six PhD students were trained in the lab of which four are ongoing. Two of the team members teach over 260h/yr at the University, three of them 80h/yr, and most PhD students are also solidly involved in teaching. Moreover, the team leader directs the doctoral school. Team members are also active in communication towards the general public, e.g. patient associations. It is remarkable that despite the very heavy teaching load at the University, the team has a very solid, original, and productive scientific activity.

Context-related weaknesses and risks

The historic scientific theme of the team was "autophagy". Given that polymorphisms in genes involved in this process are associated with inflammatory bowel disease, the recruitment of clinicians working in this field was a logical and coherent choice. However, extending the scientific activity beyond the field of autophagy, as for example by searching for biomarkers in the field of gastro-enterology but unrelated to autophagy, comes with the risk of uncontrolled dispersion of the scientific focus.
The IBD-theme also appears quite descriptive and causative links between altered autophagy and pathology remain little studied. Studying organoids, as proposed, may help elucidate causality, but this experimental system has its inherent shortcomings.

ANALYSIS OF THE TEAM'S TRAJECTORY

The project of the team proposes is a coherent follow-up of its current activity. It will further decipher the contribution of autophagy to infection by measles virus (MeV) and its virulence, assess the physiological role of two identified autophagy receptors targeted by MeV and the perturbation of autophagy caused by MeV, and study the potential selective pressure on MeV imposed by autophagy. This part of the project will provide valuable knowledge on the involvement and the subversion of the autophagy machinery in viral infection. The strong expertise of the team and the tools of which it disposes should allow the successful implementation of the project.

The team will also continue its intriguing work on the involvement of autophagy in inflammatory bowel disease. It will analyse the autophagosome-cargoes of dendritic cells from patients with altered autophagy-flux, at steady-state and upon infection. A promising novel scientific goal is the study of broader implications of autophagy dysfunction in intestinal immune responses, using organoids and dendritic cells from patients. In this part of the project, the team will need to carefully consider how it will assess the causative link between

autophagy-dysfunction and chronic inflammation in the gut. The team proposes to study potential defects in autophagy-flux in a cohort of genotyped patients. It will need to develop a strategy to make the to-be-obtained descriptive results contribute to the understanding of how such defects participate to IBD.

In conclusion, the intriguing scientific project proposed by the team is based on solid expertise in the field of autophagy and infection. The part of the project on autophagy in IBD, which has developed more recently, will require careful consideration of how causative links will be established.

RECOMMENDATIONS TO THE TEAM

The team is encouraged to continue their excellent work. For the studies on autophagy and co-infection, the team should focus on clinically relevant combinations and avoid thematic dispersion. The team should also develop strategies to establish causative links between altered autophagy and inflammation in IBD.

Team 2: Influenza viruses, from emergence to control (VirPath)

Name of the supervisor: Mr Bruno Lina / Mr Manuel Rosa-Calatrava

THEMES OF THE TEAM

The VirPath team focuses on emerging and re-emerging respiratory viruses that represent major threats to global public health. The team is structured into two complementary groups that explore different aspects of respiratory virus biology, ranging from the mechanisms driving viral emergence and pathogenesis to the functional interactions between viruses and host cells, and key host factors. VirPath also investigates antiviral resistance mechanisms and develops innovative antiviral approaches and vaccine platforms.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The recommendations of the last evaluation highlighted

- the need for the team to publish its results in high-impact multidisciplinary journals

  Over the period 2020-2024, the team has published its results in several generalist journals (ex: Nature, J Exp Med, Lancet infect dis, Cell Rep Med)

- to focus strategically on key areas to avoid dilution and ensure successful results

  The team has focused on its areas of expertise: clinical studies, respiratory virus/host interactions, antiviral drugs and vaccines

- to strengthen its bioinformatics capabilities.

  The team has significantly strengthened its bioinformatics analysis capabilities, both in the clinical field (genEPII genomics platform) and in the fundamental/applied field (Nexomis platform).

- to extend its involvement in international teaching and training in medical virology

  Over the last period, 19 PhD students and a large number (not indicated) of master students were trained. The Team is involved in teaching activities (900-1000 hours/year) and four MCU-PH or MCF are responsible for teaching programs in fundamental or clinical virology at the Université Claude Bernard Lyon 1 and training activities for healthcare professionals (Hospices Civils de Lyon).

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	4
Maitres de conférences et assimilés	7
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	10
Praticien hospitalier	2
Sous-total personnels permanents en activité	**27**
Enseignants-chercheurs et chercheurs non permanents et assimilés	4
Personnels non permanents d'appui à la recherche	6
Post-doctorants	2
Doctorants	13
Sous-total personnels non permanents en activité	**25**
Total général	**52**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent to outstanding. The team has an outstanding publication record with 207 original articles and 27 reviews. It has also filled 17 patents and created four start-ups. The team has supervised 19 doctoral theses and is highly involved in teaching activities. The reputation as a leading group in the field of respiratory virus infections is internationally recognized and the team has been involved in numerous evaluations in national or international committees. The team has secured more than 9M€ euros through 33 grants, including 19 as coordinator.

Context-related strengths and opportunities

The team is strongly involved in numerous collaborations at the local and national levels. The team has responded swiftly to the COVID-19 crisis. In early 2020, the team isolated, sequenced, and characterized the first French clinical strains of SARS-CoV-2, establishing viral quantification protocols and human airway epithelial infection models. This rapid response led to extensive collaborations and to an excellent publication record: 50 research articles (29 as first, last, corresponding, FLC) and 157 clinical articles (53 in FLC) including over 90 SARS-CoV-2-related publications in major generalist journals (Nature, Nature Comm, Science Transl. Medicine, The Lancet, The Lancet Public Health, The Lancet infectious diseases, Scientific reports…). The team contributed to describing the first European COVID-19 cases, developed and evaluated diagnostic assays, and studied several patient cohorts. It also participated in monitoring the molecular and antigenic evolution of SARS-CoV-2 and evaluated therapeutic antibodies and antiviral candidates within major clinical trials (Discovery trial). The team investigated cellular pathways involved in respiratory virus infections using physiologically relevant models. This expertise enabled important contributions to understand SARS-CoV-2-induced ultrastructural changes and infections in organotypic and specific preclinical models, in which it helped to demonstrate the lack of efficacy of hydroxychloroquine. The team played a key role in defining the importance of type I interferon defects and anti-IFN autoantibodies in severe COVID-19, and extended this work to severe influenza pneumonia. Beyond COVID-19, the team studied influenza and RSV circulation, including pandemic-related shifts in RSV seasonality and the impact of Nirsevimab. These activities were supported by major European projects and 33 grants (19 as coordinator) for a total amount of 9 M€ (ANR, RHU, PEPR, ERC). The team developed innovative models to study viral-bacterial and viral-fungal co-infections, elucidating mechanisms that worsen respiratory diseases.
It also explored viral–viral co-infections and metabolic impacts, contributing to several national and international projects. The team assessed hundreds of antiviral candidates and identified diltiazem as an anti-flu agent which led to the development of phase II clinical trial (FluNext). It contributed to the development and clinical transfer of the BIMERVAX vaccine and advanced a live attenuated bivalent hMPV/RSV vaccine. This work in the field of antivirals, vaccines or diagnostics led to the filling of 17 patents (at least 2 licensed) and to the creation of four start-ups. The team outreach activity was particularly high during the COVID-19 pandemic, with several members appearing in the media for the public as well as for specialist audiences. In addition, the team is regularly involved in scientific outreach activities and in initiatives to promote scientific careers to young people.

Context-related weaknesses and risks

One weakness of the team is the limited recruitment of postdoctoral researchers and foreign students. Also, while the team successfully secured more than 9 M€ in numerous national grants, it may lack international funding.

ANALYSIS OF THE TEAM'S TRAJECTORY

For the upcoming period, the previous VirPath team will be restructured. Manuel Rosa-Calatrava and his group will join the team GIMAP while two other members will head a new team (CARVI) which will be an evolution of the historic team. The CARVI team will develop an integrative strategy to study conventional and (re)emerging respiratory viruses such as influenza, RSV, and SARS-CoV-2. Its goal is to improve understanding of viral mechanisms in order to design innovative diagnostic and therapeutic approaches. This comprehensive program combines clinical, fundamental, and translational research, with a specific focus on virus–host interactions and co-infection dynamics. The team is organized through three main axes:
Axis 1: Viral determinants. This research focus on the identification of molecular traits linked to pathogenicity and monitoring of viral evolution through surveillance conducted at the National Reference Centre and the genEPII platform. The team will continue research focusing on viral envelope glycoproteins, functional balance

between Hemagglutinin and Neuraminidase in influenza viruses, and the impact of genome mutations on fitness and antiviral susceptibility.
Axis 2: Virus–host and inter-pathogen interactions. This research axis investigates interactions between respiratory viruses, other pathogens, and the host. Using metagenomics, experimental co-infection models, and patient cohorts, the team studies the virome, virus–bacteria and virus–virus dynamics, and host responses such as IFN signalling. It also analyses spatial and seasonal factors influencing transmission, with a focus on RSV.
Axis 3: Translational research. This axis uses insights from viral and host–pathogen studies of the two other axes to develop tools that improve diagnosis and identify patients at risk of severe respiratory infections. Projects include the VORTEX project (PEPR-MEI), to detect infections via exhaled volatile organic compounds; the REVIDA industrial chair (ANR and INSERM) to create host-based diagnostic and prognostic tools; and the BARISTA project (ERC) to design antiviral strategies targeting viral genomes with small interfering RNAs.
All of these projects benefit from funding from national agencies: RHU COVIFERON, PEPR-MIE (3D-Lungo, ZOOFLU), ANR (NARECO) and through the REVIDA industrial chair (ANR) and also from the ERC (BARISTA) for a total amount of more than 2.9 M€.

RECOMMENDATIONS TO THE TEAM

The team will be restructured for the next period, with a new direction which could constitute a threat, but the new PIs in charge have already secured funds for the upcoming projects, and have already demonstrated their leadership in the field of respiratory viruses. In addition, the team is relocated in the new CIRI building, which will further improve its interaction with the other teams of the unit.
Recommendations are to hire more post-doctoral researchers and to maintain the high-level of publication and fund-raising capacity in order to conduct the ambitious projects combining clinical, fundamental, and translational research.

Team 3: Epidermal Immunity & Allergy (EIA)

Name of the supervisor: Mr Marc Vocanson

THEMES OF THE TEAM

This team focuses on the pathophysiology of chronic inflammatory and allergic skin diseases (CIADs), such as atopic dermatitis, allergic contact dermatitis, drug allergies, and hidradenitis suppurativa. It aims to understand how environmental antigens (chemicals, drugs, and skin microbiota) interact with the immune system to disrupt tolerance and trigger allergy/inflammation. They investigate the formation, phenotypes, persistence, and functions of tissue-infiltrating and tissue-resident memory T cells (TILs and TRMs) in the initiation, maintenance, and regulation of these skin disorders. The team combines fundamental, translational, and clinical approaches with the aim of developing diagnostic and therapeutic approaches to prevent or treat CIADs, restore skin immune homeostasis, and improve patient care.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Recommendations to the team in the previous evaluation campaign included increasing the level of publication, securing more academic funding, recruiting full-time researchers, PhDs and post-docs, strengthening academic interactions, and focusing on high-impact questions.

The team has increased the level of publications by publishing in leading international journals, including Science Advances and Journal of Allergy and Clinical Immunology. It has obtained academic grants and has consolidated its structure by recruiting several permanent researchers: three MCU-PH (50 %), one PU-PH (50 %) and one CRCN (20 %) as well as four PhD students and two postdoctoral researchers. The team has also collaborated with several groups at CIRI to acquire new technologies and expertise.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	4
Maitres de conférences et assimilés	2
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	3
Praticien hospitalier	3
Sous-total personnels permanents en activité	**14**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels non permanents d'appui à la recherche	2
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**8**
Total général	**22**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent. The team has demonstrated highly recognized expertise in allergic skin diseases, and one of its main strengths lies in its ability to combine fundamental, translational, and clinical approaches. The team was supported by multiple sources of funding. It has been highly productive, with a very good level of publication.

Context-related strengths and opportunities

The team has solid and well-recognized expertise in the pathophysiology of chronic inflammatory and allergic skin diseases. Its ability to integrate fundamental, translational and clinical approaches represents a major strength that enhances both the relevance and impact of its research. The recruitment of MCU-PH and PU-PH researchers should further strengthen the team's clinical and translational potential.

The team coordinates the "Department of Allergology & Clinical Immunology", which facilitates access to patient samples and ensures the translational aspects of the projects and clinical studies. It is also responsible for a histology/immunohistochemistry platform at the CIRI Gerland. The team is actively involved in several national and international scientific networks, which contributes to its scientific visibility and recognition within its research field.

Over the past five years, the team has made several substantial achievements and produced a significant number of publications: 18 non-clinical research articles, including 11 as FLC; and 186 clinical research articles, including 52 as FLC. They have also published 25 reviews, editorial comments, or book chapters, including 17 as FLC. Several publications, with the team as lead authors, were published in excellent journals such as Science Advances and The Journal of Allergy and Clinical Immunology and specialized journals such as Allergy, J Am Acad Dermatol, JAMA Dermatol.
The scientific production of the PhD students is very strong, with first-author publications in Science Advances, JACI, J Am Acad Dermatol, JAMA Dermatology, and Allergy."

The team is implementing a phase I/II clinical study using a commercial monoclonal antibody that targets a biomarker (CD38) identified on cytotoxic $CD8^+$ T cells from toxic epidermal necrolysis patients. It has been involved in four translational clinical trials and 10 clinical studies (phase II-III).

The team plays a major role in teaching (medical and scientific students), coordinating several university and speciality courses in allergology, clinical immunology, dermatology, and skin biology (>360 h/y). It is recognized as a European reference centre for both the management of skin inflammatory diseases (ADCARE) and allergology training, including the UEMS diploma.

The team has secured various sources of funding (such as 1 Inserm MESSIDORE, 1 ACTERIA grant, 1 PHRCi, 1 ANR FWF Franco-Austrian and 1 PHRC), including 13 as coordinator and one as partner, for a total of €1.7 million. The team also secured 8 industrial contracts (such as MEDAC, DBV technologies, Leo Pharma and Abbvie) for €1.5 million. It actively engages with the public through patient associations by organizing annual events. Since 2020, it has organized 22 webinars, contributed to press articles, and produced several videos to disseminate scientific knowledge.

Context-related weaknesses and risks

While the team has successfully recruited several permanent part-time researchers (3 MCU-PH at 50 %, 1 PU-PH at 50 %, and 1 CRCN at 20 %), it currently has only one full-time researcher. Several grants end in 2025 or 2026, limiting long-term visibility regarding the feasibility of the four projects currently under development.

ANALYSIS OF THE TEAM'S TRAJECTORY

For the next period, the team will be co-led (DR2, Inserm and PU-PH, Lyon 1 University, Hospices Civils de Lyon). This co-leadership should be highly complementary, with an expert in fundamental and translational research, and an expert in translational and clinical research.

The team will continue to investigate how environmental factors (such as allergens, irritants, pollutants, and the skin microbiome) activate epidermal innate immunity and tissue-resident lymphocytes, thereby triggering or amplifying allergic and inflammatory skin responses. Their ultimate goal is to transform the management of chronic inflammatory and allergic skin diseases (e.g., eczema, drug allergies, hidradenitis suppurativa) by developing guided diagnostic tools, more effective therapies that both treat symptoms and prevent disease chronicity, and preventive strategies.

The team will develop four major, well-structured axes addressing key mechanisms in chronic inflammatory and allergic skin diseases:

- Axis 1: Role of tissue-resident memory T cells in skin allergic diseases
- Axis 2: Role of cytotoxic T cells and neuroinflammation in severe drug allergies
- Axis 3: Role of mucosa-associated invariant T cells (MAITs) in Hidradenitis Suppurativa
- Axis 4: Clinical and translational research

The team demonstrates a clear integration of basic, translational, and clinical research. It successfully integrates clinical trials and patient-oriented studies, ensuring that mechanistic findings inform therapeutic strategies and biomarker discovery. This strengthens the team's impact on patient care and disease management. Its translational focus, combined with good methodological expertise, positions the team to continue to produce important publications and to develop innovative therapeutic strategies.
Each project is coordinated by a designated PI and supported by specific grants from both public and industrial sources. It should be noted that some grants end in 2025 or 2026, limiting long-term visibility; however, new applications are currently in progress.

RECOMMENDATIONS TO THE TEAM

It is recommended that the team be further strengthened by recruiting a full-time CRCN and increasing the number of postdoctoral researchers. Substantial efforts should also be made to continue securing academic and industrial funding to support the development of the four proposed projects.

Team 4: Microbial Molecular Genomics (GenoMic)

Name of the supervisor: Mr François Rousset

THEMES OF THE TEAM

The team studies the evolutionary arms race between bacteria and phages. They aim to discover new bacterial defense enzymes as these systems are major sources of molecular innovation. They also aim at identifying eukaryotic immune proteins that evolved from bacterial systems, and uncover phage anti-defense strategies. By exploring how bacteria resist infection and how phages evade these defenses, the team seeks insights into immune mechanisms shared with or mirrored in eukaryotic and human viruses.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team was created in 2024 and was therefore not evaluated previously.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	0
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	0
Praticien hospitalier	0
Sous-total personnels permanents en activité	**2**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	1
Post-doctorants	2
Doctorants	2
Sous-total personnels non permanents en activité	**5**
Total général	**7**

EVALUATION OF THE TEAM

Overall assessment of the team

The team was created in 2024 and is composed of one CRCN, one IE and two PhD students. In addition, one ENS lecturer and two post-docs joined the team in the second half of 2025. The PI publication record of the past three years is very strong with four papers in generalist journals (Nature, Science, Cell and Cell host & Microbes) and three reviews. He has obtained the ATIP-Avenir label, and he obtained grants from ANR (317k€), from the Inserm Impact Santé program (338k€) and an ERC starting grant. The team and its projects are highly promising.

Context-related strengths and opportunities

The team's field of research is experiencing considerable growth in both microbiology and immunology, which increases the visibility and appeal of its scientific objectives. The Pi has received excellent training from world-renowned experts during his PhD and during his postdoctoral work providing a solid foundation for leading this new research direction. The goal is to assemble a team with diverse and complementary expertise, spanning bioinformatics, molecular biology, and biochemistry, to encourage effective knowledge exchange and strengthen the team skills. To this aim, the PI has obtained an ERC Starting Grant, which, that will ensure substantial financial support for the next five years and greatly accelerate the team's development. Additionally, CIRI offers a rich environment with complementary strengths in immunology and virology, creating fertile ground for long-term collaborations, and he has already started a partnership with another CIRI group, which focuses on the evolutionary conservation of innate immunity from bacteria to mammals.

Context-related weaknesses and risks

Launching a new team in a highly competitive field presents significant challenges. To address this, the Pi is establishing collaborations with leading groups in the CIRI and outside the CIRI including at Institut Pasteur, IST Vienna, and Weizmann Institute of Science. The team has obtained substantial funding that allowed to recruit one IE, two postdoctoral researchers and two PhD students. Of note, bioinformatics resources are fragmented across different units on the CIRI campus, reducing the overall efficiency and accessibility of these tools.

ANALYSIS OF THE TEAM'S TRAJECTORY

In 2025, the team launched several new projects aiming at discovering and characterizing new bacterial defense systems against phage infections, and new countermeasure strategies developed by the phages in response to bacterial defense mechanisms.
The first project investigates the functional landscape of phage small genes, defined as encoding proteins of 50 amino acids or less, which are often missed by genome annotation pipelines. While phages are known to counter bacterial restriction and CRISPR-Cas defense systems, anti-defense mechanisms have been identified for only ~15 % of known bacterial defense systems, suggesting many remain to be discovered. Comparative genomics predicts thousands of small genes families in phages, representing a largely unexplored sequence space. The team is developing a high-throughput functional genomics framework to systematically assess the role of tens of thousands of small genes in modulating bacterial defense systems, using advances in DNA synthesis and deep sequencing. This project, funded by ANR JCJC SHINE (2024–2027), is the main project of the PhD student.
The second project, EcoDefense, aims to generate a collection of 96 E. coli K-12 strains, each expressing a single defense system from a natural E. coli isolate under its native promoter. This collection addresses limitations of plasmid-based overexpression studies and provides more natural experimental conditions. The strains will be integrated at the Tn7 site, arrayed in 96-well format, and made available to the community. EcoDefense will be used for further studies, including identifying anti-defense genes and assessing defense systems' impact on conjugation. The project began in 2024 and is funded by ANR (2024–2027).
The third project, within the Evocure consortium, focuses on innate immune modules conserved from bacteria to humans. Some human immune proteins have evolutionary origins in bacterial defenses. The consortium involves several partners from Institut Pasteur, Institut Curie, IBMC and aims to discover and characterize novel human immune proteins by leveraging bacterial homologs. Candidate human proteins will be identified through computational analyses and screened in mammalian and insect cells, while the team studies their bacterial counterparts during phage infection to understand conserved antiviral mechanisms. This project is funded by Inserm Impact Santé (2025–2028) and by an ERC starting grant will be conducted by the two hired post-doctoral researchers.
Together, these projects explore the interplay between phages, bacterial defenses, and conserved immune mechanisms, combining high-throughput functional genomics, engineered bacterial collections, and evolutionary analyses to advance our understanding of innate immunity.

RECOMMENDATIONS TO THE TEAM

The projects developed by the team are highly promising as demonstrated by the excellent funding record (ERC, ANR and INSERM) that allowed to build up a team of seven peoples. Recommendation is to continue to obtain this level of funding and publication record (4 papers in generalist journals, Nature, Science, Cell and Cell host & Microbes during the past 4 years).

Team 5: Pathophysiology of mucosal infections (GIMAP)

Name of the supervisor: M. Stéphane Paul

THEMES OF THE TEAM

The team focuses on the development of neutralizing antibodies and novel vaccines such as those that elicit both mucosal and systemic immune responses. The team is strongly interested in developing methods to induce mucosal immunity and memory against acute and chronic respiratory infections.
The team is now also associated with the Center of Vaccinology of the Pasteur Institute and the U1223 - "Pathophysiology of the immune system".

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has addressed the recommendation of recruiting full-time researchers and international researchers to reinforce basic research by hiring a CNRS researcher. Moreover, two INSERM DRs plus an INSERM CRCN will also join the team. The team has obtained a junior PU chair in vaccinology and a MCU position is currently open. Finally, the team has recruited a research engineer as well. Regarding international recruitments, a major effort has been made to bring in international PhDs and post-docs from Cuba, Spain, China, Pakistan, Russia, India and Canada, and scientific discussions are now being held in English.
In order to exploit the clinical potential of the unit, the clinical protocols have all focused on mucosal vaccination and on the role of IgA and microbiota. Regarding the scientific focus, the unit has refocused its research activity on mucosal immunity and inflammatory diseases, and on the development of mucosal vaccination.
In order to increase the interactions between the unit and the CIRI, the team is extensively collaborating with numerous CIRI teams and sharing students and postdocs with several research groups.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	10
Maitres de conférences et assimilés	3
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	8
Praticien hospitalier	5
Sous-total personnels permanents en activité	**30**
Enseignants-chercheurs et chercheurs non permanents et assimilés	4
Personnels non permanents d'appui à la recherche	3
Post-doctorants	0
Doctorants	19
Sous-total personnels non permanents en activité	**26**
Total général	**56**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent to outstanding. The team exhibits a very high level of scientific excellence, international visibility, and translational impact in their field. Its strong publication record, successful acquisition of competitive funding, and strategic integration of immunology and virology support a coherent and ambitious research program with significant clinical and societal relevance.

Context-related strengths and opportunities

The team focuses on understanding mucosal immunity and memory against acute and chronic respiratory infections, and, in particular, secretory immunoglobulins in microbiota selection. However, the team has benefited with the arrival of new researchers who will broaden the team´s focus towards other inflammatory diseases such as IBD, nephropathy, anorexia, etc.) as well as T cell immunity at the mucosal interface.
The team is internationally recognized for the development and evaluation of translational strategies for mucosal immunotherapy, including mucosal vaccination and adjuvants. In fact, they have been involved both in the evaluation of mucosal response of COVID19 and RSV vaccines and the development of new vaccination strategies based on secretory IgA for antigen delivery. Particularly, the team benefits from a methodology that has the potential to be used in future human trials. As a result, the team has been invited to present in international meetings or seminars in institutes as well as to collaborate in international networks.
The team benefits from 3 full-time researchers, 8 support staff researchers, 3 temporary technicians, 19 PhD students (14 students ongoing), plus the 5 members of the hospital staff who are involved in clinical research.
Amongst the scientific tasks of the team are reaching duties such as Master lectures, clinical tasks such as direction of Departments/laboratories or outpatient consultations or acting as evaluators for societies and public/private foundations, as well as Editors/Reviewers of journals and organization of conferences.
Another strength of the team is their output in publications in outstanding journals in the field and beyond (e.g. Nature, Nature Communications, JCI, Sci. Transl. Med., etc.). The team has published 42 research articles and 82 clinical papers on which team members appeared as first, last, and/or corresponding authors. Additionally, the team published 106 more research-papers, 198 clinical papers in collaboration and a total of 131 reviews/editorials.
The team´s research output has made possible the successful acquisition of funds. They obtained 13 grants coordinated by team members for over M€3,2 and 15 grants as partners. These funds were obtained from public grant agencies (e.g. ANR) and European networks (EU-Proact, Preps 2023 Vaccibaby). Moreover, the team has benefited from their industrial liaisons with different pharmaceutical companies raising over K€3800 and three patents.
The team supports public outreach and dissemination of the information through interviews for TV, journals and radios, Université pour Tous, Fete de la sciences, dedicated workshops, etc.
After the merge with the Virology team, the current team will benefit from the new group's experience in public-private collaborative research with the pharmaceutical industry, and, in particular, with the technological research platforms as well as expanding the international outreach and becoming an international reference in mucosal immunity and vaccination against respiratory infections.

Context-related weaknesses and risks

A clear weakness of the team is the difficulty to attract postdocs, given the raising international competition in the field of vaccine and mucosal immunity. However, they have succeeded in negotiating the incorporation of several DR. Moreover, given the high amount of funds raised by the team, the level of funding seems difficult to maintain. Clinical research does not help to overcome this problem.

ANALYSIS OF THE TEAM'S TRAJECTORY

For the next contract, the team merges one virology team thus integrating virology and immunology. The overall aim will address functional interactions between respiratory viruses (e.g.: influenza, COVID19, etc.) and the airway epithelium, as well as the development of novel therapeutic and vaccine strategies against emerging and re-emerging infectious diseases.
The new team will particularly focus on three independent research axes: (i) Pathophysiology of chronic inflammatory diseases of the mucosa; (ii) pathophysiology of emerging and re-emerging respiratory viral infections (influenza, RSV, COVID-19) and (iii) the development of novel vaccine strategies for mucosal infections.

The team will take part in major national and international projects such as the Biocluster BCF2I, France Vaccin 2030 and Sanofi Pasteur's IPCEI santé "mRNA to the end".

RECOMMENDATIONS TO THE TEAM

It is recommended to increase their industrial partnership in order to maintain the high level of funding needed for such a big team, apart from the participation of the team in European networks- such as the current one aiming to describe the effect of RSV maternal vaccination combined to Nirsevimab treatment of Infants.

Team 6: Enveloped viruses, Vectors and Immunotherapy (EVIR)

Name of the supervisor: Mr François-Loïc Cosset

THEMES OF THE TEAM

The team aims to decipher how major human and animal viruses interact with host cells and immune defenses to guide new therapeutic strategies. Focusing on hepatotropic viruses, SARS-CoV-2, CCHFV and related pathogens, it uses structural, cellular, molecular and immunological approaches, together with humanized preclinical models, to study viral entry, replication and immune modulation. These insights are integrated with patient cohort studies and the development of innovative gene-delivery platforms, including technologies that reprogram immune cells and support translation through a dedicated start-up.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has effectively addressed the recommendations from the 2020 review. In line with the call to maintain an excellent level of scientific production, the team reports sustained or enhanced productivity and continued high-quality research output. Although organizational aspects were not previously evaluated, the team highlights a very positive and dynamic working environment and the implementation of both collective and individual leadership coaching to support the transition period.
Regarding scientific strategy, the team has met the recommendation to strengthen immunology and clinical expertise by recruiting a new researcher, whose arrival has expanded research on innate immunity, B-cell dysfunction, and viral pathogenesis, while also contributing to immunotherapy and vaccine development programs.
Finally, the team has successfully responded to the recommendation to secure stronger funding capacities, obtaining significant support—such as the FRM "Equipe" label and multiple national grants—thus ensuring the robust development and continuation of its research projects.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	1
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	3
Praticien hospitalier	0
Sous-total personnels permanents en activité	**9**
Enseignants-chercheurs et chercheurs non permanents et assimilés	5
Personnels non permanents d'appui à la recherche	4
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**12**
Total général	**21**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent. Between 2020 and 2024, the HEAL team advanced scientific and translational research, making key discoveries in viral entry, assembly and host responses and reinforcing its international standing in hepatotropic viruses, orthonairoviruses and SARS-CoV-2. Progress in synthetic immunology, gene-editing tools and lentiviral vectors expanded therapeutic potential. Strengthened immunology expertise, strong cohesion, high-impact publications, increased funding, training, patents and start-up activity highlighted its broad societal impact.

Context-related strengths and opportunities

The HEAL team benefits from a rich multidisciplinary environment that integrates virology, immunology, synthetic biology, structural biology and clinical research. This unique combination allows the team to pursue a unified and highly productive research program spanning fundamental mechanisms, translational development and therapeutic innovation. The full reintegration of the last director of the unit as a leader team strengthened strategic leadership and institutional visibility, while the recruitment of a new researcher expanded the team's immunological expertise, enabling new research lines in HBV immune dysfunction and immunotherapy. Strong internal cohesion and a positive working atmosphere create conditions conducive to creativity and efficient project execution.

The team has established itself as a national and international reference, as reflected in very recognized publications (more than 100 publications in excellent journals such as Nature Com, Nature, hepatology, J Hepatol…), major scientific awards and participation in influential networks and infrastructure. This visibility is further amplified by extensive collaborations, leadership in national programs and coordination of scientific communities.
The team's capacity to secure competitive funding has increased significantly, supported by prestigious labels and multiple grants from ANR, ANRS, PEPR (representing a total of 3M€ and except one, all as coordinator) and industrial partners. Its technological innovations, including synthetic immune circuits, nanoblades and targeted lentiviral vectors, create substantial opportunities for therapeutic development and industrial partnerships. With numerous patents and successful start-up creation, the team is well positioned to expand its translational activities**.** The growing societal relevance of emerging viruses, gene therapy and cancer immunotherapies offer additional opportunities for impact and future investment. Moreover, seven PhD students have been trained during the period.

Over the past two years, the HEAL team has undertaken an in-depth reflection on its scientific and organizational trajectory through a series of structured meetings, seminars and workshops held between May 2023 and February 2025. This collective process has strengthened internal cohesion, clarified long-term strategic objectives and reinforced a shared scientific vision. The team has institutionalized this dynamic through regular weekly lab meetings, thematic group discussions and strategy seminars, ensuring continuity in communication and decision-making.

Context-related weaknesses and risks

The broad scope of the team's research, although scientifically rich, poses risks in terms of workload distribution, long-term prioritization and maintaining coherence across diverse activities. Sustaining excellence across multiple virus families, therapeutic technologies and translational domains may challenge resource allocation and could increase reliance on key individuals for strategic leadership.
Despite strong funding success, the continuation of several large-scale projects will depend on maintaining or increasing grant acquisition in a highly competitive environment. The fast-changing landscape of gene therapy, synthetic immunology and antiviral strategies presents uncertainties regarding regulatory pathways, intellectual-property competition and industrial uptake. Translational ambitions, including the development of emerging start-ups, require sustained technological maturation, which may divert effort from fundamental research.
Recruitment remains essential to support growth in immunology, clinical translation and bioinformatics. Potential turnover or delays in hiring may slow key projects that depend on specialized expertise. External risks include evolving biosafety regulations, fluctuations in access to humanized models and dependencies on international clinical cohorts, all of which could impact timelines. Finally, the increasing complexity of interdisciplinary research could strain internal coordination, requiring continuous management efforts to preserve cohesion and strategic clarity.

ANALYSIS OF THE TEAM'S TRAJECTORY

Organizationally, the team has consolidated a coordinated leadership structure in which senior scientists jointly supervise major virology and immunology programs. This co-coordinated model reflects the team's culture of collaboration, shared responsibility and mutual scientific enrichment. It is widely supported by all team members, who recognize its added value for mentoring, project development and efficient resource allocation. The structure also aligns with the team's international profile, where joint PI-driven initiatives are increasingly essential for ambitious, interdisciplinary programs.

Scientifically, the team's trajectory is marked by a strategic narrowing of focus to maximize the impact. While significant achievements in HCV and SARS-CoV-2 research continue to produce publications, these themes will be gradually concluded to concentrate efforts on hepatotropic pathogens such as HBV, HDV and CCHFV, areas where the team has unique expertise and strong translational potential. This deliberate prioritization reflects both scientific opportunity and a desire to deepen the mechanistic understanding of viruses that remain major global health burdens.

The future research program follows three major axes. The first focuses on host factors and pathways that regulate viral life cycles, aiming to identify and characterize cellular components hijacked during assembly, entry and replication of HBV, HDV and CCHFV. New imaging approaches, proximity labelling and proteomics will be used to locate viral replication and assembly sites and reveal the determinants of host–virus interactions, with the explicit objective of identifying therapeutic targets. The second axis emphasizes hepatotropic viruses within their specific hepatic environment, leveraging the team's strong expertise in humanized-liver preclinical models. The third axis addresses the transmission of CCHFV, particularly from bovines to humans. By combining field sampling in high-prevalence regions with mechanistic virology, the team will map viral circulation in animals, define molecular determinants of cross-species transmission and investigate how human and bovine entry factors and immune pathways shape susceptibility.

This combined trajectory demonstrates a clear, coherent and ambitious evolution. It builds on the team's longstanding strengths in viral entry, assembly and host interactions while expanding into clinically relevant domains such as immune dysfunction, zoonotic transmission and therapeutic target identification. The integration of fundamental virology, field epidemiology and animal models position the HEAL team at the forefront of research on emerging hepatotropic and zoonotic pathogens.

Through its consolidated leadership structure and strategic refocusing, the team has established a robust trajectory for the coming years, characterized by scientific depth, translational relevance and strong collaborative potential.

RECOMMENDATIONS TO THE TEAM

The HEAL team should consolidate its strategic focus by completing ongoing HCV and SARS-CoV-2 projects and ensuring timely publication to maximize past investments. Future efforts should prioritize HBV, HDV, and CCHFV, while periodically monitoring emerging hepatotropic and zoonotic viruses to anticipate shifts in research priorities. Translational potential should be strengthened by continuing identification and validation of therapeutic targets, expanding collaborations with clinical and industrial partners, and formalizing processes for patenting and technology transfer. Interdisciplinary integration should be enhanced by leveraging expertise in immunology, lipid metabolism, and viral biology to connect molecular, cellular, and in vivo studies, and by fostering cross-axis collaborations linking CCHFV transmission with host-pathogen and immune response research. Organizational cohesion should be maintained through structured meetings and seminars, continued mentoring, and careful monitoring of workload to prevent bottlenecks. Risk mitigation should include diversification of funding sources, contingency planning for fieldwork and animal models, and tracking of viral variants to adapt experimental approaches. Finally, the team should increase visibility and international recognition through participation in high-profile conferences, publication in high-impact journals, and outreach activities to highlight societal relevance.

Team 7: Interplay between HBV and HDV and liver host factors (HepVir)

Name of the supervisor: Mr David Durantel

THEMES OF THE TEAM

The main research topic of the team is the interplay between hepatotropic viruses and liver cellular pathways/factors to identify novel targets for developing antiviral strategies that promote viral clearance and liver protection. In the previous funding period, the unit focused on Hepatitis B, delta and E, and expanded their research focus to other hepatotropic viruses including Yellow Fever flaviVirus (YFV), DENgue flaviVirus (DENV), Crimean-Congo Hemorrhagic Fever orthonairoVirus (CCHFV), Rift Valley Fever phleboVirus (RVFV), and other possible ones in the context of preparedness strategies.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has demonstrated their fast adaptation to CIRI as it is shown by their productivity (65 papers published, 25 of them as FLC) and five patents since they moved in 2021.
They have implemented their academic vs industry balance by leveraging 2.90 million EUR in academic grants (including a MSD-Avenir), and 1.32 million EUR from industrial contracts.
The team created an account on Twitter in order to promote scientific events and publications which is now moved to Bluesky.
Regarding teaching activities, the team participates in seminars and master programs. Their involvement in teaching will likely increase by a new incomer member.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	0
Praticien hospitalier	0
Sous-total personnels permanents en activité	**3**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels non permanents d'appui à la recherche	3
Post-doctorants	0
Doctorants	6
Sous-total personnels non permanents en activité	**10**
Total général	**13**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent to outstanding. The team is highly visible and shows a strong track record in basic and translational research on hepatotropic viruses, combining expertise, state-of-the-art experimental models, and outstanding scientific output in leading journals. Its ability to attract talent, secure substantial academic and industrial funding, therefore translating research into patents and partnerships, and demonstrating both scientific leadership and innovation capacity. Overall, the team is very well positioned to maintain its excellence and impact in the next period.

Context-related strengths and opportunities

HepVir, is a team composed of 10-12 members during the evaluated period which has conducted basic and translational research projects with the objective of gaining relevant knowledge mainly on hepatitis B virus (HBV) +/- hepatitis D virus (HDV) replication strategies and their interactions with host-factors/pathways in liver cells (hepatocytes, Kupffer cells and dendritic cells). The second scientific objective is to identify/get knowledge on novel targets of antiviral agents or immune strategies targeting the viruses or the host.
A team´s major asset is the attractiveness of their research topic which easily makes students, postdocs and other staff to enroll. In fact, the team has attracted three novel tenured researchers for the next period.
The team benefits from three full-time researchers plus one coming in January 2026, four PhD students, two post-docs, three technicians and three Master students.
The team is composed of tenured researchers with complementary backgrounds and no overlap with career developments who have developed a great variety of molecular and cellular tools of high quality as well as preclinical models.

Amongst the scientific tasks of the team are evaluation activities for societies and public/private foundations (ANRS), acting as members of national and international panels and Editors/Reviewers of journals (Antiviral Research, Gut, J Hep, Hepatology) and organization of conferences and as invited speakers. As part of the career development, the team has regular teaching activities such as lectures.
The team has produced a total of 16 original scientific publications, and 10 review articles/editorials/book chapters published as a first author. The quality of these papers is outstanding and published in prestigious journals such as J Hep, Antiviral Res, Hepatol Comm, J Hep Rep or PLOS Pathogens). Moreover, the team collaborated in another 31 publications and 10 reviews/editorials/book chapters.
Another strength of the team is the securement of academic funding of nearly M€3,0, mostly from national grants (ANRS), nine of which they act as coordinators. Moreover, the team leveraged over M€1,3 with industrial partners (Grifols, Pulsalys, Enyo Pharma, etc) and five licensed patents, demonstrating an excellent capacity for technology transfer and entrepreneurship (start-up creation, valorization possibilities). Furthermore, it is expected that short-term funding opportunities will emerge from industrial partners in HBV/HDV research and academia.
The team benefits from a high expertise and visibility of tenured researchers in their respective fields with a broad scope of research going from basic to translational aspects and vice versa. Moreover, the novel data (mostly epidemiological) has increased the medical impact of other hepatotropic viruses.
The team supports public outreach and dissemination of information such as the writing of popularization articles/opinion letters accessible to all public, the launching of a web page on liver diseases, press conferences, meetings with stakeholders, participation in science fairs and uploading videos in social platforms (Youtube, X). Notably, the PI of the team has collected a scientific prize in recognition of his career dedication to Antiviral Research.

Context-related weaknesses and risks

A major weakness is the limited number of technical staff who are permanent versus the high number of temporary contracts which makes it very difficult to maintain the level of research in the laboratory, and negatively affecting experimental productivity. However, the team externalizes technical knowledge to overcome this problem.
A clear risk is the most likely decrease in funding for viral hepatitis in the near future.

ANALYSIS OF THE TEAM'S TRAJECTORY

For the next contract, the team will aim to decipher the interplay between the liver and hepatotropic viruses (not only HBV, HDV, HEV, but also, YFV, CCHFV, etc.) in order to develop new antiviral strategies. This is a wise

decision given the shortage of funding in the field of viral hepatitis. In short, they will use a novel cell culture model and they are developping innovative others preclinical model. Both the in vivo and the in vitro model are aimed at enhancing basic research on liver cells/viruses interactions.
The team´s research program for the next mandate is divided in four interconnected axes: (1) Interplay between hepatotropic viruses and the liver metabolism; (2) Host factors related to hepatotropic viruses; (3) Interplay between hepatotropic viruses and innate responses and (4) Preparedness to combat the expansion of arthropod-borne viruses (still seeking funding).
In short, the HepVir program for 2026-2031 is very suitable to expand their knowledge into novel topics which constitute unmet needs of research.

RECOMMENDATIONS TO THE TEAM

To keep interacting with industrial partners in order to expand the funding available.
Within the new lab space, it is expected that the in vitro and in vivo models (a novel facility to work on high-risk human viruses is being implemented) proposed in the trajectory of the team are done in their own lab rather than in collaborator´s labs.
The team is recommended to continue participation in international consortia with the aim to reinforce the development of research axes in resource-limited countries where preparedness is needed and viral hepatitis is far from being eradicated. Moreover, national and international collaborators can reciprocally benefit from the expertise of the unit.
The team is recommended to seek funding for technical staff, given the amount of study models that they employ.

Team 8: Horizontal gene transfer in bacterial pathogens (Horigene)

Name of the supervisor: Mr Xavier Charpentier

THEMES OF THE TEAM

The project of the team focuses on the process of horizontal gene transfer in two bacterial pathogens, Legionnella pneumophila and Acinetobacter baumannii, which promotes pathogenesis and resistance to antibiotics (AMR) respectively. The aim is to explore the mechanism of transformation from a structural and physiological point of view and to reveal its role in the control of AMR acquisition and genome evolution.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has satisfactorily addressed the recommendations of the previous report. It gained a better visibility by organizing an international meeting which has become a recurring international event over the past five years and by reviewing 37 manuscripts and 10 national and international grant applications. It has proven difficult to obtain prestigious EU grants on AMR; nonetheless the group received a MSCA post-doctoral grant. The team established a research contract with a startup and hosted a researcher of the company for six months. At the same time, the team submitted a patent with Inserm transfer but this patent was not licensed and subsequently not renewed. The team has also reinforced its public outreach by giving interviews on national media and by contributing articles for the general public. Finally, the team attracted post-docs during the period to support the team and train PhD students.

The Horigene group has changed its internal communication by implementing a slack discussion group, bi-mensual group meetings and short weekly meetings. The team has broadened its activity on HGT pathways by measuring its impact on cell physiology and its interplay with mobile genetic elements. The team has established new collaborations with four different groups following its moving to the Gerland campus.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	1
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Praticien hospitalier	0
Sous-total personnels permanents en activité	**6**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels non permanents d'appui à la recherche	0
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**5**
Total général	**11**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent to outstanding with important contributions in three different lines of research. The level of publication is excellent to outstanding considering the size of the group. The visibility of the team is excellent to outstanding as assessed by the publications, invitations to international conferences and organization of webinar series, recruitment of PhD students and post-docs, collaborations, and the obtention of regular funding and awards. The team is heavily involved in teaching and has been engaged in tech transfer.

Context-related strengths and opportunities

This is a well-established team composed of four permanent members (one DR, one CR, one Prof, one MCU), two PhD students, two post-docs and one engineer during the period.
The team is working on three different and complementary aspects of natural transformation and the horizontal gene transfer. On each of these themes, the team has obtained original and important results contributing new insights and paradigms of the transformation process and the control of HGT.

In the first axis, they focus on the molecular characterization and regulation of natural transformation. They determined in collaboration the crystal structure of a partial complex of the core regulation component RocC/RocR for natural transformation in L. pneumophila. It revealed the key features of the interaction between the sRNA RocR and its chaperone RocC, demonstrating how the broadly conserved ProQ/FinO-domain RNA chaperone interacts with the non-coding RNA. They also identified all the genes required for transformation in Lp revealing the type IV pilins and the newly characterized YraN nuclease forming a nuclease-helicase complex with the ComM helicase.

In the second axis, the aim is to reveal the contribution of HGT to genome evolution, with a focus on natural transformation. Remarkably, they showed that counter-intuitive role of natural transformation in curing the genome of antibiotic resistance islands. Furthermore, they revealed that mobile genetic elements interfere with transformation.

In the third axis, they demonstrated the high-rate transfer of large resistance islands carrying carbapenem resistance between Ab isolates by natural transformation.

Considering the size of the team, the production is outstanding with ten senior author papers in primary journals (1 PLoS Biology, 2 PNAS, 1 Nature Communications, 2 mBio, 1 Antimicrob Agents Chemotherapy, 1 J. Bacteriol, 1 Applied Environ Microbiol and 1 Microb Genom) and three reviews (in Methods in Mol Biol).
The team has an excellent national and international visibility. The team has been very successful in obtaining national and international funding (3 grants from ANR, Labélisation FRM, EU MSCA fellowship, CNRS 80 Prime program). The PI has been invited to three international meetings. The PI has been involved in the organization of two international meetings series. Finally, the team has been very attractive and trained ten PhD students (two still ongoing). Four out of six students who defended their PhD before 2022 have contributed a publication as first author while three PhD students who defended their PhD in 2024 did not publish their work yet. Two post-docs were recruited recently.

Context-related weaknesses and risks

The heavy teaching duties may impact the results of one axis.

ANALYSIS OF THE TEAM'S TRAJECTORY

The group proposes to continue its work on the characterization of the RocC/RocR system and the role of the nuclease-helicase YraN/ComM complex in the recombination process and acquisition of AMR. The second line aims to analyze the interplay between bacteria and mobile genetic elements, and how MGE can modulate natural transformation. This will be complemented by other studies to reveal how bacteria defend against MGE and how these interplays modulate AMR resistance.

The proposed projects are a natural continuation of those carried out to date, and the expertise of the permanent team members as well as the established collaborations with well-known groups should guarantee the success of these exciting programs.

RECOMMENDATIONS TO THE TEAM

The team is encouraged to continue its original and important research project from a fundamental and translational perspective. Given the small size of the team, it is recommended that it focus on a limited number of projects. The PI is encouraged to apply for European funding.

Team 9: Host-pathogen interaction during Lentiviral Infection (LP2L)

Name of the supervisor: Mr Andréa Cimarelli

THEMES OF THE TEAM

The team investigates host-virus mechanisms shaping antiviral responses and replication in emerging and established infections. Research is structured around two complementary axes: The first, identifies and characterizes cellular antiviral proteins (ISG20, IFITMs, Trim69) that restrict HIV-1 and other viruses (VSV, EBOV, SARS-CoV-2), using cell biology, biochemistry, virology, imaging. The second, applies an evolutionary strategy to probe virus–host interactions and molecular arms races driving cross-species transmission, combining comparative genomics, bioinformatics, and molecular virology to reveal adaptations across viruses (HIV, SARS-CoV-2, poxviruses) and hosts (humans).

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous report recommended to « provide examples on how their findings can be useful for issues beyond basic research (antiviral treatment, HIV-1 cure) ». The team should also « intensify public outreach with regards to industrial collaborations ».
Although the team's research is primarily fundamental, its focus on antiviral mechanisms naturally carries translational potential. This has been further developed through two concrete examples: (i) the Inserm Impact EvoCure project (2024–2028), which aims to identify and validate druggable antiviral targets through integrated approaches ranging from evolutionary-guided discoveries to molecular biology assays and preclinical models; and (ii) the SAMD9/9L project, which explores host defense factors also implicated in severe genetic diseases, in collaboration with F. Roucher (HCL Lyon; ANRS).
Even though no specific progress in industrial partnerships was reported during the period, the team has clearly strengthened the translational orientation of its research, in line with the previous recommendations.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
Praticien hospitalier	0
Sous-total personnels permanents en activité	**3**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels non permanents d'appui à la recherche	1
Post-doctorants	0
Doctorants	5
Sous-total personnels non permanents en activité	**8**
Total général	**11**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent. Through complementary expertise, the team has delivered original, high-quality, and internationally visible research, with significant contributions to the understanding of antiviral mechanisms. Its strong scientific productivity, capacity to secure competitive funding, and integration into national and international networks highlight a robust and dynamic research environment. The team also shows a solid commitment to training. Taken together, it stands out as a highly dynamic and internationally competitive team.

Context-related strengths and opportunities

The team has made major contributions to the understanding of virus–host interactions, combining molecular virology, cell biology and evolutionary biology to elucidate how cellular factors control viral replication and adaptation. These studies encompass not only HIV-1 but also a broad range of other viruses, and rely on complementary expertise across two independent yet closely interconnected subgroups. This organization provides strong internal synergy, supported by a wide range of experimental and methodological approaches. The team's work is firmly anchored in fundamental research, providing mechanistic insights into antiviral processes and host adaptation across species.
This research output has resulted in a total of 20 publications, including 15 publications with lead authorship (FLC) in highly recognized international journals such as Science Advances, PLoS Pathogens, PLoS Biology, Nucleic Acids Research, PNAS, Scientific Reports and Journal of Virology, as well as five collaborative publications reflecting its integration into national and international research networks. In addition, the team has published nine reviews and one book chapter.
The team has developed extensive national and international collaborations, leading to joint publications and shared research funding. Between 2019 and 2025, the two PIs have coordinated 21 national and international grants (ANR, ANRS, Sidaction, CNRS, University of Arizona, UC Berkeley) and are partners in four others, representing a total of €3.6 M, including €1.2 M in salaries.
The team has achieved strong scientific recognition and visibility, with numerous invitations to speak at national and international conferences. Both PIs serve on evaluation and advisory committees (ANR, ANRS, Sidaction) and are regularly involved in grant reviewing, journal peer review, and external audits. The team demonstrates clear international visibility and attractiveness, illustrated by the recruitment of several foreign PhD students and postdoctoral fellows, and by its participation in international collaborative networks. It also benefits from an excellent environment within ENS-Lyon and CIRI, fostering interdisciplinarity and access to cutting-edge facilities. Both PIs are actively engaged in science communication and public outreach, contributing to debates with society.
Finally, the team demonstrates a sustained commitment to training, having supervised or currently supervising 11 PhD students and eight postdoctoral fellows (including 6 international), as well as 20 Master's and Bachelor students (M2/M1/L3/IUT) and nine technical or research support staff. Most PhD students and postdoctoral researchers have authored first-author publications, and the technical staff are also regularly included as co-authors in scientific papers. Moreover, PhD students and postdoctoral fellows regularly participate in national and international conferences.

Context-related weaknesses and risks

The small number of permanent staff represents a potential vulnerability, creating some reliance on postdoctoral researchers and project-based funding. The absence of intermediate-level permanent positions may also limit the distribution of responsibilities and long-term consolidation of the research axes. Strengthening the team with additional permanent support would help reinforce continuity and ensure sustained technical and/or bioinformatics capacity.
The current laboratory and office space, while sufficient at present, may become a constraint if the team continues to expand.
While the team's projects are strongly anchored in fundamental research, translational and valorization components remain relatively modest and could benefit from further development through dedicated partnerships. Although interactions with clinical collaborators have increased, no patent or technology transfer has yet emerged.
Finally, the broad thematic range of the projects, although a clear source of innovation and interdisciplinarity, requires careful prioritization to ensure strategic coherence over the next evaluation period.

ANALYSIS OF THE TEAM'S TRAJECTORY

The proposed trajectory of the HIVE team builds logically on its previous scientific achievements, maintaining the strong complementarity between molecular virology and evolutionary biology. It articulates a coherent and highly ambitious research program that consolidates the team's dual expertise in dissecting cellular antiviral mechanisms and tracing their functional evolution across species. The transition to a co-leadership by Lucie Étienne and Andrea Cimarelli is well prepared and should ensure strategic continuity and long-term stability.
The first axis, centred on the molecular basis of broad-spectrum viral restriction, capitalizes on the team's solid expertise in cell biology and biochemistry to explore emerging antiviral mechanisms involving ISG20, IFITMs, and Trim69. These studies are well anchored in the group's previous successes and benefit from robust collaborations with experts in structural biology, imaging, and host–pathogen interactions.
The second axis, focusing on the functional evolution of antiviral immunity in mammals, brings a highly original and interdisciplinary dimension. By combining computational and evolutionary approaches with functional virology, the group aims to uncover how ancient immune genes such as SAMD9/9L and GBP5 have diversified in specific preclinical models and how they participate to antiviral functions. This work, integrated within international initiatives such as the Inserm Impact EvoCure consortium, positions the team as a leading actor in the emerging field of evolutionary virology.
Overall, the trajectory is scientifically sound and methodologically well supported. It leverages the team's established strengths, existing collaborations, and secured funding (ANR, ANRS-MIE, Sidaction, CNRS IRP, Inserm Impact and one ERC CoG). The balance between mechanistic and evolutionary studies confers a distinctive and highly competitive profile within the broader field of host-virus interactions.

RECOMMENDATIONS TO THE TEAM

The team is strongly encouraged to pursue its highly dynamic and innovative scientific trajectory. Its ability to combine molecular virology, cell biology and evolutionary approaches across multiple viral systems represent a major asset, and further diversification into additional viruses or reservoir hosts is likely to amplify its originality, international visibility, and capacity to attract competitive funding. Maintaining clarity in project prioritization will help sustain this momentum and ensure efficient allocation of human resources as the scientific program expands.
Strengthening the permanent staff base, whether through mid-career researchers, engineers, or dedicated bioinformatics support, would further consolidate the team's expertise, reinforce continuity, and secure the long-term structuring of its research axes.
The team has already demonstrated promising steps toward European integration (MSCA fellowship, ERC application). Building on these achievements to take leadership roles in European consortia would significantly enhance its international positioning and competitiveness. Expanding collaborations with industrial partners could also unlock new avenues for translational research and increase the impact of the team's findings.

Team 10: Inflammasomes-Bacterial Infections and autoinflammation (I2BA)

Name of the supervisor: Mr Thomas Henry

THEMES OF THE TEAM

The team is focusing on innate immune responses to bacterial infections and in autoinflammatory syndromes, specifically the pyrin inflammasome, the ALPK1-NFkB response, and host-pathogen interactions of Francisella tularensis infection. The research spans fundamental work on innate immune mechanisms involved in responses to F. tularensis such as guanylate binding proteins (GBPs) and caspase 4, to translational and clinical work on anti-inflammatory diseases such as Familial Mediterranean Fever (FMF) and ROSAH syndrome (Retinal dystrophy, Optical nerve oedema, Splenomegaly, Anhidrosis, migraine Headaches).

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The number of HDR should be increased to reduce workload in PhD supervision from the PI. The team has three new HDRs; one CRCN Inserm researcher, one PU-PH and one MCU-PH.

Interactions with industry should be fostered. The team now has contact with Drug Farm on the ROSAH syndrome, but industrial contacts are still limited.

Overall, the international profile of the team could be enhanced. Currently, only five team members are of non-French origin. The team had several international PhD and fellows from other countries in the evaluation period. The team relies on NGS and data analysis, however this is not covered by bioinformatic support by the CIRI and relies on outside collaborations. Bioinformatic support for the team should be provided by CIRI. This was not addressed during the evaluation.

The integration of the team into several cohorts and consortia will aid conduction of the pyrin-related work. The team is a member of ImmunAID (European H2020 project on rare inflammatory diseases), CeRéMAIA (the French reference centre for auto-inflammatory diseases) and part of multi-centre cohorts on Pyrin-associated autoinflammatory disease and on ROSAH syndrome.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	0
Maitres de conférences et assimilés	3
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	2
Praticien hospitalier	0
Sous-total personnels permanents en activité	**7**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels non permanents d'appui à la recherche	4
Post-doctorants	0
Doctorants	6
Sous-total personnels non permanents en activité	**12**
Total général	**19**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent. The team produces high-quality research and are internationally recognized for it. They have done wise strategic choices by ending some lines of research to pursue new, promising ones – which is also reflected in some of the recent promotions/recruitment.

Context-related strengths and opportunities

The team is internationally recognized for work on the pyrin inflammasome, encoded by MEFV, whose mutations cause FMF. They showed pyrin activation is a two-step process, with the second step constitutively active in FMF and can be triggered by steroid sex hormone catabolites. They identified new FMF mutations and developed a diagnostic test. A new research line focuses on ALPK1, a sensor of bacterial ADP-heptose and mutated in ROSAH, which they helped define as an autoinflammatory syndrome. Clinical and research papers on these diseases appear in iScience, Cell Reports, Ann Rheum Dis, Lancet Rheumatol, etc.

The team previously did seminal work on GBPs in Francisella defense and human caspase-4. Using Francisella and Shigella models, they and collaborators characterized GBPs and IRF2 in caspase-4 regulation, published in EMBO Reports; one paper was Pathogens and Disease's best of 2023; one paper was Pathogens and Disease's best of 2023. GBP work has ended, while Francisella/IRF2 studies continue.

Overall, the team was highly productive: 31 papers as FLC, 60+ contributing, 35+ reviews/book chapters/editorials. PhD students published well, including first authorship. 29 members gave oral presentations at international meetings; no data on invited talks. The leader co-organized two international conferences (pyrin, tularemia) and chaired a national symposium.

The team was successful for gathering funding with a total of k€ 2375, coordinating all 6 grants listed (3 ANR, FRM, PEPRI-MIE, Drug Farm) of total 14. The team shows a strong translational research stems from clinician-researcher balance, especially in autoinflammatory diseases. The team is part of CeRéMAIA (national reference centre for autoinflammatory diseases/amyloidosis) and FAI2 (rare autoimmune/autoinflammatory network). Collaborations within CIRI (Py team, others) offer further excellence opportunities. A PU-PH was recruited in 2023 and co-directs the tularemia reference centre, fostering translational research and international collaborations in Francisella.

Outreach includes training teenagers, engaging patient organizations for FMF, and creating an inflammasome/autoinflammatory pamphlet for the public with ImmunAID partners.

Context-related weaknesses and risks

The team focuses on Francisella and anti-inflammatory diseases, and both research lines are strengthened with new, permanent recruits from basic- and clinical science. There is a risk that the team grows in different directions.

The team is successful in obtaining funding, but some of the younger researchers should be supported in applying for their own grants (e.g.: ERC starting or consolidator grants). It will be important for their career to become independent, and it is not clear what strategies the team or the unit has for career development for younger PIs. Some of the researchers/ postdocs are not visible in the research described or the selected publications and have heavy teaching duties which may delay progress.

Overall, the outreach activity could be better (social media, talks to the general audience, news/magazines/media)

Finally, the team is now four HDRs, thus they have capacity for supervising more PhD students and postdocs. Only three PhD students are listed for the next mandate.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team presents a plan for continuing the research lines on pyrin, ALPK1 and tularemia, based on previous published and unpublished discoveries. Importantly, the new recruits are centrally positioned in driving the

research proposed for the next period. For pyrin, they will look at other autoinflammatory conditions associated with pyrin dysregulation to identify mechanisms, including by developing a preclinical humanized model of pyrin-associated autoinflammatory disease (PAAD). The ALPK1 pathway is less characterized, and the team has done a CRISPR-screen where they identified potential regulators that will be investigated, including in a preclinical model they will develop for ROSAH. They propose an exciting hypothesis that mutated ALPK1 may recognize self-nucleotide sugars, and this could underlie the autoinflammation, which will be tested. The team plans on developing phenotypic diagnostic assays for both pyrin and ALPK1 using patient cells.

The tularemia work will divide in two projects, one following up on the findings that IRF2 is regulating inflammasomes and the anti-bacterial activity of NK cells with an aim to understand the mechanisms. The long-term goal is developing NK cell-based therapy to intracellular infections – though this part is not described in detail. Funding is needed and will be requested for the PI on this project. The other Francisella axis is focused on bacterial virulence factors – the mechanism of two T6SS secreted factors involved in phagosome permeabilization, and identification of new factors.

All four research projects are based on sound hypotheses or preliminary findings by the team, and several new discoveries of both fundamental and clinical relevance can be expected. The team is well suited to complete the proposed research, and they have a competitive edge in being strong in fundamental, mechanistic research, as well as having strong connections to the clinic – including through disease cohorts and consortia on autoinflammatory diseases and tularemia.

RECOMMENDATIONS TO THE TEAM

Further strengthen the CIRI, national and international collaborations on autoinflammatory diseases – the translational approach in the team is great for this type of research, and the team already has a standing on FMF/pyrin. The same goes for the ALPK1 project.

Ensure there are good career plans for young investigator talents, and support these to apply for own funding to become independent (e.g. ERC starting or consolidator grants).

More PhD students and postdocs should be recruited with the growing number of senior team members (HDRs) to supervise and mentor. Look to obtain MSCA postdoc grants to recruit from abroad. Although there are links between the research lines/project, the Francisella and the anti-inflammatory disease projects are drifting apart. The team is recommended to discuss their research strategy during the next mandate.

Team 11: Normal and Pathogenic B cell responses (NOPAB)

Name of the supervisor: Olivier Thaunat

THEMES OF THE TEAM

Using patient samples and experimental models, the team investigates mechanisms involved in rejection of allografts. It also studies "opportunistic" infections in immunosuppressed patients. In both themes, the team also develops innovative therapeutic approaches. Finally, the team develops tools to monitor immunosuppression, with the goal to optimize protocols.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

- Pursue recruitment of high-profile PhD-students and postdocs and international recognition: Several French and foreign young scientists (11 PhD students, 6 postdocs) were recruited. The team was involved in three EU- and one NIH-funded project and the team leader is chairman of the ESOT.

- Communication with the public needs to be improved: Team-members have given media interviews on organ transplantation and immunosuppression in COVID-19 and have participated to fund-raising events.

- The focus on preclinical transplantation models should be extended with analysis of immune-parameters in human transplant recipients: A dedicated structure was set up in the hospital to collect patient data and samples that then feeds back to the laboratory for testing of hypothesis developed based on these data.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	2
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	4
Praticien hospitalier	1
Sous-total personnels permanents en activité	**9**
Enseignants-chercheurs et chercheurs non permanents et assimilés	4
Personnels non permanents d'appui à la recherche	3
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**11**
Total général	**20**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment is "excellent". The team has very successfully described previously unknown mechanisms of graft-rejection and developed tools to monitor immunosuppression in allograft-recipients. It has done so using an elegant combination of the study of animal models and analysis of clinical material.
Results were published in good to outstanding journals and the team and its members have developed a very good (inter-)national reputation allowing it to obtain substantial funds for its research. The proposed project is a coherent follow-up of current work and includes innovating aspects related to transplantation-medicine.

Context-related strengths and opportunities

In the evaluated period, the team identified two novel mechanisms involved in allograft rejection. Using an elegant combination of preclinical models and clinical material, it described that an early and transient wave of donor-specific antibodies is generated with the help from graft-derived T lymphocytes (Sci Transl Med 2022). It also found that microvascular injury can develop in the apparent absence of donor-specific antibodies. Data suggested that host NK-cells may be involved (Nat Comm 2019). In a more clinic-oriented part of its activity, the team developed a blood Torque Teno Virus DNA-based approach to carefully monitor immunosuppression in transplant-recipients (J Med Virol 2024); reported increased COVID-19 mortality risk in patients that had received allografts or that were on haemodialysis (e.g. Am J Transplant); and found that transplant-recipients needed a third COVID-19 vaccination to develop neutralising antibodies (Sci Transl Med 2022). Finally, the team described that expression of the integrin alpha5/beta8 by type I conventional dendritic cells favours TGFbeta production and thus facilitates IgA production upon Rotavirus infection (Mucosal Immunology 2021).
This impressive work was published in good to outstanding journals such as Science Translational Medicine and Nature Communications. The team published a total of 18 research and 21 clinical publications and 35 review/editorials/book-chapters in first/last/corresponding position and 39 more research and 66 clinical papers in collaboration.
The work of the team provided it with a solid (inter-)national reputation. The team was involved in three EU- and one NIH-funded project and the team leader is chairman of the European Society for Organ Transplantation (ESOT). Members of the team were invited to give numerous oral presentations in (inter-)national meetings, staff-members ensure numerous scientific responsibilities (committees, chairs, reviewing) at the local, national and international levels, they have received scientific awards (e.g. FRM), and were involved in the organization of (inter-)national meetings (ITC, CFCD, SFI, etc.).
The team succeeded in obtaining solid financial support for its work. For example, its members coordinated three ANR projects and two PHRC (hospital programs for clinical research), participated to an NIH program and an EU Horizon-project, and were partners in other ANR grants. The total amount of grant-derived financing of the team was close to M€4.5.
The team (with four HDR) is very active in training young scientists. It trained 11 PhD students, of which four are ongoing, and 18 Master-students. Three of its members are (associate-)professors at the medical faculty, teaching 30 to 60h/yr.
In terms of socio-economic interactions, team members were active in consulting positions and advisory boards in the private sector. They gave interviews to several media on transplantation and during the COVID-19 pandemia.

Context-related weaknesses and risks

This team has developed very solid logistic and scientific interactions with the clinic. Its scientific work is characterized by the use of preclinical models and analysis of clinical material. The solid financial support it has acquired allows it to recruit sufficient personnel to realize its ambitious programs. The panel has not identified any weakness or threat worth mentioning.

ANALYSIS OF THE TEAM'S TRAJECTORY

The project proposed by the team is a coherent and logical follow-up of its past work and includes ambitious and intriguing innovating aspects. It thus proposes to develop therapeutical approaches to target NK-cell-mediated microvascular rejection; it has the ambition to identify the mechanisms causing microvascular injury not involving donor-specific antibodies or NK-cells; it plans to further develop TTV-based management of immunosuppression in the clinic. The team will assess the implication of myeloid cells in clinical allograft rejection,

as suggested in the literature, and develop therapeutic approaches to tackle this mechanism. It also proposes to develop novel (e.g. cellular) therapies against CMV-infection in transplant-recipients. Finally, it will develop a novel very ambitious project on the generation of rejection-resistant allografts (e.g. pancreatic islets, vascularized allografts).
Given the team's size, expertise, tools, and financial means, these projects should prove feasible and contribute greatly to the understanding of mechanisms involved in rejection and to the development of novel therapies against rejection and opportunistic infections.

RECOMMENDATIONS TO THE TEAM

The committee recommends to the team to continue its excellent work. They should investigate, using animal models, the relative contribution to organ-loss of the identified allograft rejection-mechanisms (. early donor T cell-dependent antibody responses and potentially NK-cell-mediated microvascular injury). The team should carefully consider the consequences of even further weakening immune responses in transplant-recipients.

Team 12: Lymphocyte Activation and Signaling (LYACTS)

Name of the supervisor: Mr Thierry Walzer

THEMES OF THE TEAM

The team investigates the mechanisms that regulate the differentiation, metabolism, and activation of immune cells, and how genetic or acquired alterations can cause immune deficiencies, severe infections, or autoimmunity. In particular, the team studies natural killer (NK) cell biology, focusing on their development, maturation, and functional regulation, and how signaling and metabolic pathways shape their activity. They explore NK cell dysfunction, with a particular emphasis on cancer. The team also investigates how genetic or acquired mutations contribute to the development of autoimmune disorders (e.g.: lupus, Evans syndrome, juvenile idiopathic arthritis) and aims to develop new therapeutic strategies.
Overall, the team combines fundamental and translational research to understand the immune cell biology and dysfunction, with the ultimate goal of developing targeted therapies for cancer and autoimmune diseases.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous report recommended that the team increase its patent activity, apply for international grants, strengthen international and private-sector collaborations, recruit more postdocs and focus on the most promising research questions. It also suggested joining European research consortia and consolidating the lab into a single location to enhance cohesion and productivity.

The team has made efforts to address the recommendations from the previous report. They have filed a patent, maintain regular interactions with Inserm-Transfert, and obtained a pre-maturation grant (SATT Pulsalys) to create a start-up. Efforts toward internationalization and private-sector collaboration include hiring two foreign postdocs and securing three Cifre contracts. Recruitment of postdocs is ongoing, supported by recent ANR and INCA grants, and research focus has been refined to prioritize the most promising questions. The team has also strengthened its integration into European networks by organizing the 2024 German NK/ILC society meeting and unified its structure in the new Franklin building, enhancing cohesion and collaboration.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	4
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Praticien hospitalier	0
Sous-total personnels permanents en activité	**9**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels non permanents d'appui à la recherche	2
Post-doctorants	0
Doctorants	7
Sous-total personnels non permanents en activité	**11**
Total général	**20**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is outstanding. During the evaluated period, the team has been highly productive, achieving an excellent publication record in leading journals in both basic and clinical immunology. It is supported by multiple sources of funding, including academic and industrial contracts.

Context-related strengths and opportunities

Although the two main topics addressed are somewhat distinct (immune defects linked to genetic alterations and NK cell biology), the team has successfully collaborated, combining their efforts to maintain a coherent research strategy that integrates fundamental, translational, and clinical approaches. Their complementarity is illustrated by several common publications.

Over the past five years, the team has an important number of publications with over 70 non-clinical articles (including 20 as first, last, or corresponding author), more than 110 clinical articles (including 12 as first, last, or corresponding author), and 36 reviews, editorial comments, or book chapters (including 20 as first, last, or corresponding author). They have made important achievements and published several articles as lead authors in prestigious journals such as Nature Metabolism, Science Advances, Journal of Experimental Medicine, Nature Communications, and Science Immunology. They have also published clinical articles as lead authors, notably related to the COVID-19 pandemic, in excellent journals such as New England Journal of Medicine, The Journal of Allergy and Clinical Immunology, and Lancet Regional Health Europe as well as reviews in New England Journal of Medicine, Nature Reviews Drug Discovery, and The Journal of Allergy and Clinical Immunology.

The team is internationally recognized and has raised €4 million from various funding sources, including seven grants as coordinator (1 INCA PLBIO, 1 ANRS, 3 ANR, 1 LNCC, and 1 ARC), four grants as partner (2 ANR, 1 H2020, and 1 RHU) and industrial contracts (1 Sanofi, 3 Cifre fellowships, 1 LVMH Recherche, and 1 Boehringer).

Six PhD theses were defended during the period, and seven are currently in progress. Remarkably, all PhD students have contributed to one or several publications and are typically authors of at least one first-author paper. A project leader has obtained his HDR in 2023.The team is also actively involved in teaching activities, primarily at the Master's level and in Medical School (> 130 hours/year).

The team leader assumed several scientific responsibilities. He was interim director of the CIRI from 02/2024 to 04/2025 and is the coordinator of the Immunology speciality department since 2018. He has also served on councils at Inserm, HCERES, and the German DKFZ panel.
Another project leader is Co-chair of the National network on rare autoimmune and anti-inflammatory diseases and received the 2021 FRM Prize of the Guillaumat-Piel Foundation.
The team actively participated in organizing the European NK/ILC Cell symposium in Lyon, thereby contributing to the international visibility of the CIRI.

Context-related weaknesses and risks

Only two postdocs were hired during the period, and two others will be hired soon. The number of postdocs could be increased in relation to the size of the team, which is organized into four distinct groups.

Only one patent has been filed so far, although the team intends to create a start-up and further develop the recently established cellular immunotherapy platform.

ANALYSIS OF THE TEAM'S TRAJECTORY

For the next mandate, the team will be co-led by the present PI (DR1, Inserm) and a PU-PH, and will be entitled (IMPACT). This co-leadership is expected to be highly synergistic, combining the strengths of two experts spanning fundamental, translational, and clinical research.

The four axes proposed by the team are a logical continuation of its current activity. The team will be organized into four groups, led by the same PIs as in the previous quinquennium. Each project benefits from grants that run until at least 2027.

Axis 1. NK cell differentiation: This axis will investigate how key transcriptional regulators such as IRF1 and the Mediator complex control NK cell function and epigenetic programs, using NK-specific knockout models and CRISPR/Cas9 editing. They will also explore how metabolic pathways in particular the citrate/malate shuttle shape NK cell differentiation and histone acetylation.

Axis 2. NK cell metabolism: Building on findings that NK cell dysfunction can arise from either impaired in energy production by the pyruvate-fed oxphos pathway or to a shortage in O-Glc-Nacylation, this axis will explore NK cell metabolic crosstalk with other cell types, cytokine-driven activation in higher flexibility of NK differentiation, new metabolic regulators via chemical/CRISPR screens, and metabolic defects in patients with inherited metabolic disorders.

Axis 3. Gene and cell therapy: This axis aims to develop NK- and T-cell-based therapies by optimizing NK cell expansion, engineering, and differentiation, and by testing these optimized effectors in preclinical models and forthcoming clinical applications through local and international collaborations.

Axis 4. Genetic of early-onset autoimmunity: This axis focuses on uncovering genetic causes of pediatric autoimmune diseases by combining genome sequencing, bioinformatics, and functional studies in experimental models, leading to the discovery of several Mendelian forms of autoimmunity and ongoing studies of rare variants affecting cytokine signaling, B cell tolerance, and nucleic acid sensors. They also explore immune dysregulation in conditions like MIS-C, including T cell expansions, with the aim of developing new therapeutic strategies, which could be the scope of a future start-up.

Each project will be developed in interaction with the other groups within the team. This collaborative strategy proved to be highly productive during the previous quinquennium.

RECOMMENDATIONS TO THE TEAM

The committee recommends that the team continue to actively interact with Inserm Transfert to file additional patents, which could facilitate the potential launch of a start-up and support the further development of the cellular immunotherapy platform inaugurated in 2025.

Integration into European or international research consortia, and continued efforts to secure European funding, should be considered to maintain the team's good visibility.

The team should continue its efforts to recruit postdocs and strengthen its contributions to the general public and society by involving PhD students and postdocs.

Team 13: Legionella pathogenesis (Legiopath)

Name of the supervisor: Mrs Patricia Doublet / Mrs Sophie Jarraud

THEMES OF THE TEAM

The project of the team aims to develop an integrated strategy ranging from the study of the molecular mechanisms of interactions between Legionella and host cells to the clinical microbiology of Legionnaires' disease.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has observed the recommendations of the previous committee by focusing its studies only on two major projects on Legionella, by leveraging collaborative projects with shared interests among the basic research group, the clinical microbiology team and the reference laboratory, and by recruiting a young full-time researcher. As it stands, the Legiopath project is well integrated in the strategy of the CIRI' bacteriology department.

The team has filled four patents during the period.

The team did not obtain an EU grant but nevertheless increased its fundraising to 2.46 M€ during the period.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	2
Maitres de conférences et assimilés	4
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	3
Praticien hospitalier	0
Sous-total personnels permanents en activité	**11**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	0
Post-doctorants	2
Doctorants	4
Sous-total personnels non permanents en activité	**6**
Total général	**17**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is very good to excellent. The research performed by the group is very good to excellent with several contributions in the two different and complementary lines of research. The level of publication is very good. The visibility of the team is excellent as assessed by the invitations to international conferences, the organization of international conferences, the recruitment of PhD students, collaborations, and the obtention of significant funding and awards. The team is heavily involved in teaching, in clinical work and develops tools for innovation.

Context-related strengths and opportunities

This is a well-established team composed of 12 permanent members (2 PU-clinicians, 1 PU, 2 CR, 1 MCU-PH, 3 MCU, 3 IT), 3 post-docs and 3-4 PhD students on average.

The team is working on two different aspects of the pathogenesis of Legionella: (1) Bacterial determinants of Legionella-host cell interaction, and (2) Host, microbiota and environmental determinants of LD severity. On each of these themes, the team has obtained original results contributing new insights for the pathogenesis of Legionella and severity of Legionnaires' disease.

The production of the team is very good with nine senior author articles in non-clinical journals (2 in primary journals, J Mol Biol, Cellular Microbiology) and 11 papers in collaboration with French and international collaborators (PNAS, PLoS Pathogens, 2 mBio). The team has also produced 19 papers in clinical publications (among which 9 in FLC position) and eight reviews or chapters.

The team has an excellent national and international visibility. The team has been very successful in obtaining national and fundings (grants from ANR, DGOS PROGLEGIO, Labex Ecofect, PEPR MIE / VORTEX, IDEX Breakthrough WANTED for a global funding of about 2,46 M€). Two PIs has been invited to 6 international meetings and members of the team are involved in the organization of local, national and international meetings. The team has been very attractive and trained 14 PhD students over the period.

The team is heavily involved in teaching in the faculty of Sciences, Medicine, or Pharmacy and the IUT. Members have also teaching responsibilities.

The team has been very productive for its non-academic activities. Team members obtained an industrial contract and filled three different patents.

All members of the team are involved in society outreach towards students (from secondary schools to faculties of science or medicine), patients and general public through participation to various events or communication to the media.

Context-related weaknesses and risks

The number of publications in prestigious journal is limited.

The team develops research projects on many different topics that require a wide array of technical expertise:
Axis 1: effectors of the T4SS Dot/Icm, T1SS, relationship between plasmid pLPP integration and virulence, Lp resistance to macrolides and c-di-GMP dependent signaling pathway.
Axis 2: host-pathogen-derived cell surface associated proteins, host immune response to clinical isolates, pathophysiology of severe LD, environmental determinants of human infection and severity of LD.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team wants to continue to develop its two main research axes in the fundamental and clinical study of Legionnaires' disease: i) Bacterial determinants of Legionella-host cell interactions and ii) Host, microbiota and environmental determinants of LD severity. They have already obtained funding to pursue these studies, produced a number of data sets and seven manuscripts are in preparation. Specifically, for the fundamental part, they want to i) further characterize the control of the T4SS Dot/Icm system and the role of T4SS effectors, ii) perform a comparative genomic of strains, iii) analyze the immune response to infection, and iv) explore the potential link between antibiotic resistance, tolerance and persistence of Legionella. For the clinical part, they

want to understand the relationship between and its human host and to look at factors explaining variation in the severity of the disease.
The team has a unique position through its basic research group, the clinical microbiology team and the reference laboratory. The achievement of the different projects would require a number of technical expertise, some of which will be developed in the team. Some parts of these projects will be feasible through collaborations.

RECOMMENDATIONS TO THE TEAM

The team should focus on a more limited number of projects to reinforce its international visibility.
The team should increase the publications in prestigious journals.

Team 14: Mr Laurent Genestier / Mr Emmanuel Bachy

Name of the supervisor: Lymphoma Leukemia ImmunoBiology (LLIB)

THEMES OF THE TEAM

The team brings together researchers and clinicians with complementary expertise encompassing from hematology and immunology to oncology, thus performing basic to translational and clinical research.
The team research focuses on three branches: (1) Pathophysiological mechanisms of lymphomagenesis and lymphoma progression; (2) Diagnostic and prognostic stratification tools based on RNA-seq and ATAC-seq data and; (3) Novel experimental models for therapeutic screening (PDX, in ovo, organoids).
In the last years, the unit has extended their research focus towards leukemia (both adult myeloid and pediatric B-cell acute leukemia) using preclinical models and translational research based on primary patients´ samples.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team was not evaluated in the previous evaluation.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	5
Maitres de conférences et assimilés	3
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	4
Personnels d'appui à la recherche	9
Praticien hospitalier	3
Sous-total personnels permanents en activité	**25**
Enseignants-chercheurs et chercheurs non permanents et assimilés	8
Personnels non permanents d'appui à la recherche	7
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**18**
Total général	**43**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent. The team demonstrates outstanding scientific productivity, strong clinical integration, and broad expertise in their research topic. Its high-impact publications, substantial national and international funding, and close ties with industrial partners highlight excellent translational capacity and visibility. While limitations exist in PhD funding and European grant coverage, the proposed trajectory is ambitious, coherent, and well aligned with emerging therapeutic opportunities, positioning the team for continued excellence and impact.

Context-related strengths and opportunities

The team benefits from 14 full-time researchers, four postdocs, three PhD students and 12 technical staff members (8 tenured and 4 contractual positions). Interestingly, women represent 63 % of the entire staff and, specifically 43 % of the permanent staff out of which two are PI or coPI. In addition, a total of seven students obtained the PhD during the evaluation period and two HDR defended in the last funding period.
During the last period, the team made major achievements in the areas of epigenetics and T-cell lymphomas, genomic alterations and experimental models in B-cell lymphomas, microenvironment alterations in pediatric B-cell leukemia, inflammation in myeloid hemopathies and Vexas syndrome, epigenetics and T-cell lymphomas, immuno-therapeutic intervention and CAR-T cells and OMICS, Bioinformatics and AI, resulting in an outstanding scientific production.
The team has produced 25 original scientific publications, 61 clinical articles, 33 reviews/editorial comments/Book chapters as first or last authors. Additionally, they collaborated as coauthors in 46 original papers, 210 clinical articles and 6 reviews/editorials/book chapters. It is important to highlight high quality publications such as in Leukemia, Lancet Digital Health, Blood and JCI.
Another strength of the team is the both national, and international funding raised in the last period. Overall, the team leveraged nearly M€7, obtaining a total of 68 grants, out of which they participate as coordinators in 61. These included academic grant (Ligue Nationale Contre le Cancer, CALYM Carnot Institute, ANR FLINOVO, INCA HR-HG, EP PerMed JCT2024) and industrial contracts (Servier, AstraZeneca, Roche, Bristol Myers Squibb, AMGEN). In short, the team obtained national and international funding, clinical activity and private funding, demonstrating an excellent capacity for technology transfer.
The Team benefits from fruitful collaborations as a member of the CALYM Carnot Institute and has been able to forge interactions with national and international industrial partners guaranteeing a rapid and efficient transition from bench to bed translation and thus improving patient care.
Altogether the team has an excellent capacity for technology transfer and licensed one patent.
Amongst the tasks of the team are training duties for PU-PHs/MCU-PHs (100 h/year/person university and post-graduate) such as Head of different departments and services, clinical duties, members of societies and scientific networks (LISA, GBMHM, French Hematology Society, AssHIB, OncNGS consortium, VEXAS). This also benefits the team which has access to a large number of clinical samples.
The team has an outstanding national and international recognition as observed by the invited conferences of their members including EHA, ESH, SFH, and different national liver associations.
The team supports public outreach and dissemination of the information to the general public and to the society and several members have participated in different presentations (Parliamentary and Senatorial Working Group on CAR T cells, Inserm, CNRS webinars), publications in newspapers (Le Mond), opinion articles (The Conversation, AOC).
The team benefits form a collaborative environment in CIRI that will allow strengthening their expertise with other teams of the unit (e.g.: inflammation, immuno-therapeutic intervention, etc.).

Context-related weaknesses and risks

A clear weakness is the limited source of funding for PhD students with only currently three students; however, the team seems to overcome it with excellent publications. Nonetheless, the funding raised by the team should be more noticeable in terms of training and publications.
The team participates in a European network and funding exists but is limited especially in the field of B-cell lymphoma, however, more funding is available for CAR-T cell therapies and T-cell lymphoma.

ANALYSIS OF THE TEAM'S TRAJECTORY

During the new mandate, the team will focus on the role of an epigenetic regulator in T cell lymphomagenesis and on the impact of epigenetic reprogramming and NK-like trans-differentiation on T-cell lymphomagenesis in the theme ´Epigenetics and T-cell lymphomas´. Regarding the topic ´Genomic alterations and experimental models in B-cell lymphomas´ they will decipher the dialogue between the microenvironment and leukemic cells / hematopoietic cells in refractory / relapse patients, and try to find a mechanism through Interleukins and soluble factors to stop this kind of communication. Epigenetic signatures that could be involved in the different leukemogenesis processes and leukemia outcomes for these patients around the world will be further investigated in the next funding period under ´Microenvironment alterations in pediatric B-cell leukemia´. In the area of ´Inflammation in myeloid hemopathies and Vexas syndrome´, the team will investigate inflammasomes as a potential therapeutic target for i) inhibiting autoinflammatory manifestations and ii) killing cancer cells in CMML. For the Vexas syndrome, they will implement a novel model, and regarding ´Immuno-therapeutic intervention and CAR-T cells´, the team has already largely characterized the efficacy and specificity of this CAR T cells against CD4-expressing tumor cell lines. Finally, for the ´OMICS, Bioinformatics and AI´, the team will focus on the detection of new markers, deconvolute microenvironment signals, infer gene interactions, increase classification accuracy and predict patient prognosis.

RECOMMENDATIONS TO THE TEAM

The team is recommended to both maintain the excellent industrial funding and seek more European funding by applying to Horizon calls.
In the proposal it is not clear whether the technical staff under contracts are permanent or temporary.
The team is recommended to clarify the number of publications per PhD students or at least the average and their current positions to understand career development.
The team is encouraged to foster public outreach with patients´ associations, advocacy groups, high schools and science fairs.

Team 15: Immunobiology of Viral Infections (IbIV)

Name of the supervisor: Mrs Branka Horvat

THEMES OF THE TEAM

The team studies interactions between RNA viruses (Nipah and measles viruses) and the innate immune system to develop therapeutic strategies. New projects, including leadership of a HORIZON consortium emerged with the SARS-CoV-2, focusing on the link between long COVID and endogenous retroviruses. Combining molecular, cellular, and animal-model studies, the team has developed antiviral approaches with academic and industry partners. They demonstrated the efficacy of fusion-inhibitory peptides against MeV, NiV, and SARS-CoV-2 in preclinical models and contributed to a new anti-NiV vaccine.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous HCERES report noticed as high-risk parts of the team's program, notably the objective to study mechanisms of high Henipavirus pathogenicity. In response, the team carefully assessed project risks and organized its activities accordingly, leading to strong productivity: 33 original publications in 2019-2024, including 19 with team members in FLC positions. Postdocs and PhD students were involved in different projects, contributing to high-level outputs. Following HCERES recommendations, major efforts were made to recruit permanent staff, resulting in two new CR positions (INSERM and CNRS), and the arrival of z research engineer in 2021 (High Containment activities). The team will further expand with the fusion with Prof. C. Riedel's group in 2027. Substantial national and international funding (ANR, AVIESAN, LabEx Ecofect, NIH, ERINHA-Advance, Horizon-HLTH HERVCOV) has secured the team's operations. Overall, the team has achieved strong national and international visibility in the field of Henipavirus research.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	2
Praticien hospitalier	0
Sous-total personnels permanents en activité	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels non permanents d'appui à la recherche	1
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**6**
Total général	**11**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is outstanding. The IBIV team has made major contributions to understanding henipavirus pathogenesis, virus–host interactions, including novel insights into innate immunity against RNA viruses and viral replication machinery. The team has developed innovative antivirals and vaccines, held patents, and contributed to SARS-CoV-2 research. With 33 publications, strong training activities, and significant competitive funding, the team demonstrates exceptional scientific and translational potential.

Context-related strengths and opportunities

The Team IBIV is a well-established mid-sized group composed of four permanent researchers (1 DR1, 2 CR, 1 IR), two engineers, one post-doc and three PhD students, and will expand in 2027 with the integration of Prof. C. Riedel's group (3 additional permanent members). In the fields of henipavirus pathogenesis, the team characterized Nipah virus infection in preclinical models, sequenced viral strains and the genome of Pteropus medius, and developed a specific preclinical model pluripotent stem cell line with a distinct interferon-stimulated profile. A manuscript comparing transcriptomic signatures of NiV-infected specific preclinical model and human cells is in preparation. A Pteropus aviary is also under construction with VetAgro Sup.
In the axis of virus–host interactions studies, the team has identified several key mechanisms regulating innate immune responses to henipaviruses and paramyxoviruses. Major findings include the discovery of NiV W-mediated NF-κB inhibition through 14-3-3 binding, the critical role of MyD88 and MAVS in controlling NiV and MeV in vivo, and the demonstration that the cGAS/STING axis—classically activated by DNA viruses—is also activated by RNA viruses via mitochondrial DNA leakage induced by syncitia formation. These results open new translational avenues by positioning STING as a promising antiviral target. Regarding the study of the structure and function of mononegavirus RNA synthesis machinery, the team has clarified key molecular interactions governing replication, including MeV C recruitment to the ribonucleocapsid through interaction with P and recruitment to viral factories, and determinants of P–L complex assembly. The team identified a region in henipavirus P/V/W proteins responsible for phase transition and amyloid formation by the W protein. Finally, the roles of LLPS, amyloid-like fibers and the assembly and mechanisms of the RNA synthesis machinery will be addressed using cryo-EM and functional assays (in vitro and in cellulo).
The team has strong expertise in antiviral approaches. Through an international collaboration, it developed aerosolizable fusion-inhibitory peptides effective against NiV, MeV and SARS-CoV-2, validated in preclinical models, leading to three patents. Additional developments include single-chain variable fragment–based antivirals and CD40-targeting vaccine candidates showing robust protection in preclinical settings. During the COVID-19 crisis, the team rapidly contributed insights into SARS-CoV-2 pathogenesis, early infection stages and age-dependent immunity using organotypic models.
IBIV produced major scientific outputs with 33 publications (including Science, PLOS Pathogens, Nature Communications), 19 as FLC, stemming from national and international collaborations. The team shows strong translational potential (4 patents) and has strong collaborations with regional and international (Switzerland) biotech companies, actively participating in several industry-funded research projects supported by major investors and national agencies (ANR). The team maintains active training and teaching activities, with six PhD students (four thesis defended), two HDR obtained, and involvement in biosafety courses. It also hosts the measles virus biobank. Team members contribute as experts, editors, and organizers of international meetings.
The team has secured significant national and international funding (9 as coordinator (3.465M€)/7 as partner (2.445M€)) including ANR, EU Horizon (as coordinator), NIH, AVIESAN, regional and DGA support for research and PhD fellowships. BH and OR are regularly interviewed in the press and on television.

Context-related weaknesses and risks

The only weaknesses or threats are those identified by the team itself: the high costs associated with access to and experiments conducted in specific BLS4 facility, as well as the substantial administrative paperwork required by the ANSM. The team also highlights the difficulty of obtaining clinical samples from NiV-infected patients. Finally, the lack of start-up creation is considered a weakness, particularly regarding the potential valorization of their patents.

ANALYSIS OF THE TEAM'S TRAJECTORY

The IBIV team has pursued research on RNA virus–host interactions and antiviral strategies, building a strong track record of national and international collaborations, industry partnerships, and scientific productions. In 2021, a young independent group led by former PhD student emerged from IBIV. The team's research trajectory will continue and expand within the MIHVA team (new name) from January 2027, with the integration of two researchers and one engineer, adding expertise in viral particle morphogenesis, host–virus interactions, cryo-electron tomography (ENS cryo-electron microscopy platform), and bioinformatics.
Over the next mandate, MIHVA will focus on four main axes:
Structure and function of mononegavirus RNA synthesis machinery – Using cryo-EM and functional assays, the team will study polymerase complex assembly and the regulation of RNA synthesis by NiV C. Existing data and protocols provide a strong foundation for these investigations.
Virus–host interactions and innate immunity – Using in vivo models in specific BSL2 and specific BLS4 facility laboratories, the team will further dissect STING immune pathways, cytokine signatures, and cell death mechanisms, and explore STING-targeted antiviral strategies with agonists.
Pathogenesis in natural and accidental reservoirs – The establishment of a BSL2/3 animal facility for specific preclinical models in Lyon will enable the study of the immune response in the natural NiV reservoir, aiming to understand how specific preclinical models control the infection, using Cedar virus, a closely related bat-borne henipavirus (BSL2 model).
Development of novel prophylactic and therapeutic antivirals – Translating fundamental findings into therapies, the team will advance NiV-specific antibodies, NiV-virus-like particle platforms delivering immune agonists, and diagnostic/prognostic biomarkers for COVID-19, in collaboration with academic and industrial partners.
Development of novel prophylactic and therapeutic antivirals – Translating fundamental findings into therapies, the team will advance NiV-specific antibodies, NiV-virus-like particle platforms delivering immune agonists, and diagnostic/prognostic biomarkers for COVID-19, in collaboration with academic and industrial partners.
Leadership will transition to Dr. L.-M. Bloyet and Prof. C. Riedel (retreat of B. Horvat), ensuring continuity and multidisciplinary integration. The diverse expertise of team members will facilitate applications to a broad range of national and international funding calls and strengthen industry interactions. Training of Master's students, PhD candidates, and postdocs will remain a priority, with high-level publications as an expected outcome.
International collaborations will be reinforced, including grant application and creation of a unique specific facility with the Friedrich Loeffler Institute and/or strengthened partnerships with IISER Bhopal, India, ensuring access to field samples from bat reservoirs and infected patients.
In conclusion, IBIV has made significant advances in the understanding of measles and Nipah virus immunopathogenesis. The expanded MIHVA team, strengthened by new expertise and cutting-edge facilities (including an animal facility and a cryo-EM platform), is exceptionally well positioned to continue high-impact research on viral pathogenesis, host–pathogen interactions, and the development of innovative therapeutics.

RECOMMENDATIONS TO THE TEAM

The team IBIV, transitioning to the expanded MIHVA group, has demonstrated excellent scientific productivity, strong translational potential and high international visibility. The following recommendation could be proposed to consolidate impact and sustainability: improve clinical interactions to secure the access to NiV-infected patient, promote valorization of patents and try to create a start-up, translate intellectual property into industrial applications, take advantage of the unique specific facility to foster international collaborations, continue securing competitive national and European funding (BSL4 costs).

Team 16: Group Neuro-Invasion TROpism and VIRal Encephalitis (NITROVIRE)

Name of the supervisor: Mr Cyrille Mathieu

THEMES OF THE TEAM

The Team NITROVIRE, emerged in 2021 and comprising ~10 members, aims to identify key determinants of viral neuroinvasion and encephalitogenesis using advanced ex vivo organotypic models. By studying infections of the lung, liver, and brain, the team seeks to uncover early biomarkers and mechanisms that enable viruses to reach or affect the CNS, ultimately guiding the development of next-generation antiviral and neuroprotective strategies. Research focuses on BSL-2 to BSL-4 viruses capable of causing direct or indirect brain disease, including Paramyxoviridae, Orthomyxoviridae, Flaviviridae, and Filoviruses/Nairoviruses.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Group 16 is a new team, no previous recommendations

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Praticien hospitalier	0
Sous-total personnels permanents en activité	**3**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels non permanents d'appui à la recherche	1
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**6**
Total général	**9**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment is highly promising for a young and highly dynamic group. NITROVIRE combines strong expertise in viral neuroinvasion with innovative ex vivo and organotypic models, producing outstanding, high-quality publications, securing competitive funding, training PhD students and postdocs, and engaging in patents and industrial partnerships. Key strengths include unique models and strong collaborations, while risks relate to limited permanent staff, BSL-4 dependency, and recruitment challenges.

Context-related strengths and opportunities

The team NITROVIRE is a new team that emerged in early 2021 from Team 15 (IBIV) under the leadership of a former PhD student in CIRI. The team currently includes one DR1 emeritus, one IR (retiring in 2028), and one IE as permanent staff. The team benefits from additional CDD from INSERM including one CR (until 2027) and one IE (until 2026). Taking advantage of the ex vivo tissues developed by the PI, the team characterized MeV and SARS-CoV-2 tropism and identified key mutations in paramyxovirus fusion proteins that destabilize surface glycoprotein interactions, facilitating CNS invasion. Through international collaborations, the team identified compensatory mutations restoring prefusion stability (Columbia University), and neutralizing antibodies stabilizing F, providing insights for vaccines, nanobodies, and structural studies (La Jolla). Through henipavirus reverse genetics and biochemical approaches (in collaboration), the team uncovered the role of redox regulation in phase transitions and V/W protein fibrillation, demonstrated how these proteins modulate innate immune pathways (IFN-I, NF-κB), and characterized differences in their aggregation properties, with potential implications for CNS pathology. Organotypic platforms: A broad panel of rodent and human organotypic models (brain regions, lung, liver, kidney) supports multi-omics analyses—transcriptomics, proteomics, interactomics, metabolomics—to study early infection events and organ-specific determinants of CNS invasion in collaboration with teams VIRIMI and HepVir (CIRI). In the field of therapeutic exploration, these results pave the way for developing antiviral strategies targeting both the virus and the host. The team demonstrated the limitations of remdesivir and IFN-I against paramyxovirus, and hydroxychloroquine to block SARS-CoV2, identified metabolic dependencies of flaviviridae (e.g., NAD biosynthesis, hypoxia-induced pathways) and drugs influencing RNA virus replication (MeV and NiV), and is now evaluating combinatorial, organ-specific antiviral approaches guided by ex vivo models. Since its creation, NITROVIRE has produced major scientific findings, with 35 publications, including nine as FLC (in high quality journals such as Nat comm, mBio, Cell Mol Immunol, Nat Immunol), often co-authored by the team's PhD students and post-docs. Over the evaluation period, NITROVIRE has trained five PhD (2 completed defenses), four post-docs, and numerous additional students. The team staff also maintain sustained teaching activities and contribute to the training of personnel and students for BSL-3 work. Team members contribute as experts (including co-direction of the CIRI BSL-3 facility) and serve as editors in internationally recognized journals. Dr. Mathieu is also regularly invited to give conferences. The team is engaged in translational activities through multiple industrial partnerships and has contributed to three patents supporting the development of innovative antiviral strategies. Since 2021, the team has obtained substantial competitive funding through major national (ANR, ANRS), European (H2030 as partner), intramural (AID, COPOC, Intramural-CIRI), and international programs (Columbia agreement) and institutional collaborations (6 as coordinator(778k€) / 10 as partner (1.225M€). The team members participate to numerous interactions with the general public and society.

Context-related weaknesses and risks

The NITROVIRE team faces structural and operational vulnerabilities, notably the lack of at least one permanent researcher, which limits long-term continuity, particularly for the hepato-cerebral axis. Several ongoing projects are supported by postdocs and PhD students who plan to join the lab in the future, and the reopening of BSL-4 facilities in 2026 is critical for advancing these studies. Recruitment of clinicians and specialized personnel remains a potential bottleneck. Funding of the team is good, but experimental costs, especially for BSL-4 work, are high. European procedures for BSL-4 activities can delay or block applications. Clinical interactions remain limited, and as stated by the team leader, regulatory frameworks (FSD) sometimes restrict optimal staffing and operations. The team must also ensure careful coordination to avoid internal competition with other CIRI teams working on related viruses. Nevertheless, the organotypic models developed by NITROVIRE are expected to facilitate collaborations across the institute, providing a unique platform for shared projects. Ensuring continuity of expertise, strengthening clinical links, and maintaining access to high-containment facilities remain essential to mitigate these context-related risks.

ANALYSIS OF THE TEAM'S TRAJECTORY

Over the next mandate, NITROVIRE aims to advance understanding of viral neuroinvasion and encephalitogenesis through integrated studies of the brain and peripheral organs, using BSL-2 to BSL-4 Paramyxoviridae, Flaviviridae, and Nairovirus. The team's approach combines mechanistic, molecular, and translational perspectives, leveraging ex vivo and organotypic models that allow real-time tracking of viral replication and host responses. Comparative analyses across organs, including lungs and liver, will provide critical insights into virus-host interactions, mechanisms of CNS invasion, tissue-specific responses, and host factors required for infection, dissemination, or latency.
The research is structured around three main axes:
The first, the in-brain axis, focuses on deciphering how viruses invade the CNS and behave in neurons. Using reverse-genetic Paramyxoviridae systems carrying reporter genes and tagged surface glycoproteins, phosphoproteins, or polymerases, the team will study the effects of mutations on neuroinvasion and neurodissemination, and assess the impact of metabolic modulators and compounds affecting neuronal molecular motors on viral entry, replication, and spread in the brain.

The second axis, the respiro-cerebral axis, investigates how airborne encephalitic RNA viruses, including orthomyxoviruses (IAV) and paramyxoviruses (MeV and NiV) exploit the cellular metabolism to develop host-metabolic therapies. Using ex vivo rodent and human lung models, the team will analyze virus-induced host alterations, with a particular focus on viral factory formation and genome methylation. This axis will also evaluate the antiviral potential of metabolic regulators and direct-acting antivirals to identify novel host-directed therapeutic strategies.
The third axis, the hepatocerebral axis, addresses Flaviviridae-host interactions in the liver to identify factors that facilitate neuroinvasion or trigger encephalitis. Building on findings that inhibitors of the nicotinamide biosynthesis pathway block DENV replication, this axis will extend analyses to additional flaviviruses and, where feasible, to hemorrhagic viruses such as EboV, RVFV, and CCHFV. Antiviral efficacy and consequences on innate immunity will be studied using ex vivo and in vivo preclinical models, and human organotypic cultures, with the goal of identifying early biomarkers of encephalitis.
Overall, NITROVIRE's trajectory combines innovative experimental platforms, mechanistic studies of viral replication and host responses, and translational approaches to antiviral development. By integrating studies of brain, lung, and liver infection and leveraging cutting-edge molecular tools, the team is well positioned to make major contributions to understanding and preventing viral encephalitis.

RECOMMENDATIONS TO THE TEAM

The NITROVIRE team has demonstrated strong scientific productivity, innovative ex vivo models, and high-translational potential. Continue your excellent work. To further consolidate its impact and long-term sustainability, the following recommendations could be proposed: recruitment of at least one permanent researcher to maintain the dynamism and growth trajectory of this young research group, implement collaboration with CIRI teams working with the same virus to avoid internal competition while leveraging ex vivo models for shared projects, continue securing competitive national and European funding.

Team 17: NLRP3 Inflammasome and Immune Response to Sepsis (NLRP3)

Name of the supervisor: Mrs Bénédicte Py

THEMES OF THE TEAM

The team works on the activation mechanism of the NLRP3 inflammasome and the impact of the NLRP3 signaling pathway in autoinflammatory CAPS, aging, diabetes and in sepsis. The goal is to understand pathological underpinnings and develop NLRP3 targeting drugs.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team should focus on the publication of papers currently under preparation. The published work should be used as a basis for the submission of new collaborative grants to maintain the momentum of the research to capitalize on utilizing the newly generated research resources.
The team has published well (25 FLC and 64 non-FLC) and in excellent journals in their fields both on the fundamental and the clinical side. Two clinician-researchers have been recruited with expertise in sepsis, and many new international collaborations are established to broaden the clinical spectrum of conditions the NLRP3 inflammasome will be studied in utilizing their unique resources (mutants, models). They have collaborative grants and are applying for more.

The strategy should be to fully integrate the new team members into the current team management structure. The team members seem integrated: both has published with the team and will lead a translational project for the next mandate.

The team should priorities research with backup plans to ensure the productive output stream in case competitors publish results before the manuscripts of the team will be accepted. Unclear if the team had a strategy for doing so, but the research is well published in excellent journals.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	1
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
Praticien hospitalier	0
Sous-total personnels permanents en activité	**4**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels non permanents d'appui à la recherche	1
Post-doctorants	0
Doctorants	5
Sous-total personnels non permanents en activité	**7**
Total général	**11**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent. Building on her ERC CoG, the team has developed a set of unique methods and models (mutant models) for addressing the mechanism of NLRP3 activation with a focus on PTMs, and its relevance in disease and ageing. By recruiting clinical researchers, the translational axis is significantly strengthened – as is the network of excellent international collaborators.

Context-related strengths and opportunities

The team leveraged from ERC CoG (2015–2022, extended for COVID and maternity leave) to build strong experimental platforms, including KI, KO and double KI/KO preclinical models. These tools provided a competitive edge in a demanding field and supported high-impact publications on NLRP3 PTMs and disease mechanisms: seven FLC fundamental and 17 FLC clinical papers (e.g., J Exp Med, Nature Communications, Critical Care). The team has also expanded a global network of leading collaborators, enabling joint grants and new research directions.

Major findings include identifying phosphorylation/dephosphorylation (S806) sites crucial for priming NLRP3. NLRP3 gain-of-function drives CAPS autoinflammation, but mutations vary in their response to priming or activation. The team developed patented functional tests to distinguish pathogenic mutations from polymorphisms and classified 34 mutations into 5 symptom-based groups (J Exp Med), with implications for CAPS stratification and personalized treatment.

Translational research expanded through recruitment of two PU-PH/MCU-PH, facilitating clinical and industrial funding. The team linked high and persistent inflammasome activity to immune responses in sepsis. Using a preclinical model, they showed that PD-L1+ regulatory plasma cells arise during sepsis and correlate with increased mortality (Nature Communications).

The team includes two HDRs who supervised six PhD students (2 international; one completed), three postdocs and four engineers; departing members obtained strong positions in academia, high schools, or industry. Three new permanent clinician-scientists (PH) will join in the next period, strengthening the translational capacity. Funding is strong: team researchers coordinate 13 of 15 grants (2,121 k€ total), including ANR-PRCs, RHU, UCBL-1 young investigator grants, fellowships and an extension of ERC CoG.

The team leader and members were invited speakers at international conferences and serve on juries, grant panels and PhD committees. The PI organized IRCI 2022 and two symposia and is editor/reviewer for several journals, including top-tier ones (Science, Nature Immunology). The PU-PH serves on the SAB of Immunotherapy for Infectious Disease, underscoring the team's recognized expertise and international visibility. Their results contributed to PNDS (diagnostic guidance for CAPS), and they published two reviews in Médecine/Science. Like other CIRI teams, they hosted high-school students. The team holds several patents and industrial contracts with BioAge Labs (USA), Bumper Sciences (CH), Ermium Therapeutics (FR), Volition (BE) and Hemotune (CH), totalling 101 k€.

Context-related weaknesses and risks

Highly competitive field, but the plan, toolbox and collaborators are good. Risk is on the personnel side, but lab space for the group may also be a limiting factor for hosting visitors and expanding the size of the group.

Teaching duties are considerable for one MCU-PH (200h/yr) on top of 50 % clinical duties at the Immunology lab of Lyon University hospital, which could slow down research. However, it was made clear that these duties were tied to establishment of the sepsis cohort for research (project 2) and thus complementary.

As pointed out by the team leader, non-permanent contracts for engineers/technicians may represent a risk for the continuity in methodological expertise, especially animal work, and delay progress since time and resources are spent on training students and temporary employees.

Outreach could be better, there is no information about radio/tv/news or social media, or seminars for the general public.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team will build on recent findings and preclinical models to study the role of NLRP3 during aging, diabetes and Alzheimer's disease in collaboration with top-tier researchers in the field. They will further continue the work on determining the mechanism of NLRP3 priming and investigate the underpinnings of the atypical symptoms of CAPS patients with mutations bypassing NLRP3 priming. This is a logic continuation of the team's previous work and an expansion into other diseases, which is feasible with the expertise in the team and collaborators. The recruitment of a permanent full-time researcher with expertise in inflammasomes will strengthen the team considerably. The sepsis line of research will continue with studying a possible link between hyperinflammation during and immunosuppression after sepsis, and use a preclinical model of sepsis for elucidation of a possible causal link. The strong expertise of the team and the tools of which it disposes should allow the successful implementation of both projects.

RECOMMENDATIONS TO THE TEAM

Keep on with the excellent research; the translational plans including studies of NLRP3 variants in more diseases are exciting, and the team have established collaborations with some of the best international researchers in this field. The committee recommend considering ERC Advanced grants and to try to recruit international postdocs e.g., through MSCA funding.

The team should continue to push for a permanent technician for the animal work and procedures; it is clear from the description that it is difficult to continue trained personnel on temporary contracts since they seek permanent positions elsewhere. Similarly, conversations around lab- and office space with CIRI should be initiated to ensure possibilities for expansion of the group. The committee recommends strengthening scientific and public outreach activities to increase the visibility and societal impact of the team's research.

The recruitment of a new permanent researcher who will be full-time at CIRI is great. Strategies to secure their career and independence in research should be discussed in the next mandate.

Team 18: Retroviral Oncogenesis (OR)

Name of the supervisor: Mrs Hélène Dutartre / Mrs Chloé Journo

THEMES OF THE TEAM

The team studies host-pathogen interactions in chronic viral infections leading to inflammation or cancer, focusing on HTLV-1, recently prioritized by WHO. Research addresses intra-host viral dissemination via cell-associated virions, viral manipulation of protein networks and transcriptions in infected cells, and modulation of non-infected immune cells through the microenvironment. Combining in vitro studies with viral sequences from endemic genotypes and ex vivo analyses of HTLV-1 patient cohorts and naturally infected specific preclinical models, the team integrates molecular, cellular, and organismal approaches in collaboration with clinicians, epidemiologists, and veterinarians.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has addressed the recommendations of the previous evaluation report. Public outreach has been intensified through collaboration with HTLVAware, including the development of a French-language version of the website, which will enhance awareness of HTLV-1 infection in French regions. The team has exploited translational opportunities by developing antiviral screening platforms and drug evaluation strategies in collaboration with chemists and structural virologists, although initiating industry partnerships remains challenging given the neglected nature of HTLV-1. National and international collaborations have been strengthened, securing access to HTLV-1 patient cohorts in France and abroad (Brazil, Japan), and maintaining a long-standing partnership with the CNRS primatology station to study naturally infected STLV-1 specific preclinical models. A shared biobank of STLV-1 samples now supports both national and European research projects. The previous concern regarding the integration of research axes has been addressed by reorganizing the team into three functional axes that connect molecular, cellular, and in vivo studies around a common question of HTLV-induced signaling, improving synergy and resource sharing. The team has successfully diversified funding, securing competitive ANRS, ANR, and Ligue contre le cancer grants totaling €1.559M, ensuring research continuity until 2028.
Overall, the team demonstrates strong responsiveness and strategic alignment with prior recommendations.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	0
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Praticien hospitalier	0
Sous-total personnels permanents en activité	**3**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	3
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**7**
Total général	**10**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is very good to excellent. The team advances fundamental and translational research on HTLV-1 pathogenic signaling, viral transmission, and immune manipulation, integrating molecular, cellular, and in vivo approaches. With strong expertise in viral biofilms, Tax oncogenic pathways, and non-human specific preclinical models, the team has produced significant scientific achievements, secured competitive funding, strengthened collaborations, and contributed actively to training and public outreach.

Context-related strengths and opportunities

The team benefits from a highly coherent scientific focus on HTLV-1 pathogenic signaling, enabling the integration of mechanistic virology, immunology, and translational research. Its long-standing expertise in viral biofilm biology and Tax interactomics positions the group as a recognized leader internationally. Access to unique resources, including a colony of naturally STLV-1–infected non-human specific preclinical models and large collections of endemic HTLV-1 genotypes, constitutes a rare and strategic advantage, enabling research lines that cannot be pursued in most laboratories worldwide.
The team's multi-scale methodological strengths (high-resolution imaging, proteomics, proximity interactomics, omics approaches, primary cell analyses) support comprehensive investigations of viral transmission, cellular transformation, and immune modulation. This methodological diversity strengthens the scientific impact of the work and increases the team's visibility in the HTLV field.
Their strong integration in international networks (HERN, IRVA, collaborations with Japan, Brazil, USA) ensures continued access to patient samples, facilitates comparative virology studies, and increases competitiveness for international grants.
The team produced a total of 15 peer-reviewed non-clinical publications during the last term, including seven in FLC position and eight in non-FLC position in highly regarded journals such as several Plos Pathog, PLoS Negl Trop Dis, Retovirology, etc. They also published nine international reviews.
The team has demonstrated an excellent ability to secure competitive funding (ANR, ANRS, Ligue contre le cancer, FRM), guaranteeing financial stability until at least 2028. With an FRM labelisation two ANR as coordinator and a total of 2,5 M€.
Pedagogical involvement and active participation in scientific committees and peer-review at national and international levels reinforce the team's institutional visibility.
Public engagement activities, including contributions to Médecine/Sciences and outreach via educational platforms, further increase societal relevance.
Current external trends create favorable opportunities:
- renewed institutional interest in HTLV-1 (WHO prioritization, ANRS funding focus)
- increasing global awareness of neglected viral diseases
- potential for translational development (drug screening, antiviral strategies)
- emerging opportunities for North–South collaborative programs
- planned recruitment of permanent ITA staff, strengthening technical continuity

In conclusion, altogether, the team benefits from a robust scientific environment, strong collaborations, strategic resources, and rising international interest, positioning it well for continued high-impact research and expansion.

Context-related weaknesses and risks

The team's main structural weakness is its small size, with only a limited number of PIs who must balance heavy scientific, administrative, and teaching responsibilities. This situation reduces the capacity to diversify research lines, limits responsiveness to large-scale calls, and increases vulnerability to unexpected absences or turnover. The absence of postdocs is another critical factor limiting research throughput, publication rate, and international competitiveness.
Although the team has a solid publication record, the overall number of original research papers remains moderate, partly due to the complexity of the models used (primary cells, non-human specific preclinical models) and limited manpower. Increasing publication output will require additional human resources, particularly postdocs and technical support.
Another weakness is the insufficient development of industry collaborations. Despite translational potential (e.g., antiviral screens, biofilm-targeting strategies), HTLV-1 remains a neglected pathogen with limited commercial visibility, reducing incentives for industrial partnerships. This structural constraint may hinder the development of applied research and reduce opportunities for diversified funding.

Externally, several risks threaten the long-term sustainability of some projects. The high cost of maintaining the specific preclinical model is a major concern; funding uncertainties or policy changes could reduce access to this unique resource. HTLV-1's low visibility in global health research prioritization remains an ongoing threat, despite recent WHO efforts. Competition for funding in host–pathogen interactions is increasing, and agencies may prioritize emerging or pandemic pathogens over chronic but neglected retroviral infections.
Finally, the difficulty of recruiting postdocs and attracting international students—partly due to the niche nature of the field and the limited visibility of HTLV-1 research—may limit the team's growth. Without strengthened recruitment, the team risks being under-capacitated relative to its scientific ambitions.

Overall, while the team is scientifically strong, structural constraints (size, workload), external factors (funding competitiveness, pathogen neglect), and logistical challenges represent significant risks that must be mitigated to ensure long-term resilience and scientific productivity.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team's trajectory demonstrates a coherent and ambitious continuation of its previous achievements, with a research program based on three highly integrated axes and two translational developments. Building on major advances in the understanding of the HTLV-1 virocell, viral biofilm biology, Tax interactomics and innate immune manipulation, the team has designed a project that deepens mechanistic investigations while expanding toward translational applications.
Axis 1 consolidates a decade of work on the viral biofilm, aiming to define its molecular composition, biogenesis and influence on infectivity through integrated proteomic, imaging and functional approaches. The axis is strengthened by collaborations with world-leading experts in high-resolution microscopy and HTLV cell-to-cell transmission, and by clear conceptual connections with Axis 2.
Axis 2 extends the team's recognized expertise on Tax by integrating proximity interactomics, autophagy receptor biology, imaging cytometry, kinomics and transcriptomics to understand how viral oncoproteins manipulate signaling platforms across cell types and across HTLV-1 subtypes, with multiple national and international collaborations supporting this multidimensional approach. The planned comparative analysis of viral effectors and phylogenetically diverse HTLV-1 strains will provide novel insights into viral oncogenesis and immune evasion.
Axis 3 builds directly on discoveries showing that HTLV-1 virocells impose tolerogenic or dysregulated states on innate and adaptive immune cells. The future work aims to decode the molecular and metabolic mediators of this dialogue through transcriptomics, lipidomics and proteomics, combined with functional immunology using patient samples secured through a strong clinical network spanning France, Brazil and the French Indies.
The first translational project leverages cellular models of virocell infectivity, interactomic maps and structural biology to identify vulnerabilities for antiviral development, pursuing drug screening, protein–protein interaction inhibition strategies and innovative structural approaches such as single-particle cryoEM and AI-based structure prediction. The second translational project capitalizes on a unique resource of preclinical models to investigate occult infections, a poorly documented state with direct implications for human diagnostics. The prospective monitoring of these models, combined with molecular and histological analyses, illustrates the team's capacity to bridge fundamental virology and public-health-relevant questions.

The team's trajectory is marked by clear scientific continuity, high methodological diversity, and well-established collaborations that support feasibility. The balanced combination of mechanistic virology, host–pathogen interactions, viral oncogenesis and translational objectives demonstrates a strong capacity to pursue innovative and internationally competitive research.

RECOMMENDATIONS TO THE TEAM

The team should continue strengthening the integration of its three scientific axes to ensure coherent progress and optimal use of shared technologies and datasets. Given the breadth and ambition of the program, clear prioritization and milestone planning will be important to prevent dispersion, particularly for omics-driven analyses and structural studies of viral effectors. Reinforcing bioinformatic support is recommended to manage and interpret the large volume of multidimensional data generated across axes.
The translational components would benefit from a more formal valorization strategy, particularly for antiviral screening approaches, Tax-focused structural work, and diagnostic perspectives emerging from studies of occult infections. Early engagement with technology transfer structures and potential industrial partners could enhance feasibility and impact.
Because the project relies heavily on access to patient samples and naturally infected specific preclinical models, the team should secure long-term clinical and veterinary partnerships and anticipate potential regulatory or logistical constraints. Finally, continued investment in international networking and public awareness efforts around HTLV-1 will strengthen the team's visibility, support future collaborations, and facilitate access to competitive funding.

Team 19: Staphylococcal Pathogenesis (StaPath)

Name of the supervisor: Mr François Vandenesch

THEMES OF THE TEAM

The project of the team focuses on Staphylococci's transition from the commensal to the pathogenic state, the regulation of these determinants from both a fundamental and clinical perspective, the pathophysiology of the different lineages, and the evaluation or production of innovative therapies, including therapeutic phages. The studies concern S. aureus but also non-aureus species.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has satisfactorily addressed the recommendations of the previous report by increasing the number of PhD students considering the size of the team. The team also reorganized its project into clearly identified research axes.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	6
Maitres de conférences et assimilés	9
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	10
Praticien hospitalier	2
Sous-total personnels permanents en activité	**27**
Enseignants-chercheurs et chercheurs non permanents et assimilés	3
Personnels non permanents d'appui à la recherche	5
Post-doctorants	0
Doctorants	10
Sous-total personnels non permanents en activité	**18**
Total général	**45**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent to outstanding. The research performed by the group is excellent to outstanding with several contributions in the seven different lines of research. The level of publication is excellent. The visibility of the team is outstanding as assessed by the invitations to international conferences, recruitment of PhD students, collaborations, the obtention of important funding and distinctions. The team is heavily involved in teaching, in health care and developing tools for innovation.

Context-related strengths and opportunities

This is a well-established team composed of 24 permanent members (6 PU-PH, 1 PH, 6 MCU-PH, 3 MCU), 23 non-permanent staff.
The team is working on seven different aspects of the pathogenesis of Staphylococcus species. On each of these themes, the team has obtained original results contributing new insights and paradigms for the pathogenesis of Staphylococci species.
The production of the team is excellent with 58 papers in non-clinical journals but only a few as senior authors in primary journals (1 Nature Microbiology, 1 Nature Communications, 1 ISME J, 2 Nucleic Acids Research) and 48 papers in collaboration with French and international collaborators. The team has also produced 40 papers in clinical publications (among which 26 in FLC position) and 16 reviews or chapters (8 in FLC position).
The team has an outstanding national and international visibility. The team has been very successful in obtaining national and European funding (grants from ANR, 2 RHU fundings, ERA-NET for a global funding of about 15,8 M€). Two PIs has been invited to > 20 international meetings and four members of the teams are involved in the organization national meetings. Five members of the group are involved in the organization of national and international meetings. Finally, the team has been very attractive and trained 26 PhD students over the period.

The team is heavily involved in teaching (1700 hours) in the faculty of Medicine, the faculty of Pharmacy and the IUT. Members have also teaching responsibilities. Eleven members of the group work also in the hospital with 3 clinicians, eight biologists working at the Croix Rousse hospital, including three who managed the Microbiology department and four involved in the direction of the National Reference Center for Staphylococci.

The team has been very productive for its non-academic activities. Team members obtained four grants from industrial companies, filled four different patents.

The team develops interactions with the general public through communications in the media, for example on topics concerned with the Staphylococcus menstrual shock and those related to phage therapy. The diffusion of scientific culture and to interactions with the society involved many personnel categories through more than 50 different operations such as SFV webinar, PRIMO Webinar, interviews in newspapers, etc. Members of the group comprise the founder of the French Toxic Shock Syndrome Association (patient association), a member of the communication committee of the French Society of Neonatology, co-founder of the French interdisciplinary Group for phage therapy.

Context-related weaknesses and risks

The team is relying exclusively on professors, associate professors and people working in hospital. It does not comprise any full-time researchers and did not attract any post-docs during the period.

The number of publications in prestigious journal is limited.

ANALYSIS OF THE TEAM'S TRAJECTORY

The fusion of two groups is welcome as the two groups collaborated for several years and published work together. The project aims to bridge basic science with clinical applications. The team has a unique position through its close links with the clinic and the National Reference Center for Staphylococci (NRCS), as well as the expertise of numerous university hospital members within the team.
The proposed project is composed of two axes, which are a natural continuation of those carried out to date: i) Pathophysiology of staphylococcal infections and ii) Prophage and Phage therapy- Investigating the potential of phages for the development of new anti-staphylococci therapeutics and the role of prophage in the virulence of staphylococci. The expertise of the permanent team members should guarantee the success of these ambitious programs.

RECOMMENDATIONS TO THE TEAM

The team is encouraged to focus on a limited number of projects.
The team should increase the publications in prestigious journals.
The team should attract post-docs and Chargés de recherche to reinforce the basic science part of the project.

Team 20: Unit of Biology of Emerging Viral Infections (UBIVE)

Name of the supervisor: Mr Sylvain Baize

THEMES OF THE TEAM

The UBIVE team employs an integrative approach combining diagnosis, surveillance together with fundamental, applied, and clinical research to study viral hemorrhagic fevers, with emphasis on Lassa virus (LASV), New World arenaviruses, and filoviruses. Research focuses on pathogenesis and immune responses, comparing LASV with nonpathogenic Mopeia virus (MOPV) to unravel host responses to infection and the role of viral factors in pathogenesis and immunity. Several vaccine candidates using MOPV or measles virus vectors viral platforms are in preclinical or clinical development. Vaccine testing in preclinical models allows studying pathogenesis and immunity to old-world and new-world arenaviruses.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

During the previous mandate, the team has fulfilled the prior recommendations.
- Publications and public communication
Publication record is strong, with numerous papers published in generalist journals (Lancet, Science Transl Med, Nature Microbiol, Nature Comm, Blood, PLoS Pathogens) and ongoing media engagement.
- Avoid increased workload associated with public outreach activity
Public outreach decreased, avoiding negative impacts on lab management, while scientific advisory activities increased.
- Better projects distribution among post-doctoral researchers and increasing of the PhD student number
Project distribution allowed permanent members to develop independent research areas and PhD students were favoured over post-doctoral researchers. PhD training expanded following one researcher's HDR now hosting 5–6 PhD students routinely.
- Increase the number of permanent staff
Permanent staff were reinforced with the recruitment of 1 IR and 1 medical manager
- Get appropriate access to bioinformatic analyses
Bioinformatics support was secured through long-term collaboration with the Institut Pasteur hub
- Focus more on the identification of host-factors interactions
Host-factor studies focused on NMTase and CRISPR-Cas9 approaches, generating substantial EU
- To increase the use of NHP in the specific BLS4 facility
The team is now internationally recognized for NHP experiments in specific BLS4 facility, establishing models for several haemorrhagic fever viruses, supporting vaccine and pathogenesis studies.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	6
Praticien hospitalier	0
Sous-total personnels permanents en activité	**8**
Enseignants-chercheurs et chercheurs non permanents et assimilés	5
Personnels non permanents d'appui à la recherche	0
Post-doctorants	1
Doctorants	5
Sous-total personnels non permanents en activité	**11**
Total général	**19**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent to outstanding. The team has published 30 original articles (21 in FLC position) in high-profile journals (Lancet, Nat. Microb., Nat Communications, Sci. Transl Med.) and filled 2 patents since 2020, one of which being licensed. This led to the completion of a Phase 1 clinical trial and the preparation of a phase II clinical trial. The team is internationally recognized as a leading group in the research field of VHF and models in specific BLS4 facility. The team has secured more than 12.5 M€ euros since 2022 from several European and national agencies.

Context-related strengths and opportunities

The team is composed of eight permanent staff (1 DR, 1CR, 1 medical manager, 3 IR, 1 technician and 1 administrative assistant) and six non-permanent staff (1 post-doc and 5 PhD students). The team benefits from an integrated, multidisciplinary approach combining public health activities linked to the national reference centre for haemorrhagic fever viruses (VHF) with fundamental, applied, and clinical research. Strong collaborations with clinical and field partners—including the International Pasteur institute network, ALIMA, MSF, and Bordeaux hospital—enhance both research and translational impact. Complementary expertise within the team and across platforms (bioinformatics, RNAseq, mass spectrometry and structural biology) strengthens its capabilities.
The team possesses a unique expertise in VHF research and NHP models in specific BLS4 facility. They have developed vaccines against arenaviruses, including live-attenuated platforms with broad potential. Internal immuno-monitoring of vaccine candidates in both NHPs and humans enables full control of product development. The team expertise is recognized both nationally and internationally, and it participates in major consortia (MARVAX, France Vaccins, European Vaccine Hub) and in national and international VHF working groups, aligning the team with global preparedness priorities.
The outreach activity within the period is excellent with frequent interviews in the press and generalist media (Le monde, Science&Vie, Libération, France Culture...).
WHO and ANRS MIE classifications of the VHF as priority emerging threats have generated numerous funding opportunities (CEPI, France 2030). Indeed, the team has secured more than 12.5 M€ euros since 2022 from several European (EU-HERA, EU-HORIZON, EVH) and national agencies (ANR, PEPR) and from BPI France (6 as coordinator (5.6 M€), five as partners (7 M€).
The team is now highly attractive to top students (ENS Paris, ENS Lyon, MD/PhD). Recruitment of permanent staff has strengthened its critical mass, and with more HDRs, the team can now host up to six PhD students.
Considering the difficulties inherent to the research field (BSL4 environment, in vivo studies on NHP) and the number of permanent researchers (3), the publication record over the period is excellent with 24 research publications (14 in FLC) including 6 in major generalist journals (Sci. Trans. Med., Nature Comm., Nature Microbiol., Plos Pathogens).
Due to limited access to shared facilities, the team has acquired specialized equipment, enhancing research capacity: histology platform, multiplex fluorescent staining, flow cytometer, a laser microdissection microscope, and Illumina MiniSeq sequencer. The collaboration with European specific BLS4 facility teams expands access to facilities for rodent experiments (Marburg, Hamburg, Stockholm).
Finally, recent collaborations with subcontracted industrial partners (Genibet, now acquired by Recipharm and Hilleman laboratories) broaden its operational and translational landscape.

Context-related weaknesses and risks

The team highlight overwhelming administrative workload due to regulations (ANSM), GMOs and to the national reference centre management (COFRAC) that impedes collaborations with technical platforms, resulting in limited access to high-level technologies and in acquisition of skills and equipment by the team.
The focus of the team in RG-4 agents implies time-consuming and very expensive experiments.
The team indicates that the specific BLS4 facility in Lyon has changed its access policy and management, having its own agenda in addition to collaborative research project. Also, without a dedicated scientific council or advisory board, the strategy and priority of research will be defined solely by the specific BLS4 facility director. Therefore, they emphasize delays in obtaining slots in the specific BLS4 facilities for NHP experiments, which will slow down the advance of research. In addition, the team complains that the recent changes in the BSL4 lab policy due to the new directory board have resulted in a huge increase in the BSL4 entry fees, from 126 € to 1,220 € per entry. This will result in a decrease in the amount of work that the team can perform in the specific BLS4 facility and in a substantial increase of the experimental cost.
The team also indicates issues to further expand as they have reached the maximum size of the team according to their dedicated space and staff limit.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team will pursue previous work integrating fundamental and applied research on viral hemorrhagic fevers (VHF), with public health activities through the national reference centre. Research will focus on pathogenesis, immune responses, and therapeutic targets in preclinical models to decipher disease severity mechanisms and guide intervention strategies. Six research axes are proposed:
1. Molecular bases of pathogenicity:
Characterization of interferon responses during arenavirus infection will continue, identifying proviral and restriction factors for Lassa Virus and Nipah using CRISPR/Cas9 screens and high-density cell arrays. Broad-spectrum antivirals will be tested on RG-4 viruses. Reverse genetics and chimeric viruses will clarify the role of NP and Z virulence factors in NWA to identify new therapeutic targets.
2. Lassa Fever pathogenesis and immunity:
Lassa fever will be studied in preclinical models, focusing on inflammatory infiltration, T-cell exhaustion, and viral tropism. Mechanisms of immunosuppression and immune control. Clinical studies in Nigeria will analyze soluble mediators and leukocyte transcriptomics to identify determinants of severity and early diagnostic markers.
3. NWA pathogenesis and immunity:
Diverse outcomes in preclinical models infected with NWA will be leveraged to study determinants of severe and non-severe disease. CNS studies will explore late-onset encephalitis. Transcriptomic and proteomic analyses of secondary lymphoid organs, PBMCs, and LCM-purified populations will be performed to decipher immune mechanisms of control and highlight therapeutic targets.
4. Universal NWA immunotherapy:
In collaboration with R. Diskin (Weizmann Institute), neutralizing antibodies from MOPEVAC-vaccinated animals will be isolated, cloned, and developed as broad-spectrum therapeutics. Protein baits will support isolation and characterization of highly potent NAbs.
5. Vaccines and live-attenuated platforms:
MOPEVACLAS will undergo long-term protection studies in preclinical models and a phase 1 clinical trial in France in 2026 with full immunomonitoring. MOPEVACNEW, a pentavalent NWA vaccine, will proceed toward clinical development. MOPEVACNEXT, a hyper-attenuated platform, will be optimized and transferred to industry. MOPEVAC Crimean-Congo haemorrhagic fever vaccine candidates will be evaluated to select the most effective.
6. Marburg virus (MARV) vaccines:
Measle Virus-based MARV vaccine candidates (MARVAX) will be evaluated in vitro and in preclinical models, with the best candidates advanced to further development in line with WHO priorities.
Overall, this integrated program couples fundamental, preclinical, and clinical research to advance understanding of VHF pathogenesis and immunity and to develop effective prophylactic and therapeutic tools. More than 8.6 M€ has already been secured by the team to conduct these projects through specific funding from national (BPI France, ANRS-MIE, PEPR-MIE) or European (EU-HERA EVH call, EU-Horizon) sources.

RECOMMENDATIONS TO THE TEAM

The UBIVE team is internationally recognized as a leading group in the research field of viral haemorrhagic fever (VHF) and has developed several vaccine platforms and a clinical trial.
Recommendations are to continue their excellent funding strategy and publication level, and pursue the clinical development of their vaccine platforms. The team may seek to license more of their patents to ensure clinical development. Expanding their number of full-time researchers may also help them to further increase the publication record and funding.

Team 21: Viral infection Metabolism and Immunity (VIRIMI)

Name of the supervisor: Mr Pierre-Olivier Vidalain

THEMES OF THE TEAM

The team investigates how diverse human viruses reprogram host cell metabolism to support replication and modulate innate immunity. Using an integrated multi-omics strategy—proteomics, transcriptomics, interactomics, metabolomics and chemical biology—it characterizes metabolic and signaling rewiring induced by hepatotropic and airborne viruses, including HBV, HCV, HDV, dengue, influenza A, SARS-CoV-2, measles and Nipah. These insights feed the development of innovative host-directed antivirals. The program relies on strong collaborations within CIRI and national research networks.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has effectively addressed the recommendations of the previous report. Public outreach has been significantly strengthened through the publication of popular science articles, regular engagement with secondary school and high-school students, and training activities delivered to community associations. Communication has also improved with consistent updates of the team's website and social-media presence. Doctoral training has progressed, with four PhD completions within an average duration of 3.25 years, the successful supervision of post-doctoral researchers, and a substantial current cohort of seven PhD students, reflecting improved mentoring capacity. The career advancement of several team members (AI→IE, MCU-HC, CR-HC, DR-CE) demonstrates active support for professional development. Scientific production has remained stable, with publications in high-quality journals and contributions to major collaborative papers. The implementation of advanced ex vivo models and the preparation of funded in vivo studies further respond to recommendations aimed at increasing the impact and translational relevance of the research. Finally, the creation of the start-up Hormae Pharma highlights the team's strengthened ability to translate fundamental findings toward industrial applications.

Overall, the team has satisfactorily and proactively followed the recommendations issued in the previous evaluation.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	0
Maitres de conférences et assimilés	2
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Praticien hospitalier	0
Sous-total personnels permanents en activité	**7**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels non permanents d'appui à la recherche	0
Post-doctorants	0
Doctorants	7
Sous-total personnels non permanents en activité	**8**
Total général	**15**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent. The VIRIMI team investigates how hepatotropic and respiratory viruses reprogram host metabolism and identify therapeutic metabolic vulnerabilities using multi-omics and advanced infection models. Strong translational output led to patents, clinical evaluation of FXR ligands for HDV, and creation of Hormae Pharma. The team shows solid productivity, strong collaborations, sustained funding, and growing international visibility.

Context-related strengths and opportunities

The team has a clearly defined and original scientific objective which focus on the virus–metabolism interactions, a rapidly expanding field of strategic importance for infectious disease preparedness.
There is a strong integration of multi-omics approaches (proteomics, metabolomics, spatial transcriptomics, interactomics), positioning the team at the cutting edge of systems virology.
The team uses physiologically relevant infection models (PHH, HepaRG, organotypic lung cultures, liver explants) enabling high translational potential.

The team has a major contribution to the development of FXR ligands against HBV/HDV, now in clinical evaluation, validating the scientific vision.
They have identified multiple host-targeting antiviral molecules (APY1, APY2, NAMPT inhibitors, HIF-pathway modulators).
The team has obtained ten patent applications (but no licensing) and has participated to the creation of the spin-off Hormae Pharma, consolidating the team's reputation in innovation.
The team has long-term industrial partnerships (Enyo Pharma, ATEA Pharmaceuticals) supporting the team's translational pipeline.

The team has a consistent production in high-quality journals across virology, immunology and metabolism. 41 publications including 12 as FLC in specialized journals (European Journal of Immunology, Antiviral Research, Clinical Infectious diseases…).
They have participated in European and national networks (GDR Flu, PEPR-MIE Nipah-LISA, Institut d'Hépatologie de Lyon). Four ANR including two as coordinator and six ANRS including four as coordinator…. (more than 2 M € of grants)
The researchers have increased invitations to speak at international scientific meetings.

The team has a robust supervision of PhD students with excellent career outcomes in academia and biotech (11 PhD)
The team has a strong involvement in teaching at UCBL and in medical training programs.
The team has an ability to recruit motivated students and maintain a dynamic training environment.

Context-related weaknesses and risks

The team has an insufficient laboratory space, some of it ageing or inadequate for expanding BSL-2/BSL-3 activities. This constraint may limit recruitment, experimental throughput, and capacity to host additional students or post-docs.
The research team has a strong dependence on specialized facilities (e.g., primary hepatocytes, organotypic cultures), which may lead to bottlenecks if institutional support fluctuates.

There is a need for additional post-doctoral researchers to strengthen international competitiveness and accelerate publication in the highest-impact journals.
The high proportion of fixed-term personnel (primarily PhD students) without corresponding long-term staff reinforcement may jeopardize continuity between project cycles.
There is a potential risk of PIs becoming over-extended due to substantial teaching, clinical, and institutional responsibilities.

Host-directed antivirals are promising, but they may face translational challenges such as toxicity, metabolic compensation, or limited therapeutic windows in humans. High-risk exploratory projects—for example, metabolic rewiring in organotypic models or phase-transition studies—require sustained continuity of funding. Moreover, a strong focus on a limited set of viruses may reduce flexibility in responding to emerging pathogens unless resources are expanded.

International competition in virus–metabolism research is increasing rapidly. Regulatory or ethical constraints related to humanized preclinical models or primary human tissues may delay key experimental milestones. In addition, industrial partners may shift their strategic priorities, potentially affecting existing translational pipelines such as those involving FXR ligands or H4 agonists.

Despite solid output, the team still has limited presence in generalist journals, which could affect its visibility in highly competitive funding schemes. International collaborations could also be further strengthened to consolidate its leadership in systems virology.

ANALYSIS OF THE TEAM'S TRAJECTORY

Over the evaluation period, the VIRIMI team has demonstrated a clear maturation and consolidation around the study of viral infection-induced metabolic reprogramming. Its scientific identity at the interface of virology, immunology, and cellular metabolism has been strengthened, with a coherent program structured around two major infection sites, the liver and the lung. This dual-axis organization has unified diverse projects into an integrated framework centred on central carbon metabolism and its role in viral replication. The team systematically employs organotypic cultures, multi-omics approaches, and physiologically relevant models, positioning it as a strong contributor to systems-level analyses of viral pathogenesis.
The team has deepened investigations into host metabolic pathways—including glycolysis, NAD/NADP biosynthesis, the mevalonate pathway, and the succinate/HIF axis—and identified metabolic regulators with antiviral potential. Methodological advances such as spatial transcriptomics, CRISPR-based functional genetics, and ex vivo infection systems have enabled the transition from descriptive profiling to mechanistic exploration of host-pathway dependencies, enhancing translational relevance.
VIRIMI has shown strong capacity for preclinical innovation. Host-targeting antiviral candidates identified in vitro have progressed to collaborations involving humanized preclinical models and BSL-3/BSL-4 facilities. Industrial partnerships and the creation of the Hormae Pharma start-up reflect a robust translational dynamic. Competitive national and European funding (ANR, ANRS, Astrid, PEPR-MIE, EDF) further testifies to the team's visibility and credibility.
A notable evolution is the focus on pandemic preparedness, particularly for airborne RNA viruses such as influenza, measles, and Nipah virus. This aligns with national and international priorities and leverages the team's expertise in metabolism-modulating antiviral strategies. Engagement in large consortia, including the European Defense Fund RESILIENCE program, demonstrates capacity for high-impact collaborative research.
Finally, the team has sustained productivity and cohesion, with strong inter-axis synergies and shared methodological platforms. Its trajectory reflects increasing multidisciplinary integration, consistent scientific output, and growing capability to operate across the continuum from basic discovery to early translational development.

Overall, the VIRIMI team presents a trajectory marked by consolidation, innovation and strategic alignment with emerging national and international priorities in infectious diseases and antiviral research.

RECOMMENDATIONS TO THE TEAM

The VIRIMI team demonstrates strong expertise in viral metabolism, host-directed antivirals, and translational research, with robust use of multi-omics, organotypic, and in vivo models. To further consolidate their trajectory, it is recommended to accelerate preclinical validation of promising host-targeting antivirals, ensuring mechanistic understanding and clinical relevance, while leveraging industrial partnerships to facilitate translation. Expanding focus on emerging high-risk viruses, including airborne and hepatotropic pathogens, will strengthen pandemic preparedness. Enhancing interdisciplinary integration between liver and lung axes, combining metabolic and viral lifecycle analyses, and incorporating computational modeling will optimize the discovery of broad-spectrum antivirals. Continued investment in high-containment facilities, high-throughput screening platforms, and staff training in advanced techniques will maintain competitiveness. Finally, strategic pursuit of national, European, and defense-oriented funding, together with early intellectual property management, will support long-term sustainability and translational impact.

Team 22: Épidémiologie et Écologie Évolutive des Maladies Infectieuses (PHE3ID)

Name of the supervisor: Mr Philippe Vanhems / Mr Jean-Philippe Rasigade

THEMES OF THE TEAM

The PHE3ID team focuses on the population-level dimensions of infectious diseases, including epidemiology, public health, and pathogen evolution and ecology. The team is composed of three PIs with three main axes. The first one focuses on the epidemiology of nosocomial infections, communicable disease prevention, transmission dynamics and vaccine interventions. The second group focuses on the evolutionary ecology and population genetics of antibiotic-resistant pathogens whilst the third one focuses on the epidemiology of respiratory pathogens.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

In the previous report, it was recommended to maintain and strengthen interactions with the socio-economic sector. The team reacted with the establishment of several industrial contracts (participation in the ´Immuniser Lyon´ consortium). Moreover, the team initiated a collaboration with experts in antimicrobial resistance economics at Toulouse School of Economics.
The team has also strengthened collaborations with other teams within CIRI and, as a result, six projects have been launched with five different CIRI teams.
The team was encouraged to maintain and further develop the frequency of meetings, which was increased to once per month.
In order to ensure the impact of intervention and prevention strategies, the team implemented the epidemic detection across all hospitals within the Hospices Civils de Lyon (HCL).
Moreover, in the last mandate, five postdoctoral researchers (international) have joined the team, with one researcher now holding a permanent position at ANSES plus six specialized staff members who will analyze the large volume of data collected by the team. Furthermore, three new habilitations as HDR have been completed, and more are expected.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	2
Maitres de conférences et assimilés	3
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	11
Praticien hospitalier	7
Sous-total personnels permanents en activité	**23**
Enseignants-chercheurs et chercheurs non permanents et assimilés	6
Personnels non permanents d'appui à la recherche	0
Post-doctorants	0
Doctorants	6
Sous-total personnels non permanents en activité	**12**
Total général	**35**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent. The team demonstrates strong scientific productivity and international visibility in infectious disease epidemiology, antimicrobial resistance, and respiratory pathogens, supported by a solid workforce, high-quality publications, substantial funding, and active teaching and scientific outreach. The team contributes to COVID-19, respiratory viruses, and hospital-associated infection which are particularly notable. However, structural weaknesses, including limited permanent positions, imbalance between groups, and challenges in translating epidemiological findings, need to be addressed. The proposed trajectory is coherent and relevant, but sustaining expertise in bioinformatics and strengthening collaborations, especially in vaccinology and internationally, will be critical for the future impact.

Context-related strengths and opportunities

The team is organized in three groups according to the scientific lead as follows: Public Health & Epidemiology of Infectious Diseases, Evolution & Ecology of Antimicrobial Resistance and Respiratory Pathogens & Immunization.
During the evaluated period, the team has made sound achievements related to risk factors of nosocomial COVID-19, one of the largest published studies on that topic from different countries, nosocomial influenza, respiratory syncytial virus (the team evaluated the risk of disease and prevention), evolutionary-informed models for outbreak detection, ecology of hospital antimicrobial resistance, environmental reservoirs of multi-drug resistant bacteria in hospital and Streptococcus pneumonia and other viral agents and pneumonia in low and medium income countries.
The team benefits from 18 permanent staff, four postdocs, nine PhD students and six ITA.
The team is actively engaged in training of PhDs (4 defenses during the last period contract) and one HDR.
The team shows exceptional scientific productivity and impact across infectious disease epidemiology, antimicrobial resistance, and respiratory pathogens, with several landmark studies of international relevance.
The team has produced 45 original scientific publications, 11 clinical articles and 12 reviews/editorials/book chapters as first or last authors. Moreover, they have participated as collaborators in 82 original scientific publications, 19 clinical articles and 18 reviews/editorials/book chapters. Notably, the authors published a Nat. Comm., Front in Microbiology and Elife, as well as a review published in Lancet, among others.
Amongst the scientific tasks of the team are their teaching duties (coordination of Master on Global Health, humanities and social courses in the medical school, coordinator of the Master on Epidemiology and Risk Management in Healthcare, etc.).
The team has gained national and international recognition as their PIs are Board Members of important societies as Board members, Experts, Consultants), have been invited as speakers in congresses, and are Editorial Board members (pneumonia) and actively presented in national and international conferences. Therefore, the team benefits from a strong national and international visibility.
The team has a strong capacity of securing substantial competitive funding, develop patented tools, engage with industry, and contribute to public health policy and outreach further underscores its scientific excellence and societal impact.
Overall, the team leveraged over 7M€, including national funding -six as coordinator including
ANR AAPG, and CI, SHAPEMed@Lyon and Nosocor- and private funding (Sanofi, bioMerieux), with two patents (1 licensed), demonstrating an excellent capacity for technology transfer.
The team supports public outreach and dissemination of information such as participation in the Feter de la Science, mentorship programs, TV interviews and in the European network to promote infection prevention for patient safety.

Context-related weaknesses and risks

A clear weakness is the lack of permanent contracts for researchers and engineers. During the period, there is a clear imbalance in the scientific production between the three groups. Moreover, the team struggles with the fact that translational aspect of epidemiological studies remains elusive. Another weakness of the team is related to structural and strategic issues rather than scientific quality. This together with the above-mentioned weakness of lack of permanent positions for researchers and engineers may threaten long-term continuity and expertise retention. Moreover, attention to the imbalance in the scientific output across the three groups should be paid. In addition, the translational impact of some epidemiological studies remains limited, and the lack of key expertise (notably in bioinformatics and machine learning) poses a risk if not compensated through recruitment or sustained collaborations.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team is transitioning from a broad, multi-pillar structure toward a more focused and strategic organization. At the end of the current cycle, the team will close, leading to the creation of a new emerging group at CIRI, dedicated to respiratory virus epidemiology, viral evolution, and real-world vaccine evaluation. This evolution reflects a clear alignment with global public health priorities, leveraging strong expertise in epidemiology, data science, and access to large national and international datasets.
The research program of the team will be divided in three pillars: (1) Understand the burden and epidemiology of respiratory viruses that cause disease in very young and/or older age groups, for vaccine development, (2) Monitor the genetic evolution of respiratory viruses and associated mutations, and (3) Evaluate the real-life performance of vaccines against different outcomes with the change of the PI.
Overall, the trajectory demonstrates a thoughtful reorganization that preserves scientific excellence that will enhance visibility, and position both groups for sustained impact in their respective domains.

RECOMMENDATIONS TO THE TEAM

Despite the fact that the team hired experts for data analysis, a recommendation is to include the capacities in the current report and their possible expansion in the future to allocate bioinformaticians. Thus, biomarker discovery will be affected by the leaving of the previous PI and the expertise in machine learning algorithms as wells as the use of AI will be lost, therefore it is strongly recommended to continue collaboration or look for further collaborative options.
It is recommended to strengthen collaboration with other members of CIRI who are doing excellent research in the field of Vaccinology.
The team´s visibility would increase by increasing the international collaborations.

Team 23: Persistence and Single Cell Dynamics of Respiratory Pathogens (PERSIST)

Name of the supervisor: M. Nicolas Personnic

THEMES OF THE TEAM

The team studies bacterial phenotypic heterogeneity: how genetically identical bacteria transiently form subpopulations with distinct functions and physiologies, and how these cell-to-cell variations shape infection dynamics and treatment efficacy. The research focuses on bacterial persisters using mainly Legionella pneumophila as a model organism and is organized around 3 themes: 1 - Persister Biology, 2 - Mobile Genetic Elements dynamics and 3 - Clonality and Collective Bacterial Behaviour.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Not relevant - PERSIST was founded in 2022 following the recruitment of Nicolas Personnic from the University of Zurich to establish his team at CIRI. The Team PERSIST originates from Nicolas Personnic's junior group at the Institute of Medical Microbiology (University of Zürich, Switzerland) from 2016 to 2021 and sponsored by the Swiss National Foundation Ambizione program and the University of Zürich.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	0
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	0
Praticien hospitalier	0
Sous-total personnels permanents en activité	**2**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	1
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**3**
Total général	**5**

EVALUATION OF THE TEAM

Overall assessment of the team

The team is relatively young, having been established in 2022, which makes it challenging to fully assess its performance within CIRI. Nevertheless, the team demonstrates strong potential. This is supported by the excellent track record of its leader, a distinctive methodological approach to studying pathogen single-cell dynamics during infection, and promising preliminary results. Based on these factors, the team is considered promising.

Context-related strengths and opportunities

Research on antibiotic persistence is essential to understanding how clonal bacteria without known genetic resistance evade treatment. The team builds on work initiated by the PI's group in Zurich, focusing on bacterial persisters using Legionella as a model. Many reported findings and high-quality publications stem from the team leader's pre-CIRI work (no CIRI affiliation); these are considered background and not evaluated.

The team currently includes two permanent members and three PhD students, with planned recruitment of one postdoc, one PhD student, and one technician. A CRCN CNRS researcher will join in the next mandate. Since 2022, the team has published two chemistry papers, one protocol, and three reviews as FLC authors (with CIRI affiliation). Funding is strong (1.8 M€, including 0.6 M€ pre-PERSIST) with three ANR PRC grants (one coordinated, two as partner), plus local seed, transversal, and PhD funding.

The team has built a solid methodological pipeline for studying single-cell bacterial dynamics during host infection, including fluorescent reporters, high-resolution microscopy, omics, and genome-wide loss-of-function approaches. A key tool is the Timer plasmid-based growth-rate reporter, developed by Personnic's group in Basel, enabling dynamic discrimination between persisters, growth-resuming, and replicating Legionella.

Before joining CIRI, the PI's group used the Timer reporter to show that persisters activate a virulence program subverting macrophage function and that quorum sensing regulates persister formation in host cells and biofilms. These themes continue at PERSIST, which developed "PhenoQuant" to process large time-lapse microscopy datasets. Using a human macrophage model, they showed persisters form a heterogeneous non-replicating subpopulation capable of resuming growth after antibiotics. Another key result: persister formation and antibiotic susceptibility are heterogeneously regulated by chromosomal excision and autonomous replication of the mobile genetic element pP36 ICE. These results correspond to manuscripts in preparation.

PhD students are highly productive, having published one protocol, two reviews (including Trends in Microbiology), and three manuscripts in preparation on persisters (single-cell dynamics, MGE). This reflects a strong research environment. The MCU handles 278 h/year teaching plus courses and program responsibilities. One PhD student contributes moderate teaching; all members manage lab tasks.

The team leader is invited to speak nationally and internationally. Collaborations include partners in India, Denmark, and Switzerland. The supervisor of the team represents CIRI in the Biosantexc mobility program, supporting Franco-Indian collaborations and training, offering opportunities for international recruitment. Past industrial interactions existed but none are ongoing. Outreach activities include contributions to the national biology Olympiad, science festival, and MT180.

Context-related weaknesses and risks

The personnel plan includes several future recruits contingent on securing grants. Research articles originating from PERSIST are planned but not yet published.

The team's SWOT analysis identifies key threats: insufficient technical support, limited career opportunities, lack of international PhD/postdocs, and absence of major funding (e.g., ERC). Addressing these issues, along with publishing, should be a priority for the next period.

ANALYSIS OF THE TEAM'S TRAJECTORY

The planned research is structured around three themes: 1 - Persister Biology, 2 - Mobile Genetic Element (MGE) Dynamics, and 3 - Clonality and Collective Bacterial Behaviour. Building on previous work characterizing single-cell dynamics of Legionella in human macrophages, the team now aims to uncover molecular mechanisms and host-cell heterogeneity underlying persister formation, survival, and regrowth. This will involve exploratory -omics, genome-wide CRISPR screens, and targeted approaches based on prior studies of bacterial virulence and host antimicrobial factors such as NO. Theme 2 will investigate whether interactions between MGEs (e.g., pP36 ICE) and bacterial phenotypic heterogeneity drive antimicrobial persistence and Legionella evolution, using experimental and mathematical modeling approaches. Theme 3 focuses on how transient phenotypic changes enhance intracellular community performance through mechanisms such as bistable motility and spatial organization. Finally, the team is establishing a patient-derived airway tissue model for high-content single-cell analysis of phenotypic variation of the ESKAPE pathogen Klebsiella pneumoniae, which is a new research direction for the team. This is a strategic move that enhances clinical relevance and opens opportunities for global health and One Health initiatives, as well as collaborative consortia and additional funding streams. However, Klebsiella is an extracellular pathogen, and it is not clear how the airway infection model will perform and which research questions will be addressed using it.

Overall, these themes represent a logical continuation and expansion of prior work and are feasible given the team's expertise and collaborations. Plans include national and international partners, preliminary data, and strategies for personnel and funding.

RECOMMENDATIONS TO THE TEAM

To address risks identified in the SWOT analysis, the team should actively pursue international funding and recruitment opportunities. Programs such as MSCA and HFSP can help attract international postdocs, while major grants like ERC and Horizon Europe should complement the current focus on national funding. The team's strong expertise and toolbox in bacterial persister biology should be attractive for industrial and clinical partnerships.

For internationalization, PhD students and postdocs should be encouraged to undertake research visits with international collaborators. Inviting leading international scientists to CIRI for seminars and networking would further strengthen visibility and collaboration.

Finally, outreach should be intensified through media engagement, opinion pieces, and public talks. Antibiotic resistance and persistence are topics of high public interest, offering an excellent opportunity to raise awareness and visibility.

Team 24: RNA Expression in Viruses and Eukaryotes (REVE)

Name of the supervisor: M. Théophile Ohlmann

THEMES OF THE TEAM

The team investigates the molecular mechanisms governing viral and cellular RNA expression during infections by HIV-1, SARS-CoV-2, and EBV. Its research combines fundamental and translational approaches. The fundamental axis focuses on the interplay between viral and cellular proteins and the intrinsic structural features of viral and cellular mRNAs that regulate translation and RNA metabolism. The translational axis aims to develop innovative biotechnological tools for gene therapy, including virus-like particle-based delivery systems and optimized mRNA platforms for therapeutic applications.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The recommendation to improve the balance of publication output has been addressed: all researchers have now published during the period, except one on long-term medical leave.

The recommendation to support early-career researchers in developing independent projects has been successfully implemented: the researcher previously identified has now established clear independence, evidenced by two Nature Communications papers, an HDR, and PhD supervision.

Regarding human resources, the previous shortage of full-time researchers, postdocs, and PhD students has been partially alleviated, with several recruitment (five PhD students, including two ongoing and one post-doc). However, long-term strategies to secure continued PhD and postdoctoral recruitment should be further strengthened.

All recommendations concerning scientific strategy have been taken into account. The team refined or reoriented research axes, established new collaborations to deploy state-of-the-art technologies (TurboID-dCas13, Nanoblades), and incorporated more mechanistic approaches. One project was discontinued after publication, and its PI successfully redirected research efforts toward productive new avenues, illustrating the team's adaptability.

Finally, early-career researchers have been encouraged to become more involved in seminars and outreach, as recommended.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	0
Maitres de conférences et assimilés	2
Directeurs de recherche et assimilés	3
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	2
Praticien hospitalier	0
Sous-total personnels permanents en activité	**9**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels non permanents d'appui à la recherche	0
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**3**
Total général	**12**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent.
Over the evaluation period, the group has delivered solid and innovative contributions in molecular virology, RNA biology, and the development of RNA-based translational tools. The team has also demonstrated a strong commitment to training, effectively supporting the development of young scientists, and its members are actively involved in scientific evaluation at national and international levels. Overall, the team presents a research environment with recognized expertise and valuable contributions to both science and academic life.

Context-related strengths and opportunities

The team maintains a strong balance between fundamental and translational research. Its work combines the study of molecular mechanisms regulating viral and cellular RNA expression during infection with the development of innovative biotechnological tools for gene editing and mRNA optimization. This dual orientation reinforces both the scientific impact and the societal relevance of the team's research activities.
Scientific production is strong and consistent, with 38 publications and reviews over the evaluation period, including 15 peer-reviewed research articles with leading authorship (FLC) in internationally recognized journals such as Nature Communications, PNAS, Nucleic Acids Research, Viruses, Cells, Metallomics, and IJMS. Three patents, one of which is licensed, and several industrial contracts (Vetophage, Labo'Life, LVMH) illustrate the team's capacity for technological innovation and knowledge transfer.
The team has demonstrated its ability to secure competitive funding, coordinating 11 national grants (ANRS, Ligue Cancer, Inserm Transfert, CNRS "metallomix" and "Isotop") for a total of €736,000, complemented by the industrial contracts mentioned above (€110,000). These achievements reflect the team's capacity to establish productive partnerships across academic and applied research sectors.
The team has supervised five PhD students over the period, three of whom have already defended with first-author publications, while two new PhD students started in 2024. It has also trained 41 students at all levels (L3/M1/M2, BTS, IUT, engineers) and supervised one postdoctoral researcher. This strong involvement in mentoring demonstrates the team's commitment to high-quality training. Career development of engineers is also actively supported, with opportunities to publish, supervise students, and pursue HDR accreditation.
The team is strongly engaged in academic and community life. It contributes extensively to higher education (one assistant professor and two ATERs), participates in doctoral governance (members of the BMC doctoral school), and holds responsibilities in national and European evaluation and funding bodies (Hcéres, Horizon 2020, ElSMA, Marie-Curie, EIC path finder, CNRS, INRAE, ANR). Members are also involved in organizing scientific meetings (SFERETE-SFVB, HerPAs, Journées Francophones de virologie), demonstrating a solid commitment to the scientific community.
Overall, the team demonstrates sustained productivity and scientific impact, and its integrated positioning at the interface of molecular virology, RNA biology, and biotechnology offers a strong opportunity to expand toward competitive translational programs and emerging RNA-based therapeutic applications.

Context-related weaknesses and risks

During the evaluation period, the team experienced significant turnover, including the retirement of a senior researcher and the departure of a maître de conférences, partially offset by the recruitment of a new faculty member. These changes likely disrupted the continuity of several research themes and required internal reorganization.

Although the team obtained a relatively high number of grants, the overall financial income remained modest. According to the team, this reflects the predominantly in vitro nature of their research, which limits the justification for large funding applications. However, this modest financial capacity also constrains the recruitment of postdoctoral researchers and investments in technological developments, potentially affecting long-term competitiveness. The funding portfolio remained centred on national programs and moderately sized industrial collaborations, with no international or European contracts during the period. This limits opportunities for scientific mobility, visibility, and participation in larger collaborative initiatives.

Finally, the team's activities were distributed across multiple scientific directions (HIV and SARS-CoV-2 RNA biology, EBV splicing, trace-element metabolism, VLP-based delivery systems, mRNA engineering). While productive, this breadth may have fragmented human and financial resources and limited consolidation around a smaller set of high-impact axes, thereby reducing potential thematic coherence and strategic visibility.

ANALYSIS OF THE TEAM'S TRAJECTORY

According to the decision of the CIRI management, the REVE team will not be renewed in the next contract. However, a transition trajectory has been defined, allowing the group to continue its research within the institute until December 2028. This configuration provides a valuable timeframe to consolidate the most active scientific lines, ensure the transfer or integration of ongoing activities, and complete the supervision of current PhD students.
The proposed trajectory reflects a strong effort to maintain scientific continuity while reorganizing activities in a coherent manner. The planned progressive closure of the EBV axis appears consistent with the transition context. The refocusing on HIV-1 and SARS-CoV-2 RNA translation mechanisms is scientifically robust and builds on well-established expertise and innovative methodological developments, including advanced approaches for mapping RNA–protein interactions.
The continuation of research on trace elements and the selenoproteome is justified. This line of work has generated original insights at the interface of virology, cell biology, and metabolism, and it offers complementary mechanistic perspectives that remain compatible with the future scientific focus of the group.
The translational research program is a major strength of the team. The development of biotechnological tools, such as virus-like particles for genome editing and optimized mRNA constructs for therapeutic applications, illustrates a productive continuum between fundamental discoveries and applied research. Collaborations with clinical partners, including those at Necker Hospital, provide a clear translational perspective and support the potential for further development toward gene therapy and RNA-based medicine. These activities are well aligned with institutional priorities in biotechnology and represent promising opportunities for integration into national or industrial partnerships.
Overall, the trajectory is scientifically coherent and builds on the team's recognized expertise and past achievements. Its feasibility will depend on maintaining sufficient human and financial resources throughout the transition period.

RECOMMENDATIONS TO THE TEAM

The team is encouraged to further consolidate its scientific focus, building on the efforts already undertaken to streamline research themes. A clearer concentration on a reduced number of coherent axes would help increase scientific visibility and enhance competitiveness.
Securing additional funding, both national and international, would further increase research capacity, for instance by enabling the recruitment of postdoctoral fellows or supporting the development of innovative methodological approaches.
Expanding collaborations, particularly with national and international teams, as well as with clinical or industrial partners, would also help reinforce the translational dimension of the research and facilitate access to broader technological and biological resources.
Overall, these efforts would support the team in maintaining a strong scientific dynamic and in maximizing the impact and continuity of its activities during the transition period.

Team 25: Immunity and Cytotoxic Lymphocytes (ICL)

Name of the supervisor: Mrs Jacqueline Marvel

THEMES OF THE TEAM

The central theme of the team is a development of CD8 T cell memory. It studies the diversity of memory CD8 T cells, how these cells develop, and the involvement of cytokines in this process. The team also studies CD8 T cells in pathology and contributed to the characterization of the immune response to vaccination during the COVID-19 pandemic.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Greater engagement with the public: The team leader very actively communicated with the media during the COVID-19 pandemic.

Longer-term plans: With the retirement of its director, this team will cease its activity.

Too heavy involvement of the team in research platforms: The team leader handed over the responsibility of the "federative research structure" (SFR) to her colleague in the team and a facility (IMMOS) is still run by an Inserm engineer.

Translate expertise on preclinical model CD8 T cells to humans: The expertise on preclinical model T cells was successfully translated to the study of T cell-responses to SARS-CoV-2.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	2
Praticien hospitalier	0
Sous-total personnels permanents en activité	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	0
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**2**
Total général	**7**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent. The team very substantially contributed to our understanding of the development of CD8 T cell memory, of the diversity of this population, and of its implication in pathology. During the COVID-19 pandemic, it was very proactive in studying immune responses to SARS-CoV-2 vaccination and in communicating with the general public. Its scientific production in terms of publications is impressive, qualitatively and quantitatively. The team very importantly contributes to structuring and running research-infrastructures, at the local and national level.

Context-related strengths and opportunities

The team demonstrated that memory CD8 cells develop from effector cells, in accordance with a "linear" differentiation model. It found that exogenous IL-2 favoured differentiation of effector cells and limited their further differentiation into memory T cells. The team found that LY49-expressing CD8 T cells develop in the thymus upon agonist selection and have innate like functions. Upon vaccinia virus infection, these cells are differentiated without acquiring typical CD8 T cell-effector functions.
Chronic osteomyelitis is frequently caused by S. aureus infection. The team showed that CD8 T cells can recognize and be activated by an SA-encoded antigen. During the SARS-CoV-2 pandemic, the team found that heterologous vaccination elicited the most robust response.
The team found that exposure of SPF-models to pathogens led to stronger immune responses to viral infection but relatively resistance to gut inflammation.
The team generated C57BL/6 models with a targeted single nucleotide modification changing the *Ptprc(b)* allele
into Ptprc(a). These preclinical models should prove very valuable in research in immunology.
These and other important scientific findings of the team and its collaborators were published in a total of 22 scientific papers. Team members appeared as the first, last, and/or corresponding position on seven of these publications (of which one in Nature). This scientific production should be considered outstanding, given also the small size of the team.
The team obtained contracts from several agencies, regional and local sources, charities, and the private sector, as coordinators (ANR 2018, k€200) and as partners (AURA 2018, FUI 2018, IDEX 2020, BioMérieux 2021, LNCC 2021, and ANRS 2021, 2022, for total of k€753).
Over the years, the team gained important recognition and very substantially contributed to structuring research facilities. The team-leader ensured numerous important functions at local and national levels, in public bodies as well as in charities. The team leader thus structured local research facilities ("SFR"), seated at councils at the Inserm, the "Plan Cancer", the Liliane Bettencourt charity, and was a member of the strategic council of CelPhedia, a national operational research infrastructure. She also was deputy director of the CIRI from 2012 to 2023. Other members of the team were also heavily involved in these and other activities and a staff member first was deputy director and then took over the direction of the SFR, others headed immunophenotyping facilities at the local and national levels and seated in the animal-experimentation ethics committee.
The team also has a substantial training- and teaching activity. It trained six PhD students who all defended their doctoral theses. One staff member obtained his HDR. Members of the team participated in ten thesis juries. A staff member organizes a yearly ten-day Master's course at the ENS and teaches 25h per year at the Lyon-University.
During the COVID-19 pandemic, the team leader was very regularly interviewed by the press, radio, and television at the local and national level.
The Hcéres committee regretted that, for personal reasons, the team leader could not present the achievements of the team during the site visit.

Context-related weaknesses and risks

No weaknesses identified.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team will close at the end of the evaluated period.

RECOMMENDATIONS TO THE TEAM

The team will close at the end of the evaluated period.

Team 26: Molecular Basis of Viral Pathogenicity (MBVP)

Name of the supervisor: Mr Viktor Volchkov

THEMES OF THE TEAM

The team investigates the molecular basis of pathogenicity in Henipaviruses (Nipah) and Filoviruses (Ebola). Using structural biology and reverse genetics, it elucidates how key viral proteins, particularly the Nipah phosphoprotein, control RNA synthesis, adopt dynamic conformations, and counteract innate immunity. The team also analyses the production and release of soluble Ebola GP in a recombinant VSV system, which may affect VSV-based vaccine platforms. Studies of host-adapted Ebola variants in preclinical models provide insights into tissue tropism, persistence, and disease progression. Overall, the team's research clarifies how these viruses hijack host processes and drive severe pathogenic outcomes.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous report recommended that the team increase its publication output and explore opportunities to translate its fundamental findings. During the evaluation period, the team maintained scientific activity but with a reduced publication output (5 articles and 2 reviews, none as FLC). However, in line with the recommendations, the team developed more translationally oriented projects, notably through studies of Ebola GP expression in a recombinant VSV platform with relevance for vaccine development, and through the establishment of an adapted Ebola model.
The team was encouraged to expand its training capacity by increasing the number of PhD students, which was difficult to achieve given the small group size. The PI nonetheless supervised two PhD students.
Concerning the recommendation to securing new funding, progress was mixed. The PI successfully obtained one ANR grant as coordinator and one as partner, as well as two contracts with industrial partners. However, no new funding was secured after the 2018–2024 ANR, possibly due to the limited personnel and the uncertainty surrounding the long-term future of the team. Finally, the previous report highlighted the need for succession planning as the PI approaches retirement. This point remains unresolved.

TEAM WORKFORCE: in physical people as of 31/12/2024

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is very good. Despite limited publication output, the group has produced scientifically valuable work and generated unique expertise on high-risk emerging viruses, including innovative translational directions. The team has remained scientifically active, visible internationally, and strongly committed to training despite structural constraints and its upcoming closure.

Context-related strengths and opportunities

The team benefits from a strong and unique expertise in the study of highly pathogenic, emerging and re-emerging viruses, particularly filoviruses and henipaviruses, an area of increasing global importance for human health and epidemic preparedness. This niche expertise is rare at the national level and contributes to the strategic positioning of the research. The team has well-established collaborations, notably with structural biology laboratories, which have supported five collaborative publications in peer-reviewed journals (eLife, Emerg Infect Dis., Biophys J., J Mol Biol., Biomolecules) and two reviews (Med Sci). Its research program has also evolved toward more translational directions, including work on Ebola GP expression in a recombinant VSV system and the development of an adapted Ebola model.
The PI enjoys strong international recognition, reflected in invited lectures at prominent meetings such as the Hans Klenk Symposium on Influenza and Filoviruses (Marburg), the European Meeting on Viral Zoonoses (2019 and 2023), and seminars at the University of Alabama at Birmingham. His visibility is further supported by substantial editorial and reviewing activities for leading journals (Science, EMBO Reports, PLOS Pathogens, Journal of Virology), and by his participation as a member of a DFG evaluation committee.
The team contributes significantly to education and training: despite its small size, it supervised two PhD students, hosted two postdoctoral researchers, and trained 17 M1/M2 students between 2019 and 2025. The PI provides

204 hours per year of teaching across a diverse range of virology courses at UCBL1 (Fundamental Virology, Advances in Virology, Biosafety and Biological Risk Prevention, Virology Practical Training, Technical Workshops), strengthening the attractiveness of the master's programmes. The team has also demonstrated capacity for valorization through industrial partnerships (ABIVAX, Sanofi-Pasteur), and has secured competitive funding, including one ANR grant as coordinator and one as partner.

Context-related weaknesses and risks

The scientific output of the team remains limited over the period. Although the ITA staff contributed to publications, neither the PhD candidates nor the postdoctoral researchers produced first-author articles, and only one PhD student appears as second author. The overall publication record therefore remains modest, and the absence of major authorship contributions restricts the visibility of the team.
No public-engagement activities are documented. Despite the team's specific expertise in BSL-4 virology, access to high-containment facilities within CIRI has been limited, constraining the development of projects directly involving highly pathogenic viruses.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team will not be renewed, the PI will focus on completing ongoing manuscripts and continuing teaching activities, while the future affiliation of the team members within other CIRI groups remains to be defined.

RECOMMENDATIONS TO THE TEAM

The team will not be renewed.

Team 27: Virus, Innate immunity and vesicular trafficking (VIV)

Name of the supervisor: M. Marlène Dreux

THEMES OF THE TEAM

The team VIV investigates how innate immune cells detect virus-infected cells, combining molecular and cellular analyses with in vivo and clinical approaches. The project of the team has integrated a cohort SARS-CoV-2 patients to characterize innate immunity, and developed tools and methods to assess the host response against Sars-cov2 at the single-cell level, identify alternative sensing mechanisms, and define predictors of disease severity. The team aims at understanding interferon signaling dynamics, viral strategies to evade or hijack antiviral pathways, and the impact of viral protein trafficking on innate responses. This multidisciplinary project integrates virology, immuno-virology, cell biology, and clinical research.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The last HCERES report highlighted the excellence of the team's strategy and five-year project, and encourage them to continue along this path. However, two main recommendations were made: try to develop the translational aspect of the team project, and increase the number of permanent senior scientists. Although no direct industrial translation was developed, the team VIV expanded its clinical research and conducted a longitudinal study of a sars-cov2 patient cohort (in collaboration with HCL), leading to a publication in Nature Communications. The committee had also advised increasing the number of permanent senior scientists; in response, an MCF (ENS) joined the team in 2023.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectif
Professeurs et assimilés	0
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
Praticien hospitalier	0
Sous-total personnels permanents en activité	**3**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	0
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**3**
Total général	**6**

EVALUATION OF THE TEAM

Overall assessment of the team

The overall assessment of the team is excellent. The Team VIV produced major contributions, with 14 research papers, one review, two book chapters (9 FLC), and ongoing manuscripts, in strong national and international collaborations. Despite difficult circumstances, output was excellent, including publications in high impact factor journals. Major achievements include discoveries on Zika immune escape, NLRP3–IRGM–mediated Golgi membrane remodeling, and HEV–host interactions, and a longitudinal clinical study of a SARS-CoV-2 patient cohort. The team secured major grants and maintained active training, teaching, and scientific leadership.

Context-related strengths and opportunities

Over the evaluation period, the VIV Team produced significant scientific contributions to the field, resulting in a total of 14 research articles and one review, published in important international journals (e.g., publications in Nature Communications, Communications Biology, PLOS Pathogens, Science Immunology, and Cell Host & Microbe), as well as two book chapters (Total 9 FLC). These publications result from national (intra-CIRI and external, including Institut Pasteur, IBPC, IGFL) and international collaborations (UK, Germany, Norway, among others). Team members, in particular doctoral students, appear as the first authors on several publications (even though some of these students are not listed in the team's human-resource records). The team leader is the corresponding author/last co-author on the articles directly related to the research themes developed within the team. Among the scientific achievements of the team, the team leader has chosen to present three published papers and one currently in submission to eLife (with PhD students as 1rst authors). The first study (FLC) presents the genetic pathway by which Zika virus escapes TLR3-mediated antiviral pressure, combining deep viral population sequencing, bioinformatics analysis (quasi-species evolution). They identify and validate a key adaptive mutation in the E protein that enhances infectivity and reveals a mechanistic route for viral immune escape. In the second study, the authors identify that HCV-induced NLRP3 inflammasome regulates immunity-related GTPase M (IRGM)-mediated remodeling of the cell membranes (Golgi). Zika virus also induces NLRP3-dependent Golgi fragmentation. These findings reveal the inflammasome/IRGM pathway as a broadly relevant mechanism controlling virus-induced Golgi remodeling, offering new opportunities to investigate its involvement in diverse viral infections. The following productions focus on glycosylated ORF2 forms and an arginine-rich motif in the ORF2 capsid protein of HEV modulate plasmacytoid dendritic cell–mediated antiviral responses and regulate key steps of the HEV lifecycle, highlighting critical host–virus interaction mechanisms that may control HEV replication. The team VIV has also conducted a longitudinal clinical study of a SARS-CoV-2 patient cohort, resulting in a publication in Nature Communications. Finally, an article is in preparation, involving a PhD student of the team. The team leader obtained numerous grants from various agencies (ANR, ANRS, FRM, ERC), 60 % of them as coordinator (FLC (1.01M€)/no FLC (792k€)), providing support for PhD students until they defend their thesis. The team also has a sustained activity in training and teaching, as well as in evaluation committees and the organization of international meetings. The team leader benefited from international recognition and was invited as a speaker for plenary sessions and lectures. The team leader was interviewed during the COVID-19 pandemic by international press and radio (podcast), and also communicated the team's publications at institutional and national levels.

Context-related weaknesses and risks

No weakness identified.

ANALYSIS OF THE TEAM'S TRAJECTORY

N/A Team closed on December the 31st 2024.

RECOMMENDATIONS TO THE TEAM

N/A. Team closed on December 31st of 2024. The leader of the team passed away, and the members of her team joined others CIRI teams.

CONDUCT OF THE INTERVIEWS

DATES

Beginning: 2 December 2025 at 09 h 00

Ending: 4 December 2025 at 18 h 30

Interview conducted: on-site

PROGRAMME OF THE INTERVIEWS

Day before the interview – Monday 1st of December 2025

18 h 00 **Arrival of the committee at the hotel**

20 h 30 **Work dinner**

Interview day 1 – Tuesday 2nd of December 2025
08h50 at CIRI gate 50 avenue Tony Garnier, Lyon

09 h 00 – 09 h 10 **Hcéres committee welcome**

09 h 10 – 09 h 30 **Hcéres committee meeting**

09 h 35 – 09 h 40 **Hcéres rules and procedures by J. Dutrieux**

09 h 40 – 10 h 40 **Administrative and scientific presentation of the unit's achievements and future by T. Walzer and D. Lavillette**

10 h 40 – 11 h 00 **Committee debriefing and coffee break**

11 h 00 – 11 h 15 **Visit Franklin Building CIRI**

11 h 15 – 11 h 30 **Transit to ENS Lyon**

Teams audition #1 *Public session (15min presentation + 15min discussion)*			
Time	**Room**	**Team**	**Presentation by**
11 h 30 – 12 h 00	*Salle des Conseils ENS de Lyon*	NOPAB	O. Thaunat
12 h 05 – 12 h 35		LP2L	A. Cimarelli
12 h 40 – 13 h 10		EVIR	F-L. Cosset

13 h 15 – 14 h 25 **Lunch break and committee debriefing**

Teams audition #2 *Public session (15min presentation + 15min discussion)*			
Time	**Room**	**Team**	**Presentation by**
14 h 30 – 15 h 00	*Salle des Conseils*	HepVir	D. Durantel
15 h 05 – 15 h 35		NLRP3	B. Py
15 h 40 – 16 h 10		UBIVE	S. Baize
16 h 15 – 16 h 45		LIB	L. Genestier / E. Bachy
16 h 50 – 17 h 05		MBPV	V. Volchkov

17h15 – 18h45 **Committee debriefing and coffee break**

18 h 45 **End of day 1 Interview**

19 h 30 **Dinner**

Interview day 2 – Wednesday 3rd of December 2025
08h45 at CIRI gate 50 avenue Tony Garnier, Lyon

08 h 45 – 09 h 00 **Hcéres committee welcome**

Teams audition #3 *Public session (15min presentation + 15min discussion)*			
Time	**Room**	**Team**	**Presentation by**
09 h 00 – 09 h 30	*Salle des Conseils*	I2BA	T. Henry 10
09 h 35 – 10 h 05		VirPath	B. Lina / M. Rosa-Calatrava 2
10 h 10 – 10 h 40		GIMAP	S. Paul 5

10 h 45 – 11 h 15 **Committee debriefing and coffee break**

Meeting with unit staff *(In the absence of managing staff)*			
Time	**Room**	**Committee Number**	**Meeting**
11 h 15 – 12 h 15	*Salle des Conseils*	1	Meeting with ITAs (*in French*)
	Salle Condorcet	2	Meeting with researchers
	Amphi B	3	Meeting with PhD students and postdoctoral fellow

12 h 20 – 13 h 30 **Lunch break and committee debriefing**

Teams audition #4 *Public session (15min presentation + 15min discussion)*			
Time	**Room**	**Team**	**Presentation by**
13 h 30 – 14 h 00	*Salle des Conseils*	VIRIMI	P-O. Vidalain 21
14 h 05 – 14 h 35		LegioPath	P. Doublet / S. Jarraud 13
14 h 40 – 15 h 10		REVE	T. Ohlmann 24

15 h 10 – 15 h 45 **Committee debriefing and coffee break**

Teams audition #5 *Public session (15min presentation + 15min discussion)*			
Time	**Room**	**Team**	**Presentation by**
15 h 45 – 16 h 15	*Salle des Conseils*	IbIV	B. Horvat 15
16 h 20 – 16 h 50		Horigen	X. Charpentier 8
16 h 55 – 17 h 25		APY	M. Faure 1
17 h 30 – 18 h 00		Stapath	F. Vandenesch 19

18 h 00 – 18 h 30 **Committee debriefing**

18 h 30 **End of day 2 Interview**

20 h 15 **Dinner**

Interview day 3– Thursday 4th of December 2025
08 h 45 at CIRI gate 50 avenue Tony Garnier, Lyon

08 h 45 – 09 h 00 Hcéres committee welcome

09 h 15 – 10 h 15 Meeting with institutions representatives

Teams audition #6 *Public session (15min presentation + 15min discussion)*			
Time	**Room**	**Team**	**Presentation by**
10 h 20 – 10 h 50	*Salle des Conseils*	PHE3ID	P. Vanhems / J-P. Rasigade 22
10 h 55 – 11 h 25		EIA	M. Vocanson 3
11 h 30 – 12 h 00		OR	H. Dutartre / C. Journo 18
12 h 05 – 12 h 35		LYACTS	T. Walzer 12

12 h 35 – 13 h 30 Lunch break and committee debriefing

Teams audition #7 *Public session (15min presentation + 15min discussion)*			
Time	**Room**	**Team**	**Presentation by**
13 h 35 – 14 h 05	*Salle des Conseils*	NITROVIRE	C. Mathieu 16
14 h 10 – 14 h 40		GenoMic	F. Rousset 4
14 h 45 – 15 h 15		PERSIST	N. Personnic 23

15 h 15 – 16 h 00 Coffee break and committee debriefing

16 h 00 – 17 h 00 Meeting with the unit direction

17 h 00 – 18 h 30 Redaction of the final report

18 h 30 End of the interview

GENERAL OBSERVATIONS OF THE SUPERVISORS

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69622 Villeurbanne Cedex
France
direction.recherche@univ-lyon1.fr

Haut Conseil de l'évaluation de la recherche et de l'enseignement supérieur
19 rue Poissonnière
75002 Paris

Réf. : *Observations de portée générale sur le rapport d'évaluation DER-PUR270026007 - CIRI - Centre international de recherche en infectiologie*

Villeurbanne, le 9 mars 2026

Madame, Monsieur,

Je vous remercie de m'avoir transmis le pré-rapport d'évaluation de l'UMR5308/U1111 **Centre international de recherche en infectiologie – CIRI.**

Je tiens à souligner la très grande qualité du travail réalisé par les membres du comité d'évaluation.

Après lecture attentive et analyse du document, je vous précise que ce rapport n'appelle pas d'observation de la part de l'Université Claude Bernard Lyon1.

Je vous prie de croire, Madame, Monsieur, en l'expression de mes sentiments les meilleurs.

Université Claude Bernard Lyon 1
Pour le Président et par délégation

UNIVERSITE CLAUDE BERNARD LYON I

Le Vice-Président Recherche
Arnaud BRIOUDE

Annexe : retour de l'UMR5308/U1111 CIRI sur le rapport d'évaluation du laboratoire.

Dimitri Lavillette, PhD, Dr. Habil, DR2 CNRS
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http://ciri.inserm.fr

Lyon, 4 Mars 2026

To the attention of:

Madame the President of HCÉRES,

The Scientific Advisors,

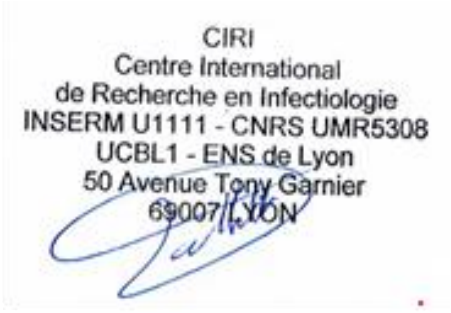
and Members of the Expert Committee

Subject: Observations on the HCÉRES Pre-Report (Wave A) – CIRI

We thank the HCÉRES committee for their work. We have no general observations to make regarding the report.

We have taken note of the recommendations and had already anticipated some changes. We will do our utmost to implement the others.

Sincerely,



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