Evaluation of Research

EVALUATION REPORT ON THE UNIT:

LPHI - Laboratory of Pathogens and Host Immunity

UNDER THE SUPERVISION OF INSTITUTIONS ANS RESEARCH BODIES:

Université de Montpellier

Centre national de la recherche scientifique - CNRS

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

EVALUATION CAMPAIGN 2025-2026
GROUP A

Report published on February, 18 2026

High Council for the evaluation of research and higher education

On behalf of the committee of experts:

Chetan Chitnis, 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.

MEMBERS OF THE COMMITTEE OF EXPERTS

Chair:	Mr Chetan Chitnis, PR, Institut Pasteur, Paris
	Ms Laurence Delhaes, PU-PH, Université de Bordeaux (representative of Inserm CSS)
	Ms Céline Henry, IR, INRAE, Jouy-en-Josas (supporting personnel)
Experts:	Mr Hervé Isambert, DR, CNRS, Paris
	Ms Corinne Mercier, PR, Université Grenoble Alpes (representative of CNU)
	Mr Etienne Meunier, DR, CNRS, Toulouse (representative of CoNRS)

HCÉRES SCIENTIFIC ADVISOR

Ms Birke Bartosch

REPRESENTATIVES OF THE UNIT'S SUPERVISING INSTITUTIONS AND BODIES

Mr Jean Paul Cristol, Université de Montpellier
Mr Jacques Mercier, Université de Montpellier
Ms Agnes Mignot, Université de Montpellier
Mr Mathieu Nigues, Inserm
Ms Eve-Isabelle Pecheur, CNRS
Ms Patricia Renesto, Inserm

UNIT CHARACTERISATION

- Name: Laboratory of Pathogens and Host Immunity
- Acronym: LPHI
- Label and number: CNRS UMR5294, Inserm UA15
- Number of teams: 7
- Composition of the executive team: From 01/2021 to 07/2024, Mr Georges Lutfalla (director) and Ms Rachel Cerdan (deputy director). Since August 2024, Ms Rachel Cerdan (director) and Ms Maryse Lebrun (deputy director).

SCIENTIFIC PANELS OF THE UNIT

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

THEMES OF THE UNIT

The unit's research is focused on understanding the basic biology of pathogens and host-pathogen interactions at the molecular level. The unit uses this knowledge to develop novel intervention strategies including drugs and vaccines that target the pathogens selected for study.

The unit has evolved from an important protozoan division (4 teams) to a unit with three axes, one on Apicomplexan parasites (4 Teams); a second on bacterial virulence and innate immune responses (2 Teams) and a third on Computational Biology (1 Team).

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The unit is located on the Montpellier University Campus Triolet with a surface area of ~1800 m2. The unit was previously led by Catherine Braun-Breton (Pr Univ-Montpellier UM) from January 2007 to December 2014; then Georges Lutfalla, DR CNRS, led the unit from January 2015 to July 2024. Since July 2024, Rachel Cerdan (Pr UM) leads the unit with Maryse Lebrun (DR INSERM) as deputy director.

The teams of Michel Vidal (retired), and Virginie Molle and Karima Kiss departed from LPHI at the beginning of the quinquennial. A new team led by Anne Blanc-Potard and Audrey Bernut has recently emerged from Georges Lutfalla's group and is now integrated in the unit as a team. In addition, an ATIP-Avenir team on P. falciparum gene regulation (T. Hollin) has been recently added to the parasitology division and is not assessed here.

UNIT RESEARCH ENVIRONMENT

LPHI is a mixed unit supported by the University of Montpellier, the CNRS and more recently Inserm. It is composed of seven teams that are organised into three major research axes, namely Apicomplexan parasite biology and bacterial pathogens/inflammation and computational biology. LPHI hosts three technological core facilities (Electron Microscopy, Zebrafish lab, and Malaria L3 lab). These three facilities are open to the scientific community of Montpellier. The Zefix-LPHI facility was established in 2022, the L3-Malaria, equipped for medium-throughput screening, was operational in 2022, and the MRI-EM4Bio facility was officially created in 2023.

LPHI is a member of the PARAFRAP labex, the EuroBiomed (consortium bringing resources, skills and network of experts for innovation), and the Méditerranée Infection Foundation. At the European and international levels, LPHI is involved in European networks linked with the Actions Marie Sklodowska-Curie Action (2 international training networks, FishForPharma and ImageInLife) and MalariaGEN, a consortium for malaria genomics.

The unit has successfully integrated junior researchers who have received permanent positions through Inserm, CNRS or University of Montpellier, the three supporting agencies of the unit. The Inserm label is the most recent.
The unit proposes some re-organization in the next phase. The reorganized unit will have three scientific axes, namely, Parasitology, Computational Biology and Bacteriology/immunity with seven teams. An ATIP-Avenir team working on post-transcription gene regulation in *P. falciparum* has been added (T. Hollin) and the bacteriology team has been divided into two teams due to its growing size. Several teams are jointly managed by a senior and junior researcher, which is very healthy to ensure a smooth transition in the coming years.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maitres de conférences et assimilés	3
Directeurs de recherche et assimilés	4
Chargés de recherche et assimilés	10
Personnels d'appui à la recherche	24
Sous-total personnels permanents en activité	**43**
Enseignants-chercheurs et chercheurs non permanents et assimilés	3
Personnels non permanents d'appui à la recherche	8
Post-doctorants	9
Doctorants	14
Sous-total personnels non permanents en activité	**34**
Total personnels	**77**

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
U Montpellier	5	1	5
CNRS	0	5	17
Inserm	0	8	2
Total personnels	**5**	**14**	**24**

GLOBAL ASSESSMENT

LPHI has a long history of excellence in microbiology research at the University of Montpellier (UM). They have remained competitive at an international level over a long period and are recognized for their highly original and important contributions in understanding pathogen biology, host-pathogen interactions and pathogenic mechanisms. The unit has continued to attract excellent new talents and skills over the years, due to its international competitiveness. The unit is now poised to develop three axes, including studies on Apicomplexan parasites, P. falciparum and T. gondii, bacterial pathogens and host immunity, and computational biology with a focus on infectious diseases. The unit has outstanding teams in each of these areas, which includes a combination of experienced and junior scientists, who are well placed to lead the unit in the future.

The overall objective of LPHI is to understand the biology of pathogens and their interaction with the host. In addition, the unit is interested in exploring the development of novel interventions based on the basic discoveries made by its teams. Each team of LPHI has made important fundamental contributions to our understanding of pathogen biology and host-parasite interactions. Two landmark discoveries include description of the molecular machinery responsible for rhoptry secretion in T. gondii and identification of transcriptional regulation as the mechanism for sexual differentiation in P. falciparum. Such fundamental discoveries present novel approaches to target these pathogens. For example, interference with sexual differentiation can be used to prevent malaria parasite transmission and inhibition of rhoptry secretion can block parasite multiplication. Studies on pathogen biology proposed for the LPHI unit will continue to provide additional breakthroughs. The unit is encouraged to develop an effective strategy to guide their translational research activities to improve chances of success in the stated goal of developing novel therapeutics against the pathogens selected for study within a reasonable timeframe.

The LPHI unit has established 2 important core facilities, one for electron microscopy and the other for zebra fish biology. These facilities have greatly enhanced the capacity of its teams to undertake novel approaches and cutting edge research in pathogen biology and host immunity. These platforms have an impact in the local research ecosystem beyond the unit. These are unique resources that need to be supported and strengthened by the agencies. There is a need to ensure that key staff in the unit have permanent contracts to ensure stability of these important facilities.

LPHI has been very successful at recruiting outstanding young researchers who have gone on to obtain permanent contracts with CNRS, UM or Inserm. Several of the teams are jointly managed by a senior researcher and a junior colleague. This healthy mentorship is laudable and will help the unit in the long run to provide the next generation of leaders ensuring the longevity of the unit. The unit also has a healthy environment with many common activities that provide plenty of opportunities for scientific and social interactions. Such interactions are important to inform each team about ongoing research in neighboring teams thus opening the possibilities for potential collaborations. This is particularly important for the core facilities and teams such as the Computation Biology Team, whose success depends on such collaborative projects. The Computation Biology team is well embedded in the unit with interactions and ongoing projects with several teams.

The unit has achieved remarkable success in securing funding with six European, eighteen ANR, two labex and other national grants totaling to 2.5 M€ from external sources annually since 2022.

LPHI has a highly positive visibility with team leaders as well as junior researchers invited to present their work at national and international meetings. Together, the unit has published over 200 research articles and reviews with unit members holding leading positions (first author or corresponding author) on 60% of the publications.

The unit has engaged in outreach activities at different levels including undergraduate students in university as well school students.

Overall, the LPHI has an outstanding record of achievement over the past five years and should achieve continued success with the plan proposed for the next five years.

DETAILS OF THE EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous Hcéres evaluation in 2019-2020 made three recommendations regarding the future of LPHI. The unit has responded to the major recommendations of the Hcéres evaluation.

A – Recommendations on scientific production and activities (criterion 1). The committee recommended to develop a clear research strategy with enhanced internal synergies and collaborations with industrial partners. This strategy should then guide future hiring's.

The overarching objective of LPHI is to study host-pathogen interactions and develop novel drugs and vaccines to target them. Each team has identified important questions, which will not only improve our understanding of their pathogens of interest but can also provide new targets for drug and vaccine development. Sound scientific strategies to address these questions have been developed and should yield important results. Efforts have been made to build synergies between teams and establish translational research projects to exploit emerging leads. Some collaborations with industrial partners have been established. Some excellent young researchers with research interests that align with the overall strategy have been recruited.

B – Recommendations on the unit's organization and life (criterion 2). The committee commended the overall organization and life of the unit and recommended increasing both external and internal communications.

The overall organization, productivity and life of LPHI remains excellent. All teams have attracted excellent students, post-docs, and junior researchers reflecting the unit 's attractiveness. There are many opportunities for internal interactions and several collaborations have been established between teams. Efforts have been made to increase outreach activities to reach students through on-campus activities and peers by disseminating results at leading national and international conferences.

C – Recommendations on scientific strategy and projects (criterion 3). The Committee recommended increased collaborations between teams of the unit.

The unit has made efforts to encourage collaborations between different teams and provide opportunities for interaction through regular joint seminars and meetings. A special effort has been made to identify points of collaboration between the Computation Biology team and other teams. In some cases, the pathogens and

models used are too different to enable collaborations. For example, the zebrafish model is unique and may not be relevant to all pathogens studied in the unit. The establishment of a new team that will use the zebrafish model will strengthen this area and optimize the use of the zebrafish model, which is a unique strength of the unit.

B - EVALUATION AREAS

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

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

LPHI studies **host–pathogen interactions, with a focus on parasitology and immunity, inflammation, and bacterial virulence.**
It has established an appropriate governance framework including a steering committee, laboratory board, and a general assembly.

LPHI has been highly successful in raising funds at national and European levels with a marked increase in European funding (x8 compared to 2019).

Considering the scientific breakthroughs achieved, successful management of the unit and success at raising funds, the performance of the unit is rated as 'Outstanding'.

1/ The unit has set itself relevant scientific objectives and is organized accordingly.

2/ The unit has resources adapted to its scientific objectives, profile of activities and research environment and mobilizes them.

3/ The unit has premises, equipment and technical skills adapted to its scientific policy and research objects.

4/ The unit's practices comply with the rules and guidelines set by its supervisory bodies in terms of human resources management, safety, environment and data protection as well as scientific assets.

Context-related strengths and opportunities for the four references above

The unit's teams share advanced biological and technological core facilities, fostering collaboration and efficient resource use. A unique feature of the unit is the integration of mathematical modeling and artificial intelligence, providing innovative tools to support experimental research. This combination of cutting-edge infrastructure, interdisciplinary expertise, and collaborative culture positions LPHI as a leading center for research on infectious diseases.

Two landmark discoveries made by the unit include description of the molecular machinery responsible for rhoptry secretion in T. gondii and identification of transcriptional regulation as the mechanism for sexual differentiation in P. falciparum. Such fundamental discoveries present novel approaches to target these pathogens. For example, interference with sexual differentiation can be used to prevent malaria parasite transmission. Studies on pathogen biology proposed for the LPHI unit will continue to provide additional breakthroughs. Key strengths of the unit lie in its ability to bridge fundamental and applied research, thus fostering technology transfer and international collaborations (ERC grants, ITN networks), promoting career development (specially for early-career researchers), gender equality, and open access and supporting a critical scientific mindset and combating misinformation.

The unit has achieved remarkable success in securing funding, both at the European level (2 Marie Skłodowska-Curie actions, 2 ERC: totaling 6 M€) and the national level (18 ANR, 3FRM Teams, 2 ATIP-Avenir, 2 labex (EpiGEnMed, ParaFrap)). The unit's **annual budget is around 2,7 M€** (annual financial resource from supervision bodies 200 k€, external grants € 2.5 million). In terms of staff, the unit has made two new recruitments, and IR CNRS and a CPJ UM (O. Radulescu team).

Between 2022 and 2023, three platforms were established to serve the scientific community of Montpellier. 90 k€ are dedicated each year to common equipment of the unit. The unit operates three BSL-2 laboratories (parasitology, bacteriology) and two BSL-3 laboratories (Plasmodium), shared by all relevant teams. It has access to national computing platforms (CINES, GENCI, Meso@LR) and in-house servers for modeling and simulation.

LPHI benefits from full documentary resources via its supervisory bodies, and nearly all publications are openly available on HAL, supported by a dedicated referent.

The unit manages three open-access technological core facilities and plays a strategic role within BioCampus Montpellier, contributing financially and operationally, particularly to the Optical Imaging Facility.

The unit demonstrates gender parity in managerial positions and maintains balanced team composition across all categories of staff (researchers and ITA). Moreover, it actively promotes fair and inclusive recruitment policies.

The unit places strong emphasis on preventing psychosocial risks and promoting well-being at work. The director has completed specific management training, and all team leaders are encouraged to do the same. Two designated contacts ensure appropriate support for individuals at risk. Regular individual meetings with the direction foster open dialogue and trust. Flexible organization minimizes constraints related to experimental work, and collective solidarity is actively encouraged. Training, workshops, and career development support, including promotion preparation, are systematically offered, reflecting the unit's commitment to a supportive, inclusive, and respectful working environment. PhD students are also encouraged to take part in training programs.

The unit ensures health and safety compliance through dedicated staff and training, with strict access control as a Restricted Area (ZRR) due to pathogens and radioactive materials. Annual events further promote safety awareness among all members.

Data protection is a top priority in the unit, with all digital assets secured, encrypted, and managed according to the FAIR principles.

LPHI has appointed a sustainable development representative and established a working group to promote eco-friendly practices, reduce resource consumption, and minimize plastic and carbon footprints. Initiatives include optimizing freezer use, encouraging recycling, sustainable purchasing, energy savings, and promoting awareness through dedicated events and training for all staff.

Context-related weaknesses and risks for the four references above

One of the key objectives of the unit is to exploit leads for development of novel vaccines and drugs. While the unit is working on several such translational projects, it needs to develop and implement a strategy for translational research that develops new tools in a reasonable timeframe.

Despite its strong international network, the unit could better capitalize on these collaborations to secure additional international funding and coordinate large-scale research projects. Strengthening the strategic alignment between its thematic axes and major global health priorities (such as antimicrobial resistance, emerging pathogens, and climate-related infectious risks) would enhance the coherence, visibility, and competitiveness of the unit at the international level. Developing a few flagships, cross-cutting scientific objectives shared across teams could also help focus resources and increase the unit's ability to attract competitive international grants.

ANR funding appears to have been decreasing since 2022.

Regarding the staff, there is an alarming decrease in the number of permanent PAR that could jeopardize the future of some platforms, which is temporarily compensated for by hiring many people on fixed-term contracts (9 permanents PAR for all the teams). The unit faces significant challenges due to the upcoming retirement of support staff and the difficulty of replacing them.

Some infrastructures are aging (over 20 years old) and require urgent renewal to maintain optimal research conditions; for instance, the air handling unit for the L3 lab is extremely costly, making its replacement a major financial and logistical challenge. Funding for such operations is currently insufficient. The 3 LPHI core facilities are running essentially with the contribution of non-permanent technical staff (just one IR as permanent staff).

Concerning data protection, the reliance on a non-permanent replacement for the retired IT manager could expose the unit to risks in continuity and data security. It is strongly recommended to secure a permanent IT position to maintain compliance with GDPR and FAIR principles.

While the commitment to sustainable development is visible and dynamic, most actions are still limited to awareness and small-scale behavioral changes. The unit is encouraged to move towards quantifiable environmental objectives, formalize its Labos1point5.org (organization aiming to reduce carbon imprint in research) assessment outcomes into an action plan with measurable targets, and integrate sustainability criteria into purchasing and research project design.

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

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

The unit has made outstanding discoveries in understanding the basic biology of pathogens. These discoveries have led to the identification of some leads for development of therapeutic strategies. Although it has not yet yielded a viable drug candidate. Thus, strategies for translational research need to be reinforced for efficient development of novel drugs.
The unit leadership has also not taken a lead in organizing regional or international networks/consortia/conferences. The performance of LPHI unit is evaluated as excellent in this evaluation area.

1/ The unit is recognized for its scientific achievements that meet quality criteria.

2/ The research activities of the unit result in quality scientific production.

3/ The unit participates in the coordination and management of its community.

4/ The unit's scientific production respects the principles of scientific integrity, ethics and open science. It complies with the guidelines applicable in this field.

Context-related strengths and opportunities for the four references above

The unit's research aims at improving our basic understanding of host-pathogen interactions, while at the same time being aware and acting on translational research opportunities emerging from basic science to develop novel drugs and vaccines to target pathogens of interest. The unit has been highly productive with the research undertaken providing many unique insights into the biology of important pathogens and providing leads for the development of novel drugs.

The unit has collectively published over 200 articles with more than 50% of the research articles having unit members as lead or senior authors. Publications from the unit include reputed international journals such as Nature (1), Science (1), Nature Microbiology (2), Nature Communications (10), Science Advances (1), Cell Host Microbe (1), PNAS (2), EMBO J (2) and PLoS Pathogens (5). Each team of the unit has made key fundamental breakthroughs in our understanding of pathogen biology. These include a.) Identification and characterization of the rhoptry secretory machinery in Apicomplexan parasites like Toxoplasma gondii, which plays a key role in host cell invasion. b.) Identification of the transcriptional switch mechanism for sex determination in P. falciparum providing novel targets to block malaria transmission. c.) Description of G-quadruplex DNA motifs in P. falciparum genome and their role in regulation of var gene expression. d.) Understanding of P. falciparum infections in asymptomatic cases of malaria by genetic analysis of infected individuals in high transmission endemic settings e.) Mathematical modeling of HIV-1 infection dynamics based on single molecule imaging of HIV-1 transcription. f.) Use of zebrafish model to study macrophage function in bacterial infections. As described, the topics covered by the unit are wide and the unit creates a significant impact in the field of pathogen biology. The members of the unit have been recognized for their work with prestigious awards and prizes. These include the Legion d'Honneur medal and the CNRS Bronze medal. Members of the unit have also been successful at obtaining competitive national and international research grants (1 ERC Advanced, 1 ERC Starting and 2 Marie Sklodowska-Curie Action grants) as well as competitive research positions including 5 CRs recruited by CNRS (3) and INSERM (2). The unit members are invited to present their work at National and International conferences and are members of several national and international collaborative research networks, such as labex ParaFrap (French Alliance for Parasitic Diseases) and Indo-French International Research Network (IRN) for Infectious Diseases.

The unit communicates its research findings to peers at international conferences and its members are regularly invited to speak at important meetings in the field such as Gordon Conferences, EMBO meetings and invitations to speak at universities and research institutes around the world. The unit also encourages participation of young researchers, post-docs and doctoral students in scientific meetings such as the Molecular Parasitology Meeting,

International Toxoplasma meeting, iron-sulfur meeting and Conference on Systems Biology, where they are often invited to present talks and have also won awards for best presentations.

The unit promotes an open science policy, including open access to data, use of open-source licenses, and adherence to FAIR principles. Team members are encouraged to select open access journals to publish their results and to post a preliminary version of their manuscript on a pre-print server. All experimental details and data are recorded daily. Electronic laboratory notebooks and centralized data archiving have been implemented. The unit adheres to the Nagoya Protocol on Access and Benefit-Sharing.

Context-related weaknesses and risks for the four references above

The unit is strong in basic science research on pathogen biology. This impressive research effort produces leads for translational research. However, the output from translational research for drug and vaccine development can be improved. There is no clear strategy for the translational projects undertaken by the unit. Given that this is a stated goal of the unit, the strategy for translation should be clearly thought through and stated so that it can guide the projects and work plan in the future.

EVALUATION AREA 3: INCLUSION OF RESEARCH ACTIVITIES IN SOCIETY

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

LPHI has made outstanding contributions to our basic understanding of pathogen biology. However, the unit does not appear to have a very clear strategy or plans for translational research. The unit may seek the help of INSERM Transfert to develop a strategic plan for translational research to set the goal of developing a drug or vaccine candidate. The performance of the LPHI unit for developing programs that lead to societal benefit is "very good".

1/ The unit stands out for the quality of its interactions with the cultural, and socioeconomic world.

2/ The unit develops products and services for the cultural, socioeconomic world.

3/ The unit shares its knowledge with the general public and participates in social debates.

Context-related strengths and opportunities for the three references above

The unit is committed to translation of leads from their basic research on pathogens to develop novel drugs and vaccines. Towards this objective, teams of the unit have engaged with 'Sociétés d'Acceleration du Transfert de Technologies (SATT)', and this has led to develop at least two anti-malarial lead compounds identified by the unit. At least one other project based on a T. gondii protein is currently being reviewed by SATT for development as a cyto-protective and anti-inflammatory molecule. These are promising developments that can help to translate basic research findings into technologies that can be used to address important public health problems. The unit has been pro-active in filing patents with 4 patents filed and one invention disclosure in the current evaluation period. One patent relates to a novel anti-malarial compound based on a purine analog, another is based on compounds that target G-quadruplex DNA sequences in P. falciparum and two others are related to novel methods in computational biology. Protecting intellectual property is the first step to enable the development of technologies for commercial use and public good. It is encouraging to note that the unit is paying attention to protection of intellectual property arising from their fundamental research on pathogens.

The unit has also engaged in outreach activities to students in schools. The unit receives students from high schools in their laboratories and unit members also participate in the 'Science Festival' and 'Declics Initiative', an outreach activity to reach undergraduate University students. Unit members including PhD students participate in several activities including participation in MOOCs, European research night and reach community through interviews, debates and press articles.

Context-related weaknesses and risks for the three references above

The translation of research findings to technologies that are used for public awareness is a major challenge facing academic research institutes and universities. While it is positive to see that the unit is engaging with SATT to find solutions for technology transfer for commercial development, there is limited information on these activities so it is difficult to evaluate the progress made and their chances of success. While the unit acknowledges their commitment to translational research, the strategy for translation and the status of these projects have not emerged clearly throughout the evaluation process. The workplan with milestones, timelines and deliverables need to be defined better for the translational projects.

Similarly, while some outreach activities have been undertaken, there does not seem to be any clear plan for these activities. How many visits by school students are there each year? Is there a calendar of events each year? Has the unit considered using occasions such as 'Malaria Day' to engage with the public or students? A clear strategy for communication and public outreach would help streamline these activities and make them more effective.

ANALYSIS OF THE UNIT'S TRAJECTORY

Overall, the LPHI unit has made outstanding progress in their studies on pathogen biology and interactions with the host with several landmark fundamental discoveries and identification of some potential leads for development of novel intervention strategies, especially new drugs. The unit has also been successful at raising funds through national and international grants, which testifies to the recognition of their work by peers and places them in a comfortable situation to undertake their plans for the next period. The success of the unit at recruiting some excellent young researchers with permanent positions through the competitive national schemes of INSERM and CNRS places the unit in an excellent position to grow and flourish in the next phase. The unit has proposed re-organization for the next phase to create three axes, one on parasitology focused on *T. gondii* and *P. falciparum*, a second on bacterial pathogens and mechanisms of innate immunity and a third on computation biology, that will be cross-cutting and engage with the other axes and teams. The re-organization also envisions the fusion of two current teams working on malaria and the arrival of two new teams, one funded with an ATIP/Avenir grant on malaria and another on bacterial pathogens. The re-organization proposed is coherent and should lead to effective synergies whilst the new additions of young researchers will provide stability for the future of the unit.

In addition, 2 major points are relevant for a notable unit's trajectory: i) having a team of mathematicians within the unit and ii) being the 1st in French core facility to have a Leica UC Enuity Advanced ultramicrotome (along with the Zebrafish core facility).

The scientific program outlined for the next period of five years builds on the success of the last period and should yield exciting new findings in all the areas of investigation. The platforms for imaging and zebrafish established should be strengthened to enable optimal use for the unit's projects and also accommodate investigators in the community outside the unit. A clear strategy for translational research should be developed to improve the chances of success so that the fruits of research reach the community in a timely manner. Plans for outreach should also be outlined to communicate both the importance of studies on pathogens and the excellent work being done by the unit in this area. Altogether, the unit has a bright future and can continue its trajectory to be recognized as one of the leading groups internationally working in some niche areas of pathogen biology.

RECOMMENDATIONS TO THE UNIT

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

The scientific focus on understanding the basic biology of pathogens of interest and their interactions with the host should be maintained. The opportunities for development of therapeutic interventions based on fundamental discoveries should be identified and exploited. A strategy for selection of promising targets and development of therapeutic interventions should be developed so that translational research progresses more efficiently.

The unit is organized effectively, providing participation by all the teams in decision making and providing plenty of opportunity for interactions between the teams at all levels. The core facilities are key resources of the unit that make the unit attractive. The unit may consider including core facility leaders, especially the EM core facility head, in team leader meetings in the unit to provide opportunity to core facility heads to participate in the life of the unit more fully.

Supporting agencies together with LPHI leadership should explore ways to secure permanent positions for key personnel in the platforms to optimize investments made to establish this infrastructure.

During the staff interview (PAR), the issue of communication and feedback from team leaders' meetings was raised. It appeared that the feedback provided varies greatly from one team to another. It would therefore be advisable to share the agenda of these meetings with all staff members, and possibly make the meeting minutes available as well.

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

The unit is already publishing high quality papers in leading international journals describing many important results. The unit is well recognized internationally for important scientific breakthroughs in pathogen biology through their publications and participation in national and international meetings. These activities should continue.

Given their success, team leaders can now take more active leadership roles outside the LPHI to broaden their impact. For example, they can take on roles as coordinators or principal investigators of collaborative multi-partner projects/consortia at the national, European or international levels. The unit can also organize and host international meetings once in 2-3 years on topics relevant to the activities of the unit. This can provide wider exposure to unit members to international experts, provide more visibility to the work of the unit and potentially lead to collaborations that can enlarge the scope of activities of the unit.

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

In addition to studying the basic biology of pathogens, a key stated objective of LPHI is to develop novel therapeutic strategies based on targets emerging from the fundamental studies. The translational research activities of the unit need to be strengthened. This requires a clear plan to guide researchers for translational research once a promising discovery is made. This may require some advice and hand holding for researchers interested in pursuing translational research based on their leads. The unit should reach out to INSERM Transfert and requests a consultation or on-site workshop on the subject. A pro-active effort from the unit to put in place a clear strategy and plan for exploitation of leads is needed to make translational research more effective.

TEAM-BY-TEAM ANALYSIS

Team 1: Cell biology of apicomplexan parasites

Name of the supervisors: Ms Maryse Lebrun & Mr Sébastien Besteiro

THEMES OF THE TEAM

The team, composed of three groups, focuses on the understanding of the molecular determinants that allow the intracellular parasites *T. gondii* and *P. falciparum* to invade into, replicate within and egress from the host cell. M. Lebrun's group (biology of rhoptries), S. Besteiro's group (search for *Toxoplasma* metabolic specificities that could be exploited to interfere with the parasite's multiplication) and M. Lamarque's group (role of phosphatases during the Plasmodium egress) used similar (functional genomics, phenotypic analyses of mutants, cutting-edge imaging techniques) and complementary technical approaches to unravel key mechanisms.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous report had requested from the team to extend their fundamental research studies to more applied projects. This was undertaken in the evaluated mandate since 1/ the vaccine potential of rhoptry proteins is being investigated in collaboration with the Uruguay Pasteur Institute in both sheep (vaccine against toxoplasmosis) and cattle (vaccine against neosporosis caused by *Neospora caninum*, the closest *Toxoplasma*-related Apicomplexa parasite); 2/ in collaboration with chemists, they have identified compounds thought to interfere with the redox or the Fe acquisition pathway, and they now need to elucidate the mode of action and the targets of these compounds before patenting them.

The previous report had requested from the team to secure more external financial supports: the team obtained, during the evaluated mandate, one ERC advanced grant, 5 ANR grants (3 as coordinators and 2 as partners), the renewal of the FRM team, and a Booster Innovation grant from the University of Montpellier for a total of 600,000 to 800,000 euros per year from 2020 to 2024.

The last request was to increase their participation to outreach events: over the mandate, they were involved in the "Declics" initiative, "Jeunes Francophones et la Science", "Lycéens au labo". They were also particularly active in sharing their findings with the youngest generations to sensitize them about the potentials of research and the necessity to develop a critical mind.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	2
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	**12**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels non permanents d'appui à la recherche	1
Post-doctorants	2
Doctorants	3
Sous-total personnels non permanents en activité	**7**
Total personnels	**19**

EVALUATION OF THE TEAM

Overall assessment of the team

The evaluation of the team is "outstanding" over the evaluated mandate in terms of scientific objectives, achievements, publications, funding and attractiveness. The assessment is excellent in terms of outreach activities.

Context-related strengths and opportunities

Capitalizing on the outstanding work published on *Toxoplasma* invasion over the past years, the group of M. Lebrun has appropriately gained an internationally recognized leadership leading to the success to an ERC advanced grant (2020-25), from which the entire team has greatly benefited over the evaluated mandate. In addition to this major grant, the team was also successful in obtaining three ANRs as coordinator (+ 1 under review), two as partner, a Booster innovation grant from U. Montpellier, and in getting the renewal of their FRM team labelisation. This success contributes to major achievements: two post-docs in the team were recruited as CNRS and Inserm researchers over the period; twelve PhD students were trained, seven post-doctoral researchers were hired and fourteen Master/Bachelor students were trained over the period. This also triggered numerous invited conferences and seminars (15 invited conferences and 14 invited seminars for M. Lebrun, and a total number greater than 40, when counting the other group members), election of the PI for the co-organization of the famous International Molecular Parasitology Meeting of Woodshole, expanded the number of international collaborations with prestigious research institutes such as MIT, Univ. of Stanford, Harvard, and resulted in the publication of 43 articles over the evaluated period (2 Nature Microbiology, 2 PNAS, 1 EMBO Journal, 3 Nature Communications, 1 eLife, 3 PLoS Pathogens, 2 mBio, 1 J. Biol. Chem), four book chapters and ten invited reviews. Importantly, post-doctoral researchers and PhDs came out of their training with multiple publications including first author papers; engineers were also included in publications.

Among the major scientific achievements over the last five years, one can mention: 1/ the demonstration that bradyzoites use a moving junction (MJ)-dependent invasion process, yet of specific composition; 2/ the validation that the MJ complex can be considered as a potential vaccine that could protect against acute and chronic toxoplasmosis; 3/ the characterization of ROP55 as a novel major virulence factor that prevents host cell death and suppresses the pro-inflammatory response in absence of stimulation by IFN-gamma; 4/ using the elegant approach based on the comparison of rhoptry secretion and secretion from free-living Ciliates, the discovery and the 3D resolution of the rhoptry secretory apparatus; 5/ the validation of the apicoplast as a valuable drug target in bradyzoites; 6/ the characterization of Fe-S assembly pathways in Toxoplasma and highlighting the fact that the cytosolic pathway displays unusual features that may be exploited for drug design; 7/the identification of TgShelph as a phosphatase playing a major role in the acute virulence of Toxoplasma; 8/ highlighting the fact that PfPPI plays a major role in egress.

Over the mandate, team members were involved in the "Declics" initiative, "Jeunes Francophones et la Science", "Lycéens au labo". They were also particularly active in sharing their findings with the youngest generations to sensitize them about the potentials of research and the necessity to develop a critical mind.

Context-related weaknesses and risks

While the group of M. Lebrun is very successful and well established, that of S. Besteiro is more modest, nevertheless well recognized in the Apicomplexa community, which is attested by the numerous invited reviews, several invitations to national and international conferences, the success to several ANRs and the development of several fruitful collaborations that should contribute to further expansion and successes of the group. What is more questionable is the survival on the long term of the group of M. Lamarque, due to the planned 4 yearsleave of the group leader. The group has published in high standard reviews over the evaluated period (Nat. Comm; mSphere), which is a great achievement given that the group leader is an associate professor at University of Montpellier and has important administrative responsibilities (coordinator of one of the programs of the Master's degree, and contact officer for the Erasmus European mobility program). Emergence of the newly recruited researchers might compensate in the mandate to compensate for the "temporary loss" of the group leader during the 4 years leave.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team will appropriately continue the undertaken studies: 1/ questioning how the rhoptries' content is released into the host cell at the time of invasion, how their proteins contribute to the invasion process and how they control the host cell death (M. Lebrun's group); 2/ developing exploratory approaches to identify and validate new therapeutic targets linked to *Toxoplasma* metabolic specificity and continuing the undertaken drug design approach on identified targets to develop drugs for licencing (S. Besteiro's group). This trajectory is clear, and should be successful. Furthermore, the newly recruited researchers, while being integrated in the rhoptry secretion project, will develop their respective independent projects: 1/ investigating the biogenesis of micronemes and rhoptries in Apicomplexa, taking the elegant approach of using the free-living ciliate *Paramecium* as a model since the biogenesis of secretory organelles and their exocytosis seems to be conserved among Alveolata (Apicomplexa, Ciliates and Dinoflagellates) (one of the newly recruited researchers has strong experience in the biology of Ciliates); 2/ characterization of the secretory organelles specific to the gametocyte stage of *P. falciparum*. These new axes in the team should provide very interesting outcomes.

Some of these projects are already funded (ex: visualization of the structural changes of the Rhoptry Secretory Apparatus upon exocytosis and the role of Ca2+ in this secretion (INSERM international collaborative project 2025-29; test of MJ-based vaccine in both sheep and cows in Uruguay; ParaFrap funding to characterize the specific secretory organelles found in the sexual stages of *P. falciparum*; ANR 2025-29 to investigate the Fe6S proteome). Other funding requests are being evaluated (role of Ca2+ in the exocytosis from rhoptries: ANR and NIH grant; evaluation of the ability of TgROP55 to control necroptosis in the context of bacterial infection: CNRS pre-maturation project). The numerous grant applications attest to the dynamism of the group to search for funding sources and should guarantee their success.

RECOMMENDATIONS TO THE TEAM

While it is anticipated that the team will continue to perform great on fundamental studies, they should continue to explore more translational aspects, as their first collaborations on the development of vaccines and novel drugs are encouraging. The major point of attention is the announced retirement of M. Lebrun in 2032, which means that the team should anticipate her replacement, maybe through further expansion of S. Besteiro's group strengthened by the blooming of one of the newly recruited researchers.

Team 2: Molecular approaches for new antimalarial strategies

Name of the supervisors: Ms Rachel Cerdan & Ms Ana-Rita Gomes

THEMES OF THE TEAM

The team focuses on two key processes of the parasite P. falciparum within red blood cells (RBCs): i) the cell cycle progression and regulation of DNA replication and ii) the phospholipid metabolism for membrane synthesis and cell signalling, with a strong interest in the development of novel and efficient antimalarial compounds in a drug-to-target approach. The team is composed of two subgroups led by R. Cerdan and A.R. Gomes. R Cerdan subgroup focuses on phospholipid metabolism and antimalarial compound discovery/development and A.R. Gome's subgroup focuses on the cell cycle progression and fate of the parasite.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

It was recommended to the team to develop "a clear strategy for prioritising candidate enzymes for pursuing as drug targets, ideally in coordination with stakeholders/funders with appropriate expertise". The group prioritized enzymes involved in phospholipid metabolism, which are essential and function as rate-limiting steps. The group mentioned that this approach was funded by an ANR grant (PaluMet) from 2021 to 2025.

Furthermore, as part of their drug-to-target approach, the group developed purine analogues, for which a patent has been filed. This project went through the evaluation process of Tres Cantos Open lab foundation (TCOLF, GSK) but was stopped during the COVID-19 pandemic and not reinitiated.

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

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

EVALUATION OF THE TEAM

Overall assessment of the team

The evaluation of the team is "outstanding" over the evaluated mandate. This covers scientific goals, discoveries, publications, drug target identification and compound development, funding, attractiveness, and excellent in terms of outreach activities.

Context-related strengths and opportunities

The group has published strong work regarding P. falciparum biology (PloS Genetics, Nature, Chemistry, Cellular and Molecular Life Sciences) and virulence over the past years. In addition to the R. Cerdan subroup, the emergence of the AR Gomes subgroup also contributes to expand the international recognition and area of research of the group. Specifically, the Cerdan group has successfully raised multiple national grants (2 ANRs, 1 ANR-IDEX, MITI- 80Prime, 2 SATT valorisation grants), supervised students (7 PhD students, 3 supervisors) and obtained a strong internationally acknowledged expertise. In addition, the ANRJCJC, the ERC-tremplin and the ERCS StG grant as well as the Bronze Medal from CNRS awarded to AR Gomes also strongly contribute to the international recognition of the team as well as to the development of novel and cutting edge area of research regarding *P. falciparum*. In line with this, the group has also developed novel purine analogues in the frame of *P. falciparum* cure, for which a patent has been filed with support from the SATT-AxLR.

This, in addition to the attendance/organization of important conferences and seminars (e.g organization of the congress of French Association of Crystallography 2024 (~200 participants) and the Antifungal and antiparasitic consortium CaPF 2020 (~100 participants)), the strong teaching involvement of the group (e.g. R Cerdan is the director of the Biology-Health Master's program (350 students) of the University, each year the team's PIs give lectures to the Infection Biology track of the Master's program) and the important outreach activities (e.g Declics initiative, history and evolution of women's rights and gender equality, Radio France interview) regarding the spread of science as well as the different supports for Women in Sciences are very strong assets of the team.

The complementary experience of the two PIs and the emergence of a young researcher awarded by an ERC STG constitutes a strong positive signal for the future and solidity of the team.

Context-related weaknesses and risks

None

ANALYSIS OF THE TEAM'S TRAJECTORY

The proposed team's trajectory is clear and promising as it combines highly complementary expertise regarding *P. falciparum* biology, virulence and pharmacological targeting. The objectives will be articulated around four axes of research:
- Phospholipid metabolism of the parasite
- Purine analogues as anti-malarial drugs
- Cell cycle regulation and cell fate of the parasite
- Cell cycle progression and phospholipid metabolism of the parasite

To achieve those goals, the team has already secured numerous grants including one ANR grant on purine analogues, one ERC StG and is also supported by the novel BSL3 infrastructure for novel drug identification for malaria hosted at LPHI. The group has also submitted grants (2 ANRs) that are currently under evaluation.

RECOMMENDATIONS TO THE TEAM

Based on the current dynamic and the very strong success of both PIs, it is anticipated that the team will continue to perform great fundamental studies.

While the ANR and ERC grants are a strong support for the research success, keep applying to various grants, which will help secure the next steps of the team.
Finally, obtaining a new HDR in the team (in progress for 2026) will also support student supervision capacities of the group.

Team 3: DNA Biology in Plasmodium falciparum

Name of the supervisor: Mr José-Juan Lopez Rubio

THEMES OF THE TEAM

The team, part of the LPHI parasitology division, addresses the broad theme of host-pathogen interactions with research focused on *Plasmodium*. Specifically, the team specializes in the molecular parasitology of *Plasmodium falciparum*, with a focus on DNA/RNA regulatory mechanisms—including G-quadruplex structures, noncoding RNAs, and epigenetic controls—to unravel regulation of expression of virulence gene, and to address the development of drug resistance, which represent important innovative questions in a competitive research field.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

As recommended, team 3 participates to weekly meetings for the entire unit, to each division weekly meetings, and to set up a weekly 'Plasmodium' and 'Zebrafish' meetings, to foster collaboration within parasitology division. The proposed joining of forces with another group has led to fusion with team 4 of the unit and resulted in a positive outcome, which may lead to better synergies.

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

Catégories de personnel	Effectifs
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	0
Sous-total personnels permanents en activité	**1**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	0
Post-doctorants	1
Doctorants	2
Sous-total personnels non permanents en activité	**3**
Total personnels	**4**

EVALUATION OF THE TEAM

Overall assessment of the team

In the field of *P. falciparum* biology and drug resistance, Team 3's overall assessment is 'excellent', with several published papers and grants and a filed patent. The team was involved in co-organization of a scientific meeting, the "Montpellier non-B DNA Day" bringing together national and international experts providing visibility to their contributions and capabilities.

Context-related strengths and opportunities

Team 3 is well-established in CRISPR analysis of *Plasmodium* (*P. falciparum*), however this expertise was mainly valorized in 2019-20. However, *Plasmodium* G-quadruplex research represents a burning topic in which the team develops expertise. It recently published two articles as lead team on this topic and in particular the impact on gene expression in malaria (i.e. the identification of PfGBP2 as novel G-quadruplex binding protein in *P. falciparum;* Cell Microbiol. 2021, PLoS Genet. 2020). The team has published twelve articles in peer-reviewed journals, of which two as first and last authors (Cell Microbiol, PLoS Genet), and two further papers with team members as 1st authors (NAR, Front Parasitol).

Three PhD scholarships were obtained from Montpellier & Azerbaijan universities.
International collaborations have been established with University Hospital Bonn and University of Munich, SNRC Spain, Institut Pasteur of Dakar, UNAM Mexico. The team furthermore hosted international visitors from India and Mexico.

A patent has been filed on Naphthalene diimide compounds. The team shares resources and expertise in genome editing with external partners through workshops and short-term lab placements, aiming to accelerate therapeutics and vaccine development pipelines for neglected infectious diseases.

The team contributes to Master's-level teaching in Parasitologie Moléculaire (U Montpellier) and participates in MOOCs (e.g., Malaria MOOC) to educate a broader audience.

Context-related weaknesses and risks

The limited size of the team 3, with only one permanent researcher, two PhD students, one post-doctoral researcher and recently a research engineer, could impact its research program negatively, jeopardize its scientific outputs (articles, conferences) and visibility (conference attendance/invitations, etc). Grant leverage has been limited to few national/ regional grants such as MUSE-Epigenmed (50k€); labex ParaFrap (Partner); Equipe FRM– National (PI, 310,676€) and a collaborative ANR – AAPG grant (2023–2025). However, another ANR grant is submitted and in the 2nd round evaluation.

Probably in line with its size, the team has limited interactions with other LPHI teams.

ANALYSIS OF THE TEAM'S TRAJECTORY

See trajectory of team 4, as teams 3 and 4 will fuse. Merging with team 4 represents an opportunity for team 3 to address further the role of G-quadruplex structures in virulence and malaria disease evolution (symptomatic versus asymptomatic cases).

RECOMMENDATIONS TO THE TEAM

See recommendations to team 4, as teams 3 and 4 will fuse.

Team 4: Genomic approaches to tackle asymptomatic chronic malaria

Name of the supervisor: Mr Antoine Claessens

THEMES OF THE TEAM

Team 4 (ATIP-AVENIR in 2019) develops genomic approaches to tackle asymptomatic chronic malaria by combining field studies in Africa and advanced transcriptomics /genomics approaches. These approaches allow the tam to refine hypotheses about mutually exclusive var gene expression in a real-world setting.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

No recommendations were previously made for this team.

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

Catégories de personnel	Effectifs
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	1
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	3
Doctorants	0
Sous-total personnels non permanents en activité	**4**
Total personnels	**6**

EVALUATION OF THE TEAM

Overall assessment of the team

Team 4 is an excellent, new team that successfully emerges from an ATIP-Avenir team to decipher parasite genetic recombination & the critical role of asymptomatic carriers in sustaining transmission of *P. falciparum*. Based on its implication in both the African malaria research field & new NGS approaches, it is recognized as a pioneer team in the identification and study of the role of asymptomatic carriers in the malaria life cycle. By combining NGS tools & African studies, it refines hypotheses about var gene expression in real-world settings, thus paving the way for a new understanding of malaria disease and improved clinical management of malaria.

Context-related strengths and opportunities

As the continuation to the ATIP-AVENIR team created in 2019, team 4 benefits from undeniable dynamism, reinforced by the grants obtained (approximately £1.7 million) including a JCJC-ANR as PI and a strong synergistic collaboration with the UMR MIVEGE.

The implication of team 4 in both field research in Africa and development of new NGS tools allows it to be recognized as a pioneer team deciphering the role of asymptomatic carriers in the malaria life cycle. Briefly, the tools - especially molecular (NGS) and bioinformatic tools- developed by team 4 clearly improve the quality/novelty of its research data. Of note a PhD student is being shared with team 6 (RADULESCU team – Mathematics- Bioinformatics). In addition, by merging with team 3, it could develop mechanistic approaches based on *P. falciparum* CRISPR tools. Indeed, team 3 has already generated Tare 1-3 KO and Tare 1-6 KO parasites that will clearly benefit the future project of the fused teams. Indeed, generating these parasites KO of non-coding subtelomeric regions involved in the regulation of VAR gene expression will document further the role of VAR genes in anti-disease immunity.

The work produced by team 4 is qualitatively and quantitatively outstanding, as well as its communications (14 invited conferences). Team 4 reached a notable scientific production (15 published papers in 2020-25: Nat Microbiol. 2025, Lancet Microbe 2024, Elife 2024 as co-authors; Elife 2025 and J Infect Dis. 2022 as last authors), with international collaborations and several key papers on chronic malaria concept and physiopathology.

Team 4 participates in the animation and management of its community: It was selected to join the labex ParaFrap consortium in 2019 and actively contributes to the MalariaGEN network, which maintains the largest publicly available database of P. falciparum genomes. It hosted a researcher from the University of Glasgow, Scotland in 2023/24. From 2019 to 2023, the team PI initiated and organized the "Bioinformelles," a biweekly informal seminar for ~20 geeks bioinformatics researchers at MIVEGEC, and was a junior editor for eLife in 2021-2022.

Team 4 was also involved in several research activities to society: Inserm made a short video about the team's research as part of the Science Festival, and a blog from CNRS about the team's research in The Gambia was produced.

Context-related weaknesses and risks

The limited size of the team 4 (with only 2 permanent persons) could limit the ability to develop the proposed research program.

While the fusion of teams 3 and 4 is relevant in terms of research fields (both teams focusing on *P. falciparum,* addressing complementary biological questions), it will require great attention and development of synergies to be relevant and to produce research data with an excellent level.

ANALYSIS OF THE TEAM'S TRAJECTORY

By combining diverse resources and skill sets of teams 3 & 4, the new team will aim at having a comprehensive understanding of how subtelomeric ncRNAs shape *P. falciparum* biology (especially for genes VAR), from sequence-level changes to chromatin remodelling, ultimately guiding the development of novel anti-malaria strategies. In parallel, the team aims to understand why certain *P. falciparum* infections lead to clinical symptoms, while others remain asymptomatic (focusing on antigenic variation via VAR gene expression and CRISPR tools recently developed by Team3).

This new configuration will give the opportunity to both current groups to have more efficient interactions and collaborative work than is currently the case. Given that the current team 3 is small in size with expected and average research activity, its fusion with team 4, a larger team composed of 5 - 8 people and with a clinically relevant research project and a nice dynamism, should boost team 3 research activities.

RECOMMENDATIONS TO THE TEAM

Team 4 should ensure increased collaborations with team 3 - beyond CRISPR tools, as well as with other teams within the unit beyond the PhD student that is being shared with team 6 - RADULESCU team – Mathematics-Bioinformatics.

More shared research grants/programs and/or PhD students between teams 3 and 4 will be appreciated, even if a team 4 post-doctoral researcher is involved in a team 3 research project.

Team 3-4 proposes 2 research axes that are complementary, addressing both difficult biological questions on malaria, however more collaborative works/tasks have to be developed and attention must be paid to ensure that the input and attractiveness will be balanced between the two areas of research. Here clearly, the G-quadruplex (plus other gene regulation process such as non-coding subtelomeric region) expertise developed by team 3 could be an added value since these structures seem to be involved in VAR expression analysed by team 4.

Continue to increase promotional activities (publications/conferences) and funding.

Consider recruiting permanent staff (young researchers) for this team (to improve team size and attractiveness).

Team 5: Computational systems biology

Name of the supervisor: Mr Ovidiu Radulescu

THEMES OF THE TEAM

The Computational Systems Biology team headed by O Radulescu since 2021 develops mathematical and computational methods for multiscale systems biology, with a particular focus on infectiology.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has clearly and successfully addressed the recommendations from the previous reports by:

1) writing more review articles, covering topics such as HIV-1 latency and melanoma resistance to treatment.

2) increasing the size of the team with the arrival of a Research Engineer and a Junior Professor in 2024

3) strengthening its interactions with experimental teams within the LPHI unit, notably with a strong synergy with Antoine Claessens' team, but also with other local teams at Montpellier in IGH and IGMM and with national teams in the ICM, Paris.

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

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

EVALUATION OF THE TEAM

Overall assessment of the team

Overall, the team has produced excellent science both through methodological developments and in terms of biological applications in collaboration with both local and more distant experimental teams. The team presents also a promising trajectory with the recent arrival of a Junior Chair Professor and a Research Engineer with novel and complementary expertise for the team.

Context-related strengths and opportunities

The team has produced a number of theoretical and computational developments in a range of biological topics and applications since the last evaluation.

In particular, building on their expertise in formal analysis of biochemical networks, they developed new model reduction approaches and tools to handle multi-timescale systems (ANR/DFG SYMBIONT project) and in their integration into automated modelling pipelines (CEFIPRA project).

The team also studied long-term immune evasion through var gene expression switching and dynamic reshuffling of gene repertoires in collaboration with team 4 (LPHI) and discovered of the role of stochastic pausing of RNA polymerase II in HIV-1 latency in collaboration with a team in the IGH. In addition, the team used AI models to explore resistance of melanoma to BRAF/MEK inhibitors and to predict treatment risk during the INSERM/Plan Cancer funded project MALMO (2020-2023) coordinated by O Radulescu.

The team has recently been reinforced with the appointment of a Junior Professor in AI for biohealth thanks to the support of the Montpellier BioHealth cluster. In addition, the CNRS provided a significant support to the team with the opening of a research engineer position.

The team has clearly strengthened its position in the unit and in the Montpellier region. The team has secured around seven grants during that period, including as coordinator (PIA MUSE MELOCO (2020-2023), INSERM ITMO Cancer/Aviesan AAP "MALMO" (2020–2023), two international collaborative grants (CEFIPRA Indo-French collaborative grant (2023–2026), ANR/DFG PRCI "SYMBIONT" (2018–2022)), with 3 on-going funded projects and PhDs (CNRS MITI 80 PRIME (2024–2027), Région Occitanie "Émergence" (2024–2027), CEFIPRA Indo-French collaborative grant (2023–2026)).

The team has published both methodological developments in a range of scientific journals and conference proceedings (Nucleic Acids Research 2023, PLOS Computational Biology 2024 & 2019, Bulletin of Mathematical Biology 2024, SIAM J. Appl. Dyn. Syst. 2024, 2024, conferences on Computational Methods in Systems Biology 2021, Theoretical Computer Science 2021, Math.Comput.Sci. 2021). The team has also published collaborative application studies in high profile interdisciplinary journals (1x npj precision oncology, 3x Nat Commun) in collaboration with a team in IGMM and a team in IGH in Montpellier. This is a nice publication record for an interdisciplinary team. The team has participated to seven conferences as invited speakers during the period and acted as associate editors for several journals. The team has also produced online and standalone computational resources such as ODEbase (Radulescu) and pyULL (Orlando) for the community.

Context-related weaknesses and risks

The coordination of the recently extended team provides both clear opportunities but also some risks, for instance, if independent subgroups with little interactions eventually emerge within the team. It is important that the common projects outlined for the team's trajectory can be developed with dedicated funding in the coming years.

While the team appears to be well integrated in the unit and in the Montpellier scientific community, being the only mathematical / AI team in a primarily experimental biology unit also comes with the risk of being or feeling scientifically isolated. Continuing to participate to local as well as national and international networks with similar-minded interdisciplinary scientists will be important to mitigate this risk.

ANALYSIS OF THE TEAM'S TRAJECTORY

The two recently filled permanent positions have significantly strengthened the team's momentum and broaden its expertise in computational systems biology notably in AI-based approaches. The common projects on physics-informed neural networks (PINN) applied to disordered proteins and to ODE models of molecular networks applicable to infection are promising projects (LOI submitted to ANR 2026 call). The development of causality analysis on time series data to reconstruct regulatory networks controlling the cell cycle of P. falciparum, using phosphoproteomics data from Anna-Rita Gomes, opens also interesting novel collaborative perspectives within the unit.

RECOMMENDATIONS TO THE TEAM

The team should be congratulated for its excellent work and scientific productions as well as for its fruitful collaborations both within the unit and with other groups in Montpellier, as well as for its integration within international networks.

One recommendation would be to try organize some regular scientific exchanges with other theoretically-minded teams in the Montpellier region or beyond, so as to maintain a stimulating scientific environment for the team members, notably PhD students and post-doctoral researchers, beyond the interesting collaborations with the teams of biologists in the unit. This could be achieved for instance through joint scientific retreats with other mathematical modeling AI teams or through the participation to national consortia with regular opportunities to exchange about methodological developments in relation to on-going projects.

Team 6: Mechanisms of normal and pathological inflammation

Name of the supervisors: Ms Mai Nguyen-Chi & Ms Laure Yatime

THEMES OF THE TEAM

The team's goals are to develop integrated approaches in order to study immune and inflammatory processes in infectious and non-infectious contexts, with a strong expertise in zebrafish models. Knowledge generated aims at proposing new anti-infectious and anti-inflammatory strategies.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has addressed the following recommendations from the previous reports by:

1/ participating to more conferences (included invited conferences)

2/ training more PhD students (7) and post-doctoral researchers (4)

3/ Expanding the interactions between the different PIs of the group which was translated in more PhD students that have been trained, more co-authored publications and co-held grants within the group.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**9**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels non permanents d'appui à la recherche	2
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**5**
Total personnels	**14**

EVALUATION OF THE TEAM

Overall assessment of the team

The evaluation of the team is "excellent" over the evaluated mandate. This covers scientific goals, discoveries, publications, funding, attractiveness, training and outreach activities.

Context-related strengths and opportunities

The team is strongly expanding and now holds five research axes (that are expanding as well) focusing on immune cell activation, inflammatory mediators and modelling of chronic pathologies, on one hand, and on bacterial infections, virulence mechanisms and bacteria-driven inflammation, on the other hand. Over the period, the group developed and discovered key inflammatory processes involved in multiple diseases

(including infectious, Crohn or wound healing contexts) that were published in important international journals (34 in total, including collaborations) such as eLife, Free Radic Biol Med, Dis Model Mech, FEBS J or in PloS Pathogens for instance with students and PIs as first and senior authors. In addition, the team developed a strong novel platform of zebrafish for modelling of various pathologies, which has been of strong importance in the frame of their research program but also contributes to their international collaborations/ visibility (2 publications in collaborations in Science and Science Advances).

The group has also developed, thanks to its zebrafish platform but also thanks to two MSCA-ITN European grants, a strong international visibility (Acquifer Imaging GMBH Germany, University of Murcia, Spain, Universities of Sheffield and Edinburg, UK, University of Eotvos, Hungaria…).

Regarding international conferences, a PI of the team co-organized the European Phagocyte workshop 2024 and the Inflanet dissemination meeting in Visegrad, Hungria. PhD students of the team participated in the organisation of MIIM 2024 (Montpellier Infection & Immunity Meeting) and the group co-organized the first French Zebrafish meeting in Montpellier in 2024. Finally, one of the team's PI presented at 9 conferences (3 national, 6 international), including as a keynote speaker, another PI presented at 2 national conferences. Two additional PIs who will be leaving to form a new team presented at 8 (5 national, 3 international), and 6 national, 2 international conferences, respectively.

Regarding teaching, the group mostly relies on the strong teaching activity in the two European MSCA-ITN PhD student training networks in which they are involved.

All axes are supported by technical permanent positions as well as by a large body of grants (ANR, 2 European network funds, multiple charities funds, a total of more than >7M.euros over the evaluation period). The group is also involved in a very broad range of outreach activities (Youtube, ZEFIX platform network for training to zebrafish biology, 'La Fête de la Science', Declics or the European Researchers' Night).

Context-related weaknesses and risks

The team has a very strong expansion with various themes of research (5, and still expanding). As highlighted in the team's self assesment, some PIs that recently joined the team have not yet published. Furthermore, the group has seen the retirement of some of its members but this was compensated with a strong recruitment activity. Finally, the team is also restructuring its theme of research to a more focused theme.

A particular attention should be given to the newly recruited PIs in order to support their development (grant applications, research development, student training).

ANALYSIS OF THE TEAM'S TRAJECTORY

For the next period, the team will be renamed "Mechanisms of Normal and Pathological Inflammation". This relies on strong modifications in the team members and area of research. The axis related to infections will split and emerge as an independent team while it will focus on inflammatory processes in both physiological and pathological contexts, with the aim to decipher the molecular mechanisms and cellular communication at play, from initiation to resolution.

Specifically, the projects will embed three main research axes: 1) Dynamics of Immune Cell Activation and Inflammatory Mechanisms; 2) Pathogen- and Host-mediated Inflammation in Crohn's Disease; and 3) Hereditary Haemorrhagic Telangiectasia and Inflammation. These axes will be led by the 3 PIs of the team.

The trajectory is clear, well supported in term of people, funds and scientific ambition. Specifically, the team has already obtained three funded grants (Inflanet grant until 2026, AAP IBiSA Interfra 2025-26, AMRO grant 2025-26) and has applied to other grants (ANR, FC3R, ARC, MSCA-ITN). In addition to the PIs, permanent technical staff (2 IE CNRS) will contribute across projects and PhD students/post-doctoral researchers will be hired according to the funding success rate.

RECOMMENDATIONS TO THE TEAM

While the team holds a strong reputation and a clear line of research, particular attention should be given to the emerging PIs in term of grant support.

Team 7: Pathogenesis of chronic bacterial infections and therapeutic strategies

Name of the supervisors: Ms Anne Blanc-Potard & Ms Audrey Bernut

THEMES OF THE TEAM

In the global context of anti-microbial resistance, the team develops fundamental and translational studies on host-pathogens interactions, more precisely on bacterial infection (by *Pseudomonas aeruginosa* mainly), virulence mechanisms and bacteria-driven inflammation. They invest in particular in the development of *in vivo* models (zebrafish) and the discovery of novel anti-virulence or immunomodulatory compounds to better understand the interaction between bacterial pathogens and host innate responses (involving macrophages and neutrophils) during chronic infection refractory to antibiotic treatment in both normal and cystic fibrosis (CF) conditions.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

This section does not apply since the team was created in January 2025.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
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
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	0
Sous-total personnels non permanents en activité	**0**
Total personnels	**5**

EVALUATION OF THE TEAM (TRAJECTORY)

Overall assessment of the team

No assessment on the report since the team was created in January 2025.
The project of this new team is ambitious and, based on their former successes in the previous team from which they emerged, the team should develop with success in this novel mandate. The global assessment of the trajectory is thus excellent: they develop important projects, making use of numerous national and international collaborations (including European networks) as well as the unit's core facilities.

Context-related strengths and opportunities

The team has recently individualized itself from a large team (team 6) dedicated to immunity, inflammation and bacterial virulence in order to focus specifically on bacterial virulence and to gain more visibility. This should allow the development of collaborative projects (shared grants and PhD students) with the other part of the original team, now focusing specifically on immune cells' activation, inflammatory mediators and the modelling of chronic pathologies, and the recruitment of new staff members.

The team is headed by two researchers (an experienced research director, who joined the former team in 2023 and a CNRS researcher recruited in 2021) with complementary expertise. The team has already secured the recruitment of an assistant professor from University of Montpellier (recruitment in 2025) and two permanent technical staff members (a CNRS engineer and an University technician). The team leaders have proven experience in obtaining and managing of grants (8 grants in total over the mandate, even if these grants were obtained when the PIs were in their previous team), international recognition (5 invited international conferences and 13 national conferences over the last mandate); they have access to the BioCampus core facilities and importantly for their projects, to the Biocampus-labelled Zebrafish core facility. They also have developed a broad network of medical collaborators that allows them to correlate their findings on lab strains with strains from patients as well as a network of national and international collaborators with the help of which they can diversify their technological approaches (from human and murine cell lines to organoids and mouse models).

Context-related weaknesses and risks

ANALYSIS OF THE TEAM'S TRAJECTORY

With the zebrafish at the centre of therapeutic perspectives, the team aims at developing 3 axes: 1) the role of the intra-macrophage phase of development of *P. aeruginosa* during chronic infection (A. Blanc-Potard); 2) to understand how CTFR determines the innate immune responses and how their imbalance may promote infection (by non-pathogenic *Mycobacterium*, *P. aeruginosa*, *Staphylococcus aureus*) and associated inflammation (A. Bernut); 3) identification of anti-virulence and immune-targeted therapies (A. Blanc-Potard and A. Bernut).

The project is ambitious and coherent. However, it will require to expand the group: the team plans to recruit a novel permanent researcher and to secure a current engineer contract position into a permanent position.

It is important to notice that part of the projects are already financially supported: 1/ an ANR obtained in 2025 to investigate the role of intra-macrophage development of *P. aeruginosa* during chronic infection; 2/ an ANR obtained in 2025 to study the mixed infection by *P. aeruginosa* and *S. aureus* in zebrafish; 3/ an ANR obtained in 2025 to study the mechanistic links between CFTD deficiency and CF immunopathology; 4/ an ANR obtained in 2025 to investigate how modulators of Ca2+ channels reduce the innate susceptibility of CF patients to infections and inflammatory lung disease; 5/ a Welcome Trust funding obtained in 2025 to identify novel therapeutic strategies against multi-drug resistant Mycobacteriae. No doubt that, with these financial supports, the PIs should be able to develop outstanding research!

RECOMMENDATIONS TO THE TEAM

Although the team has valuable expertise in many pathogen models, they should try to remain focused as long as the number of scientists remains limited. Strengthening the team seems to be a priority.

The project will also require to secure more funding sources: the team should follow up on its ambition to become an FRM team in 2027 and to further apply to local, national and international grant sources.

CONDUCT OF THE INTERVIEWS

DATES

Beginning: 03 November 2025 at 08:00

Ending: 04 November 2025 at 18:00

Interview conducted: remotely

PROGRAMME OF THE INTERVIEWS

Agenda November 3rd

9:00-9:10 Hcéres Rules and procedures *Public Session (all unit members)*

9:10-10:00 *Administrative and Scientific presentation of the Unit Including Question Answer SessionPublic Session (all unit members)*

10:00-10:20 Debriefing committee and break *(closed door meeting)*

10:20-10:40 *Team 5 - Computational systems biology* Speaker *Ovidiu Radulescu Including Question Answer SessionPublic Session (all unit members)*

10:40-11:10 *Team 6 - Mechanisms of normal and pathological Inflammation* Speaker Mai N-Guyen-Chi and Laure Yatime *Including Question Answer Session Public Session (all unit members)*

11:10-11h40 *Team 7 - Pathogenesis of chronic bacterial infections and therapeutic strategies* Speaker Anne Blanc-Potard and Audrey Bernut *Including Question Answer Session Public Session (all unit members)*

11:40-12:00 Debriefing committee and break *(closed door meeting)*

12:00-13:20 Lunch Break

13:20-14:00 *Team 1 Cell biology of apicomplexan parasites* Speaker Maryse Lebrun and Sébastien Besteiro *Including Question Answer Session Public Session (all unit members)*

14:00-14:30 *Team 2 Molecular approaches for new antimalarial strategies*

Speaker Rachel Cerdan and Ana Rita Gomes *Including Question Answer Session Public Session (all unit members)*

14:30-14:50 Debriefing committee and break *(closed door meeting)*

14:50-15:10 *Team 3 DNA Biology in Plasmodium falciparum* Speaker Jose-Juan Lopez-Rubio *Including Question Answer Session Public Session (all unit members)*

15:10-15:30 *Team 4 –Genomic approaches to tackle asymptomatic chronic malaria* Speaker Antoine Claessens *Including Question Answer Session Public Session (all unit members)*

15:30-17:00 Debriefing committee and break *(closed door meeting)*

Agenda November 4th

9:00-9:40 Meeting with ITAs (in French) *In the absence of any managing staff*

9:40-10:20 Meeting with researchers *In the absence of any managing staff*

10:20-11:00 Meeting with post-docs and students *In the absence of any managing staff*

11:00-11:30 Debriefing committee *(closed door meeting)*

11:30-12:00 Meeting with institution representatives *(closed door meeting)*

12:00-13:30 Lunch Break

13:30-14:00 Meeting with the Management Team of the Unit *(closed door meeting)*

14:00-17:00 Redaction of the final report *(closed door meeting)*

17:00 End of the visit

GENERAL OBSERVATIONS OF THE SUPERVISORS

UNIVERSITÉ DE MONTPELLIER

MONTPELLIER
Le 13 janvier 2026

Monsieur Arnaud TOURIN
Directeur du Département d'évaluation de la recherche
HCERES
19 rue Poissonnière I 75002 PARIS

DRED
SERVICE DE LA COORDINATION DES STRUCTURES
ET DES MOYENS DE LA RECHERCHE
GERALDINE YVON
+33 (0)4 67 14 94 97
dred-srech@umontpellier.fr
163 rue Auguste Broussonnet
34 090 Montpellier
WWW.UMONTPELLIER.FR

OBJET : Rapport d'évaluation - DER-PUR270025817 - LPHI - Laboratory of Pathogens and Host Immunity

Monsieur le Directeur,

Je tiens à remercier le comité de visite HCERES pour la qualité de son rapport d'évaluation concernant l'unité de recherche LPHI - Laboratory of Pathogens and Host Immunity - dirigée par Madame Rachel CERDAN.

La directrice de l'unité, le CNRS et moi-même avons pris connaissance des recommandations formulées par le comité de visite.

Nous n'avons pas d'observations de portée générale à formuler.

Nous vous prions d'agréer, Monsieur le Directeur, nos salutations distinguées.

Agnès MIGNOT

Vice-présidente
Chargée de la recherche

Evaluation of universities and schools
Evaluation of research units
Evaluation of the academic formations
Evaluation of the national research organisms
Evaluation and International accreditation

Evaluation · Research · Higher Education
Hcéres

19 rue Poissonnière
75002 Paris, France
+33 1 89 97 44 00