Research evaluation

EVALUATION REPORT OF THE UNIT

Unité de dynamique cellulaire physiologique et pathologique

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Institut Pasteur Paris,
Centre national de la recherche scientifique

EVALUATION CAMPAIGN 2023-2024
GROUP D

Rapport publié le 23/05/2024

High Council for evaluation of research and highter education

In the name of the expert committee[1] :

Jörg Renkawitz, Chairman of the committee

For the Hcéres[2] :

Stéphane Le Bouler, acting president

Pursuant to Articles R. 114-15 and R. 114-10 of the French Research Code, evaluation reports drawn up by expert committees are signed by the chairmen of these committees and countersigned by the Chairman of Hcéres.

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

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

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:	Mr Jörg Renkawitz - Ludwig-Maximilians University Munich Allemagne
Experts:	Ms Florence Besse CNRS - Centre national de la recherche scientifique Mr Thomas Guilbert Inserm - Institut national de la santé et de la recherche médicale (supporting personnel) Mr Jason King - The University of Sheffield Royaume-Uni Mr Martin Loose - Institute of Science and Technology Austria Autriche Mr Etienne Morel Inserm - Institut national de la santé et de la recherche médicale Mr Pablo Vargas Inserm - Institut national de la santé et de la recherche médicale Mr Florian Gärtner - Ludwig-Maximilians University Munich Allemagne

HCÉRES REPRESENTATIVE

Mr Jacques Dutrieux

REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Institut pasteur	Mr Patrick Trieu-Cuot
CNRS INSB	Mr Patrick Blader
Délégation régionale CNRS Ile de France Meudon	Mr Eric Migevant

CHARACTERISATION OF THE UNIT

- Name: Dynamique cellulaire Physiologique et Pathologique
- Acronym: DC2P
- Label and number: UMR 3691
- Composition of the executive team: composition of the executive team

SCIENTIFIC PANELS OF THE UNIT

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

THEMES OF THE UNIT

The unit addresses fundamental principles and mechanisms in cell biology and their mis-regulation in disease, such as during infection and other cell-based pathophysiological processes. Thereby, the unit covers a broad range of fundamental topics in cell biology like cell division, membrane dynamics, autophagy, cell motility and polarity, and in infection biology like pathogenic bacterial infections and host cell behaviour. This approach is complemented with interdisciplinary projects that develop quantitative experimental and computational tools for cell biology, particularly on image analysis. Thus, the unit aims to address fundamental concepts at the interface of cell and infection biology by using state-of-the-art technologies and quantitative analysis.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The unit UMR3691 was established in 2015 (headed by S. Etienne-Manneville), bringing together six teams (PIs A. Echard, S. Etienne-Manneville, A. Subtil, R. Weill, J-C. Olivo-Marin, C. Zimmer) from the successful 'Cell Biology and Infection' department (which itself was established in 2002). Since then, the teams of J. Enninga, T. Wollert, and C. Zurzolo have joined the unit, and most recently in 2023 the team of T. Brunnet. Two teams have left the unit – R. Weil in 2018 and C. Zimmer in 2024 (C. Zimmer will maintain a small team within the department of Institute Pasteur but not within the unit UMR3691).

The individual teams (currently 9 and 1 new group) of the research unit are located on the campus of Institute Pasteur and are distributed over four buildings (Teams 3, 6, 8, 10 (new) in the Monod building, teams 2, 4, 5 in the Calmette building, team 1, 9 in the Duclaux building, team 7 in the Jacob building).

RESEARCH ENVIRONMENT OF THE UNIT

The unit is integrated into the campus of the Institut Pasteur, providing an excellent research environment and state-of-the-art technologies (such as numerous technological and animal platforms like omics, imaging, and cell sorting) to carry out the ambitious research aims of the unit at the interface of cell biology, infection biology, and computational biology.

UNIT WORKFORCE: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	9
Chargés de recherche et assimilés	14
Personnels d'appui à la recherche	32
Sous-total personnels permanents en activité	**55**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	2
Post-doctorants	20
Doctorants	23
Sous-total personnels non permanents en activité	**47**
Total personnels	**102**

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons at 31/12/2022. Non-tutorship employers are grouped under the heading 'others'.

Nom de l'employeur	EC	C	PAR
INST PASTEUR PARIS	0	14	29
AUTRES	0	9	3
Total personnels	0	23	32

GLOBAL ASSESSMENT

The unit UMR3691 was established in 2015 and includes currently nine research teams. The vision of the unit is to understand the fundamental principles and mechanisms of the cell in physiology and pathophysiology quantitatively, combining classical cell biological approaches with advanced technological and computational developments. As such, the teams investigate how cells divide, polarise, migrate, maintain their organelles like mitochondria, perform autophagy, interact with neighbouring cells via tunnelling nanotubes, and how they respond to and interact with pathogens. The unit investigates the underlying principles and molecular mechanisms of these critical cellular processes, and investigates their mis-regulation in diseases like neurodegenerative diseases, cancer, and infection. This approach is complemented with an outstanding expertise within the unit to employ and develop state-of-the-art quantitative experimental and computational approaches, such as on bioimage analysis.
Each research team in the unit is led by a principal investigator, together comprising a mix of established, mid carriers, and junior principal investigators. All teams publish in broad-interest, high-profile journals, and most teams publish in an excellent/outstanding frequency, together showing an outstanding research output of the entire unit. Further, the unit and its teams are impressively successful in acquiring national and international grants. This is complemented by frequent invitations to scientific meetings and seminars, dissemination to the public by interviews and high school interactions, and a growing interaction with industry and clinicians. The unit is highly attractive for national and international students, postdocs, and researchers. Together, the scientific objectives, performance, and output of unit UMR3691 are outstanding.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous committee report praised the output of the unit and only identified minor weaknesses. To address these weaknesses, the previous committee report recommended (i) strengthening the mentorship of young PIs (ii) reducing the administrative burden for PIs, and (iii) maintaining a critical mass of cell biologists while also (iv) strengthening the genetic analysis, modelling, imaging, and translational connections.
The unit successfully implemented the mentoring of new PIs, as exemplified by the mentorship structure established for Timothy Wai. Further, the unit maintained the critical mass of cell biologists through the recruitment of Timothy Wai, Thomas Wollert, Chiara Zurzuolo, and Thibaut Brunet. At the same time, the unit also strengthened the area of infection biology with the recruitment of Jost Enninga and also started to strengthen their translational connections (e.g. team Olivo-Marin, team Subtil). The recommendation to reduce the administrative burden for PIs is yet to be addressed, but the committee also sees the challenges in implementing this aspect.

B – EVALUATION AREAS

Considering the references defined in the unit's evaluation guidelines, the committee ensures that a distinction is made on the outstanding elements for strengths or weaknesses. Each point is documented by observable facts including the elements from the portfolio. The committee assesses if the unit's results are consistent with its activity profile.

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

Assessment on the scientific objectives of the unit

The vision of the unit is to understand the fundamental principles and mechanisms of cells in physiology and pathophysiology in a quantitative manner. This is an outstanding scientific objective, combining cell biology with infection biology and other cell-based pathologies like neurodegenerative diseases and cancer.

Assessment on the unit's resources

The unit's resources are excellent to outstanding, substantially supported by numerous international and national grants.

Assessment on the functioning of the unit

The unit functions excellently, providing the necessary structure to address groundbreaking research questions.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The vision of the unit is to understand the fundamental principles and mechanisms of the cell in physiology and pathophysiology in a quantitative manner, combining classical cell biological approaches with advanced technological and computational developments. As such, the teams investigate how cells divide, polarise, migrate, maintain their organelles like mitochondria, perform autophagy, interact with neighbouring cells via tunnelling nanotubes, and how they respond to and interact with pathogens. The unit investigates the underlying principles and molecular mechanisms of these critical cellular processes, and investigates their mis-

regulation in diseases like neurodegenerative diseases, cancer, and infection. This approach is complemented with an outstanding expertise within the unit to employ and develop site-of-the-art quantitative experimental and computational approaches, such as on bioimage analysis. Understanding how cells function in an interdisciplinary and quantitative manner is a fundamental aspect of biology and holds the promise to lay the foundation for understanding infectious and non-infectious diseases.

Weaknesses and risks linked to the context

The unit will lose expertise on quantitative computational approaches in cell biology caused by the departure of Christoph Zimmer (in 2024, to Würzburg; Christoph Zimmer will maintain a small team within the department of Institute Pasteur but not within unit UMR3691). This loss of expertise in quantitative computational approaches could be compensated by the recruitment of new teams, by collaborative efforts with research teams at the Institut Pasteur outside of the unit, or with close interactions with the technology platforms at the Institut Pasteur.

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

Strengths and possibilities linked to the context

The unit shows outstanding competitiveness in acquiring third-party funding. During the last five years, the unit acquired stably high resources through third-party funding, including ERC grants (team 6/Wai ERC-StG 2017–2022; Team 2/Enninga EC-CoG 2017–2022) and 24 ANR grants. While funds from international grants dropped slightly during the last years, funding from national sources increased in these years, maintaining impressive and constantly high resources, leading to approximately 4 million Euros of resources for the unit per year. Notably, Thibaut Brunet (team 10) recently joined the unit and acquired an ERC starting grant, underscoring the competitiveness and attractiveness of the unit.

The unit organises a weekly seminar series with external speakers, PI lunches, and a monthly internal seminar series, and participates in an annual retreat of the unit with its department 'Cell Biology and Infection'. As such collaborative crosstalk between some of the teams is evident and reflected by shared publications and grant applications.

In summary, the unit has excellent to outstanding resources and mobilises them for an outstanding research output.

Weaknesses and risks linked to the context

The number of publications that include members from more than one team could be increased. While the teams approach various scientific questions centred around cell and infection biology, the experimental and computational expertise of individual teams may complement each other to the benefit of individual collaborative projects between the teams.

3/ The unit's practices comply with the rules and directives laid down by its supervisory bodies in terms of human resources management, safety, environment, ethical protocols and protection of data and scientific heritage.

Strengths and possibilities linked to the context

The unit is composed of students, PhD students, postdocs, researchers, permanent staff, and principal investigators, summing up to 123 unit's members in total (January 2023). The gender balance among the PhD students, postdocs, and researchers as well as in the entire unit is well balanced. While only 30 percent (3 out of 9), principal investigators (team heads) are women, this percentage of women principal investigators reflects a solid number in comparison to other institutions but should be aimed at increasing in the future. Notably, some unit members are very active in mentoring and promoting women in scientific careers.

The unit shows an excellent performance in training PhD students (62 PhD students from 2017 to 2022) and appears to be excellently managed. The data management plan appears to be state-of-the-art, including electronic lab books and substantial data storage spaces on internal servers. Team members have yearly personal 1:1 conversation with their team heads. Additionally, PhD students have a tutor outside of their direct team.

Weaknesses and risks linked to the context

None.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness is outstanding, achieved by successfully establishing strong connections between fundamental and applied research. International representation is very strong (high-level conferences, strong representation of PIs on the editorial boards of scientific journals) and the UMR is very attractive to students and postdocs. The UMR enjoys high visibility, attributed to its success in securing highly prestigious grants, including European Research Council grants, and active participation in national and international research and funding committees.

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

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

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

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

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

The undeniable scientific impact of this Unit is clear through the numerous invitations extended to its members for conferences or international stays. Staff members are dynamic in organising internal, national, and international meetings and conferences. Importantly, many principal investigators assume editorial responsibilities and contribute to national and international steering committees, and also actively engage in national and international science societies. The teams' track record is equally compelling when considering additional indicators such as participation in committees or institutions, as well as prizes, in addition to the numerous awards for posters.

The Unit has consistently pursued an active policy of welcoming newcomers, especially students and postdocs. Over the last five years, the UMR has successfully attracted 104 interns, 64 postdocs, and 64 PhD students. Young researchers and trainees receive support through research, as well as professional and initial training. An impressive number of doctoral candidates have been welcomed over the period of evaluation. The unit actively contributes to the facilitation and administration of research, participating in activities such as thesis or HDR juries, and serving as mentors to both PhD students and young principal investigators.

The Unit encourages all its teams to respond to project calls. The teams have developed a certain expertise, resulting in numerous successes at various levels leading to more than three million Euros on average each year over the last five years. The most remarkable instances occur in the national public calls, including those from ANR and INCA, as well as foundations such as ARC, Ligue Nationale Contre le Cancer, FRM, and others. Among these, it is noteworthy that A. Echard and C. Zurzolo have obtained the label from FRM, while S. Etienne-Manneville has been recognised with the label from the Ligue Nationale Contre le Cancer. These funding constitute the majority of the UMR financial support. Additionally, there has been a notable success at the international level, including the acquisition of two ERC grants since 2017.

Given the highly multidisciplinary nature of the unit and its diverse equipment requirements, and the absence of a directly attached technological core facility, each team independently procures equipment through their respective grants. Consequently, every team within the unit is required to furnish a five-year strategic plan

outlining the equipment they intend to acquire, the necessary installation work, personnel requirements, operational budget, and IT support needs.

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

Interdisciplinary research projects require expertise and technical skills from different disciplines. Thus, such research projects are highly challenging, necessitating extensive training sessions for individual researchers working on the project or multiple researchers with specific expertise. This challenge could be addressed by establishing research engineer positions within the unit that specialise in state-of-the-art technologies like microfluidics or organoid cultures.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The unit has an outstanding scientific output and competitiveness, which is reflected by the continuous publication of discoveries as lead authors in broad-interest high-profile journals, as well as by the stably high acquisition of national and international grants.

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

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

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

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

The scientific output of the unit is excellent to outstanding. The teams have continuously published as lead authors in broad-interest, high-profile journals, including publications in Science Advances (2x), PNAS (3x), Current Biology (2x), Cell Reports (1x), EMBO Journal (3x), EMBO Mol Med (2x), and in Nature family journals like Nature Communications (7x), Nature Methods (2x), Nature Materials (1x), Nature Biomedical Engineering (1x) with unit members as lead authors. Further, unit members published as lead authors in more specialised but high-profile journals, such as cell biology, molecular biology, and host-pathogen journals like the Journal of Cell Biology (5x), Journal of Cell Science (2x), PloS Biology (2x), Genome Biology (1x), and PloS Pathogens (4x). In total, the unit members were authors on 274 publications (2017–2023) that were approximately 9500 times cited.

The unit members were active in the organisation of meetings and were frequently invited to meetings and seminars, underscoring the worldwide recognition of the unit and most of its principal investigators. Further, the unit members contributed very actively to the research community, such as by being panel members in ERC, EMBO, and Welcome Trust boards, as well as in journal editorial boards (e.g. Current Opinion in Cell Biology), and president of the French Society for Cell Biology (A. Echard, team 1, 2015–2018). Further, J. C. Olivo-Marin (team 4) is the founding and current Editor-in-Chief of the new journal 'Biological Imaging'.

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

The success of some team members in acquiring grants leads to lab space issues. This aspect of insufficient lab space is reinforced, if the team hosts successful permanent researchers that can apply for their own grants. In the most extreme case, this aspect may lead to fewer grant applications by some teams or competition for lab space within a team.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The unit demonstrates very good to excellent interactions with research society, including excellent public outreach and very good interactions with industry and clinicians.

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

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

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

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

The unit excellently interacts with the general public through journal articles and radio interviews (e.g. a radiofrance interview in 2019 by Timothy Wai, team 6; and several radio interviews and round table discussions on AI in health by Christoph Zimmer, team 8). Further, there is an impressive involvement of some teams in high school outreach programs, such as in the DECLIC high school program from the Schlumberger Foundation. Furthermore, Sandrine Etienne-Manneville (team 3) shows impressive activity in the promotion of women in science at conferences, in interviews, and in journal articles (e.g. Etienne-Manneville S. Having it all, a scientific career and a family, Nature Cell Biology 2018). Moreover, Chiara Zurzolo (team 9) organises annually an advanced five-week theoretical and practical course 'Molecular Biology of the Cell' for students.

The interactions of the unit with industry and clinicians are very good, including collaborations with Sanofi-Pasteur (A. Subtil, team 5; C. Zimmer, team 8), involvement in three H2020 projects co-led by big pharma (J.C. Olivo Marin, team 4), and patent applications (e.g. teams 2, 4, 8).

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

None

ANALYSIS OF THE UNIT'S TRAJECTORY

The unit UMR3691 was established in 2015, bringing together six teams (Pis Echard, Etienne-Manneville, Subtil, Weill, Olivo-Marin, Zimmer) of the successful 'Cell Biology and Infection' department (which itself was established in 2002). Since then, the teams Jost Enninga, Timothy Way, Thomas Wollert, and Ciara Zurzolo have joined the unit, and most recently in 2023 the team of Thibaud Brunnet. Two teams have left the unit – Robert Weil in 2018 and Christoph Zimmer in 2024. These successful reorganisations of the unit are an excellent demonstration of its attractiveness to recruit new and successful research teams (e.g. Thibaud Brunnet is joining with an ERC Starting grant), and to yield Pis that are competitive for international appointments (e.g. Christoph Zimmer, new 'Chair of High-Resolution Optical Microscopy' at the University of Würzburg, Germany). This aspect is also showcased by the increased size of the unit from 2015 to 2020 and its continuously excellently high number of acquired national and international grants. In the future, the unit will be directed by Agathe Subtil (Team 5) with Arnaud Echard (Team 1) as a deputy director.

The current objectives of the unit aim to continue the excellent track by continuation of the investigation of fundamental aspects of cell biology and infection biology. These objectives include novel synergies and shared grant applications between the unit members, and also the implementation of new experimental approaches like microfluidics and organoids. Considering the outstanding performance of most research teams in the unit, and the excellent national as well as international recognition of the research teams, these approaches will enable the continuation of fundamental discoveries in cell biology and infection biology. Given that the interface between immunology and cell biology is a quickly growing field, the excellent worldwide recognition of the unit's research offers an outstanding perspective.

Groundbreaking discoveries at the interface of cell biology and diseases are often driven by interdisciplinary and technology-driven approaches. The unit outstandingly combined these approaches in the past. However, with the leave of Christophe Zimmer (in 2024, to Würzburg) the unit will lose expertise on quantitative computational approaches in cell biology. This loss of expertise in quantitative computational approaches could be compensated by the recruitment of new teams, by collaborative efforts with research teams at the Institute Pasteur outside of the unit, or with close interactions with the technology platforms at the Institute Pasteur. In any case, the research of the unit is highly interdisciplinary, combining fundamental cell biology with advanced imaging approaches, custom-made image analysis, disease models, and bioengineering approaches.

Overall, the unit continues to follow an outstanding trajectory.

RECOMMENDATIONS TO THE UNIT

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

The research output as well as the experimental and computational approaches by the individual teams are excellent to outstanding. Some of the teams also actively collaborate to synergize their expertise. Fostering more active internal collaborations between the teams to share their state-of-the-art technological knowledge may further facilitate groundbreaking discoveries and thus support the worldwide recognition of the entire unit beyond the research of its teams. Thus, we recommend exploring and implementing additional strategies to identify overlapping interests and synergies within the unit to strengthen an overall unit identity. A close interaction between PhDs and postdocs often facilitates the initiation of collaborative exchanges in a bottom-up manner. Currently, there are monthly seminars, monthly PI lunches, and an annual retreat between the teams in the unit. Additional, more frequent, events like joined curricula (for PhD Students), experimental workshops (such as on computational image analysis or others), or soft skill workshops may foster the interaction and collaboration between the different teams on the level of PhDs, postdocs, and researchers in a bottom-up manner. Furthermore, students and postdocs would appreciate more occasions to present their ongoing work and progress in front of the unit. Thus, we recommend to continue exploring potential synergies and interests within the unit, which may also lead to further shared grant applications within the unit, in addition to the currently ongoing shared grant application between some of the teams, and an improved visibility and identity of the entire unit beyond the excellent research of its teams.

The unit aims to regroup the unit's teams from multiple buildings to two sites to facilitate the interaction and the use of common instruments. The committee fully supports this aim to facilitate the interaction between the teams, which also includes the integration of new teams in a collaborative manner to foster interactions and collaborations from the start.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit is outstandingly attractive. Strengthening the external visibility of the unit may further support the attractiveness of the unit. Strengthening the external visibility of the unit (e.g. by a Unit's website) may further help to achieve a worldwide recognition of the beyond the excellences of its teams and may help to reach out to interdisciplinary student candidates in mathematics and physics for instance.

Recommendations regarding Evaluation Area 3: Scientific Production

The scientific production of the unit is outstanding. We recommend to continue performing outstanding research on fundamental principles in cell biology and their mis-regulation in disease. Considering the strong experimental expertise within the unit, additional research engineer positions could support the maintenance of state-of-the-art knowledge on novel experimental or computational approaches like microfluidics or organoid cultures.

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

The committee appreciates the efforts to improve the interactions with industry and clinics during the last five years. It recommends further strengthening the connections to industry and clinics.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Membrane Traffic and Cell Division

Name of the supervisor: Arnaud Echard

THEMES OF THE TEAM

The team of Arnaud Echard aims to study the molecular aspects of cytokinesis regulation in mammalian cells. In particular, they focus on interconnected aspects of membrane dynamics, membrane trafficking, and cytoskeleton recruitment during the initiation steps of cell division. The research area, although associated with very 'basic cell biology', is relevant in pathological situations such as cancer and microencephaly. The team uses cutting-edge technologies in cell biology and imaging and is considered a leader in the domain.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous HCÉRES recommendations mostly addressed the team size and societal impact while underlying the overall outstanding dynamism and quality of the team. Currently, the team size is pretty high – and probably reached the proper equilibrium – and the contribution of team members to training programs is satisfactory.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**7**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	3
Sous-total personnels non permanents en activité	**5**
Total personnels	**12**

EVALUATION

Overall assessment of the team

This team was particularly efficient over the reporting period in terms of financial support and for publications. They also succeed in young researchers' formation, through a high number of master internships and PhD students mentoring. Overall, the performance of the team is outstanding.

Strengths and possibilities linked to the context

The scientific insights generated are impressive and are of major interest for the global cell biology community. The team succeed in securing fundings for a total of approximately 4M€ over the last HCÉRES period, from diverse sources (8 ANR with one as PI, 1 ANRS as PI, FRM team labelization, Sidaction, Pasteur, etc.). The dissemination (conferences, training, editorial activities, grants evaluations) was excellent and the global scientific production is outstanding, with 31 top-quality publications in high-level journals (such as Nature Communications, PNAS, Journal of Cell Biology, EMBO Reports, etc.) with half as principal investigator.

Weaknesses and risks linked to the context

We see very little risks in the present context. However, the research theme of the lab is evolving in a very competitive field and this aspect should be kept in mind for the opportunity/risks balance concerning the future projects of the lab.

Analysis of the team's trajectory

The financial renewal of fundings is already secured for at least the three coming years. Rationale about ESCRT independent abscission processes as well as the axis on in-depth approaches for cell-division ESCRT associated membrane-related mechanisms are making sense with the team's history. Finally, the study of the importance of Flemmingsome/abscission machinery in viral dynamics is a smart project that deserves to be addressed.

RECOMMENDATIONS TO THE TEAM

The team past, present and trajectory are – overall – outstanding. Thus, recommendations proposed here could only rely on superficial aspects. We would suggest to take advantages of the team knowledge on ESCRT system to analyse its implication in other membrane-related processes that are associated with (physiological) cellular dynamics such as migration, or membrane maintenance during mechanical constraints associated with cellular movements and polarisation (for example). In this perspective, the team would benefit from engaging in local, national and/international collaborations with other research groups working with ESCRTs.

Team 2: Dynamics of host-pathogen interactions

Name of the supervisor: Jost Enninga

THEMES OF THE TEAM

The team led by J. Enninga is focused on understanding the molecular and cell biological mechanisms that allow pathogenic bacteria to survive within host cells. In particular, the focus is on understanding the membrane trafficking pathways that regulate the formation and escape from bacteria-containing vacuoles. The main focus is on Shigella and Salmonella infection, but the team is beginning to diversify further and apply their methods to a wider range of pathogens. They have a strong emphasis on adopting and developing new high-resolution imaging technologies which have provided new insights and benefits to the broader research community.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous recommendation to consolidate high productivity has been exceeded, with a further increase in scientific output over this reporting period. A reduction in administrative burden was also suggested; It is unclear how much this has changed as J. Enninga still performs major roles within the unit and externally. As recommended, some efforts have been made to engage more with national agencies (e.g. CNRS committee membership). However, trying to reduce administrative burden while managing at the same time a large and highly productive group is somewhat limited, as would be expected.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**6**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	3
Doctorants	1
Sous-total personnels non permanents en activité	**4**
Total personnels	**10**

EVALUATION

Overall assessment of the team

The team has continued to be highly productive over the reporting period, producing research of high quality, and substantial new insights into host-pathogen interactions. The group has done particularly well in adopting new technology and made excellent progress in facilitating the wider adoption of these techniques. The team has done very well in obtaining external funding to support their research and gained a high international profile. The performance of the team has been outstanding overall.

Strengths and possibilities linked to the context

The team has a very strong research profile, evidenced by a high number of publications in the reporting period, the majority of which have team members as first authors. This includes consistent publication of primary

research papers led by the group in high-profile journals, including three papers in PLoS Pathogens and two in Cell Reports within the reporting period. A major strength of the team is the adoption of new technologies such as cryo-CLEM and super-resolution light microscopy. This gives them both a competitive edge and enables broad collaboration with other groups both within the unit and externally. The new BSL3 unit will open further exciting opportunities to apply these technologies to a broader range of important human pathogens, inaccessible to many other researchers.

The group is highly successful in attracting both external funding and highly skilled postdoctoral and PhD level researchers. This is evidenced by>5M Euro in competitive funding including a 2M Euro ERC grant and multiple grants and postdoc fellowships from ANR and FRM national agencies. The group appears to be a highly supportive environment, with all students completing PhD's on time and postdocs publishing well and going onto good positions. Attracting top-level researchers allows them to sustain their high productivity.

An additional strength is the efforts in both obtaining new equipment for the unit and establishing pipelines to increase the accessibility of technological advancements. Notably, the team leader has led or partnered in almost 1M Euro of equipment grants from DIM ELICIT, making a significant contribution to the facilities available throughout the unit. This is particularly important to maximise the impact of their work and support other researchers. This supports the overall aims of the unit and means the team is well integrated into the unit. The recent development of a new advanced imaging summer school is also an excellent and welcome addition.

Finally, there is awareness of commercialisation opportunities, highlighted by a contribution to two independent patent applications within the period,

Weaknesses and risks linked to the context

There are only a few minor weaknesses identified. The main risk is that the intention to diversify further may dilute the focus of the group. The team is in a position where they have outgrown their lab footprint, so they need to carefully select where to best apply their resources to maintain a cohesive research group. Whilst the team is strongly involved in engaging the scientific community, there is less evidence in the report of connecting earlier in the career path at schools. This may be a missed opportunity given the visual nature of their research.

Analysis of the team's trajectory

The team continues to follow an excellent trajectory and is now a well-established senior researcher. The team is an international leader in the field, demonstrated by frequent conference invitations, publications, and grant successes. They continue to innovate and apply creative approaches to their research and have a strong vision and plan for continued success. The team is an asset to the Unit, providing broad benefits to their partners.

RECOMMENDATIONS TO THE TEAM

They should take some caution in establishing collaborations and new research angles to maintain research focus and not get spread too thin.

Continue developing commercial interactions to maximise the impact of their research.

Develop an ERC advanced grant application to obtain long-term external support for the team. They should be well positioned, although there are considerations around space that may need to be addressed.

Team 3: Cell Polarity, Migration and Cancer

Name of the supervisor: Sandrine Etienne-Mannevielle

THEMES OF THE TEAM

The team investigates the molecular mechanisms regulating the migration and invasion of normal (glial cells) and tumour cells (glioblastoma cells). They place a particular emphasis on understanding the role of the cell microenvironment in shaping cytoskeletal structure and dynamics, as well as the establishment of cell polarity.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No specific weaknesses were identified in the previous HCÉRES report. The only recommendation involved the establishment of stronger interactions with the industry and the clinic. However, it does not appear evident that this recommendation is still relevant or consistent with the primarily fundamental research conducted by the team. During the 2018–2022 period, the team has maintained excellence in scientific productivity and science-related activities (e.g. scientific outreach), as already stated in the previous evaluation.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	7
Sous-total personnels permanents en activité	**10**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	2
Sous-total personnels non permanents en activité	**4**
Total personnels	**14**

EVALUATION

Overall assessment of the team

The team has published more than twenty articles since 2018. The scientific production is equivalently high in the three main research areas: cell polarity, cell cytoskeleton, and mechano-transduction. This indicates thoughtfulness and equilibrium between the research topics. The PI is involved in teaching activities and the team has visibility demonstrated by national and international presence in scientific meetings. The overall assessment is outstanding.

Strengths and possibilities linked to the context

The team is excellently positioned in the cell biology community as an expert in the field of intermediate filaments and cell motility. Since 2018, the team has obtained or contributed to funding of around 3M€ (2 ANR with 1 as PI, 2 FRM contracts as PI, Cancéropole IDF, 3 ARC…). The team has a multidisciplinary profile by using microfabrication as a tool to study the cytoskeleton during mechano-transduction. In recent years, the team had 36 publications with 24 as first, last or corresponding author. Some are major publications in the journals Nature Communications and Nature Materials, which highlight the excellence of the research performed by the team.

Weaknesses and risks linked to the context

The multidisciplinary aspect of this team requires several areas of expertise that are unique. Therefore, the departure of specialised team members might be detrimental to the laboratory research.

Analysis of the team's trajectory

The team has a strong record of publications, presence in scientific conferences, invited seminars, and teaching activities. The team leader received extensive funding and recognition, and is an ambassador of successful women in science. This reflects a functional team with an excellent scientific research line. In the last years, one permanent researcher left to start its own team while two permanent young researchers joined. This shows the diversity of the team's activities in agreement with the multidisciplinarity aimed for their future research.

RECOMMENDATIONS TO THE TEAM

The team is excellently organised, funded, and productive. It is encouraged to continue in this line of excellence.

Team 4: Bioimage Analysis

Name of the supervisor: Jean-Christophe Olivo-Marin

THEMES OF THE TEAM

The team develops quantitative and automated analysis of biological images and has recently extended its projects to smart imaging, statistical imaging and implementation of machine learning, with applications in digital pathology. It is leading and constantly upgrading a worldwide recognised image processing and analysis platform called Icy.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The past evaluation pointed to only a few minor points worth to be strengthened, related to reaching a critical group size and increasing partnerships with the industry. The team has successfully followed both recommendations. It is currently composed of sixteen members, including nine with permanent positions and three 'Chargés de recherché', which should ensure the successful implementation of the proposed projects. The team has also developed several partnerships with big pharma, in particular through involvement in different European projects (e.g. H2020 HLTH DI-DIDA, H2020 IMI BIGPICTURE).

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	5
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**9**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	6
Sous-total personnels non permanents en activité	**7**
Total personnels	**16**

EVALUATION

Overall assessment of the team

The team's research activities are outstanding. The team has successfully combined innovative projects in computer science & biology, while constantly upgrading the functionalities of the image processing and analysis platform Icy.
The team's visibility is outstanding: its science is at the forefront of current worldwide challenges. It has both scientific and strategic leadership positions and it has been very successful at recruiting and training students. The team is also very actively engaged in partnerships with the industry, in particular through participation in large European projects.

Strengths and possibilities linked to the context

The team has an outstanding publication track record with 43 published articles, including nineteen research articles with team members as the last author, including articles published in Nature Communications, Nat

Biomedical Engineering, and Science Advances. The team has additionally published 27 articles in international conferences.
The team has been excellent at collaborating with biologists (in particular other groups of the Unit), publishing more than fifteen collaborative publications.
The team's capacity to raise funds has been outstanding, with participation in three H2020 European network grants (>€1.5 million), two project-based ANR grants (>200 k€) and the coordination of 4 major transverse programme grants (2 funded by the ANR – Investissements d'avenir ; €15 million).
The team has developed a rich network of interactions with the industry. It is currently involved in three H2020 projects co-led by big pharma, has supervised 4 PhD projects in partnership with national companies or start-ups, and has deposited three patents.
The team is highly visible, both nationally and internationally. Despite the very competitive context, it has been very efficient at recruiting students and staff scientists (10 PhD students and 3 postdocs, all left the lab with at least a publication and a position in academia or industry). The team leader has launched a new journal (Biological Imaging from Cambridge University Press) dedicated to methods and techniques that use imaging approaches. He is the co-coordinator of the image processing and data management (IPDM) node of the FranceBioimaging national infrastructure.

Weaknesses and risks linked to the context

The team has embarked on the development of IA approaches and the analysis of pathological samples for many years and has so far been excellent at competing with data science companies and staying at the forefront of innovative research. The current context is, however, aggressively competitive and the team needs full support, in particular for the further development of Icy and the implementation of deep learning approaches in this platform.

Analysis of the team's trajectory

The team's trajectory appears excellent and well balanced. It both proposes to build up on the team's strengths and expertise in computational cell biophysics and statistical spatial analysis and to expand its implementation of machine learning and deep learning approaches, with applications in the field of digital pathology and developments related to smart annotation methods. The team will also continue improving the performance of Icy and promote its versatility and capacity to implement AI-based approaches.

RECOMMENDATIONS TO THE TEAM

Continue performing outstanding work.

Team 5: Cellular biology of microbial infection

Name of the supervisor: Agathe Subtil

THEMES OF THE TEAM

Team 5 uses Chlamydia as a model system to investigate the fundamental cellular and molecular mechanisms that allow an intracellular pathogen to colonise and exploit host cells. Furthermore, their research extends to exploring long-term effects on the host cell, with particular emphasis on epigenetic alterations, as well as identifying hallmarks of the host immune response. The ultimate goal is to pave the way for novel antimicrobial treatment strategies and vaccine development.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has considered and implemented most of the suggestions from the previous review.
As suggested in the previous report, ongoing projects were written up and published. This increased the number of publications by doctoral students, which was criticised in the last evaluation. The documents provided now shows that 4 out of five doctoral students have published as first authors, with the fifth being in preparation. The team has developed new research priorities in the areas of cancer and antibiotic resistance, which have led to successful applications for competitive ANR and INCa funding.
It was recommended to hire an expert to increase the capacity for bioinformatics. Based on the documents provided, it remains unclear whether the team has addressed this issue. However, based on the team's self-evaluation, the possible lack of bioinformatics capacity does not seem to significantly affect productivity.
The last evaluation recommended that technologies and approaches that promote translational activities should be strengthened. To address this issue, the team has started a vaccine development project in collaboration with Sanofi-Pasteur. Furthermore, the team has expanded its toolbox by starting to use human organoid systems to bridge the gap between cell lines and patients.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
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	**4**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	1
Post-doctorants	1
Doctorants	1
Sous-total personnels non permanents en activité	**4**
Total personnels	**8**

EVALUATION

Overall assessment of the team

A. Subtil is a recognised expert in Chlamydia research. Her work has focused on understanding the interactions between an intracellular bacterium and its host cell. In particular, the team has pioneered the identification and functional characterisation of effector proteins of the bacterium that are crucial for implantation into the host cell. In this evaluation period, the team continued to be highly productive on this topic with the discovery of the interaction with ATG16L1, published in PNAS (2020) in collaboration with T. Wollert (team 7), being particularly noteworthy. In the current funding period, a new line of research has also been developed that successfully elucidates the metabolic requirements of Chlamydiae on their host cells (EMBO J 2020, JBC 2022). The third line of research focuses on the host response to chlamydial infection and is investigating the potential for vaccine development in collaboration with Sanofi-Pasteur. Overall, the team showed an excellent performance.

Strengths and possibilities linked to the context

The broad range of topics has the potential to provide a comprehensive picture of Chlamydia infection and the corresponding host response. It offers the opportunity to interact with different areas (including within the unit) and to open up new sources of funding, as has already been demonstrated during this funding period. The Team's broad expertise also offers a great opportunity for a translational research approach ranging from basic cell and molecular biology to drug testing.

In addition to A. Subtil, the team has another experienced group leader (Y. Wu) with complementary expertise who deals with the innate and cellular response to Chlamydial infections and also leads the industry project. This is an important advantage and will support the proposed multidisciplinary approach.

The team's track record since 2017 is very good to excellent (13 original articles and 4 reviews, including 9 as senior authors), including lead author publications in PNAS, EMBO J, and JBC. The team has succeeded in attracting competitive funding (including ANR-PPR-AMR, PLBIO_INCa) and establishing a partnership with a pharmaceutical company (Sanofi-Pasteur) (total funding: approximately 1.2M Euros).

Weaknesses and risks linked to the context

The broad topic harbours the risk that not all projects can be implemented at the planned high level. The proposed establishment of CRISPR/Cas9 in Chlamydia and organoid systems is extremely promising but requires appropriate resources. It will therefore be essential to acquire further third-party funding in order to maintain the current size of the group (the funds specified in the documents expire in 2026).

Analysis of the team's trajectory

The team continues to be at the forefront of its field, as reflected in its very good publication record. The plan to use CRISPR/Cas9 technology for the genetic manipulation of Chlamydia, as well as the reorientation of the topics towards the epigenetics of the host cells and the increased focus on the host's immune response is very promising. Although no publications have yet been published in these areas, they are in the pipeline (manuscript in preparation) and the team has successfully obtained funding for these topics up to 2026. The expected results should lead to further successful applications. Furthermore, the thematic focus on host cells offers opportunities for collaboration with other teams in the unit, and the planned establishment of human organoid systems could be important for improving the translational orientation of the consortium. However, there is little discussion of this potential in the documents available to us.
A. Subtil will lead the unit in the next funding period. It is not clear from the available documents to what extent this will affect the work on the projects, supervision of doctoral students, etc., and whether appropriate measures will be taken. The fact that the team has another group leader could be an advantage here.

RECOMMENDATIONS TO THE TEAM

The team works at the interface between cell biology, infectious diseases, and translational research. Their translational approach could represent an important expertise for the entire unit. We therefore recommend further increasing collaboration with other groups in the unit.

According to the available documents, participation in conferences was rather low (8 conferences in 4 years), which may also be due to COVID-19. However, this should be increased again in the next funding period.

Team 6: Mitochondrial Biology

Name of the supervisor: Timothy Wai

THEMES OF THE TEAM

The research of team 6 led by Timothy Wai is aimed at understanding the mechanisms that underpin mitochondrial biology. This approach is largely focused on how these organelles fuse and divide to maintain their morphology and understanding how this regulates mitochondrial function. Their recent work and future plans revolve around understanding genes involved in mitochondrial genetic diseases. These are poorly understood and the Wai group exploits a range of cutting-edge animal (mouse) and cell-based systems to investigate the underlying biology.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team only joined the institute as a junior group in 2018 and thus has not been covered by the previous report.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

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

EVALUATION

Overall assessment of the team

The group is now very well established at the Institut Pasteur. Scientifically the team is highly productive and well integrated into the institute. They also have a strong external profile and generated clear and sensible plans to expand the scope of their work into broader areas more relevant to human diseases. There is also a strong ethical ethos, both in supporting staff and managing their research in a sustainable way. The team is well positioned to continue and build on this success in the next years. Overall, the performance of the team has been excellent.

Strengths and possibilities linked to the context

After a couple of years of establishing the research team, they are now becoming very productive. Even as a small team, they have had multiple impactful papers in the past two years (13 publications, including three senior author papers: Nature Comms, EMBO Mol Med, Brain, Cell Reports). This has built on their previous work to generate strong international recognition, evidenced by regular conference invitations (e.g. Keystone symposia, EMBO workshops and courses), high-profile review articles (e.g. in Developmental Cell), and co-organising an upcoming Keystone symposium. This visibility will also help recruit top-quality researchers to work within the group.

The team has been highly successful in acquiring international and national grants, including an ERC-StG and ANR grants, in total 2.75M Euro). This is supported by a highly open and collaborative approach. Whilst there is a risk of being scoped, this is far outweighed by the advantages as indicated by high-profile collaborative

papers (Brain, Science Advances, Cell Reports) and regular visiting scientists. This aspect is important, particularly for a small junior group, and extends possibilities for fruitful collaboration and funding opportunities.

The future plans of focusing more on health and disease are also sensible and will take advantage of high-quality local collaborations. The team has made considerable efforts in developing tools and is now well positioned to capitalise on this. Their plans to start mitochondrial drug screening with an industrial partner are also a nice addition and step towards broader societal impact.

Weaknesses and risks linked to the context

The open collaborative spirit can run the risk of being spread too thin – especially for a small group. It is also of concern that whilst they have had success in bringing in external postdoc funding, all except the ERC grant are only short 1–2 years positions. Given the highly technical nature of this research and the timescale required, this will be quite inefficient, with long training periods followed by only a brief time of productivity. It will be important to maintain long-term staff to minimise the risk of losing technical expertise, as well as find longer-term support if possible. To achieve their goals, the team may also consider collaboration with more unit members than currently, to profit from the local experimental or computational skills within the unit. The planned collaboration with team 5 (Subtil) on the morphology of mitochondria during Chlamydia infection may be a first step towards this direction.

There is little else to criticise – the group is doing exceptionally well for this stage.

Analysis of the team's trajectory

The team was newly established in 2018 in the unit and is doing excellently well for this stage of the research career: the team has an excellent publication output and shows a well-balanced research plan for the next years, which is based on their profound expertise on mitochondria morphology and genetics, as well as on the implementation of new research facets such as disease models.

RECOMMENDATIONS TO THE TEAM

We recommend to continue excellent research and only identify one minor suggestion:
The new interest in screening drugs is a strength, but the challenges of working in this area are unique and should not be underestimated. Thus, we suggest mentoring and support on this aspect, such as by mentoring through unit members who are experienced in collaborations with industrial partners.

Team 7: Membrane Biochemistry and Transport

Name of the supervisor: Thomas Wollert

THEMES OF THE TEAM

Thomas Wollert is a well-known expert in studying the molecular mechanism of autophagy. This cellular recycling pathway sequesters cytoplasmic material into specific intracellular compartments called autophagosomes, which are then transported to lysosomes for degradation. Autophagy plays a central role in cell maintenance and survival, and defects in this pathway can contribute to different human diseases, including cancer, neurodegeneration, metabolic and immune diseases. Autophagy involves many complicated steps, from the selective capturing of cargo, to membrane growth and expansion. The research focus of this team fits well into the broader theme of the unit.

To understand the fundamental molecular mechanisms of autophagy, the research team uses a combination of approaches, including purified components in vitro and the controlled manipulation of biochemical pathways in vivo. They apply fluorescence, electron and atomic force microscopy techniques for the characterisation of these experimental systems. Since the group was established at Institute Pasteur in 2017, it has successfully moved from yeast as a model system towards mammalian systems to study autophagy in the context of neurodegenerative diseases, cancer, and the replication of coronaviruses.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The research team is one of few in the world that is able to perform this particular kind of in vitro reconstitution experiments and it is well known for its excellent work uncovering the molecular mechanism of autophagy. In the previous report, the committee acknowledged the strong competition that the team is facing in his area. This speaks for the timeliness and importance of the field as well as for the medical relevance of the research topic. Such strong competition bears some risks, in particular for young researchers early in their careers. It was the recommendation of the committee to take advantage of the strengths of the team and the expertise of the unit, to develop a strategy to mitigate this risk and that would allow for continuous scientific output while avoiding direct overlap with competing groups.
The research team has followed this recommendation by slightly broadening, evident by the noteworthy publication with the group of Agathe Subtil from 2020 and active collaborations with Jost Enninga and Timothy Wai. We acknowledge and support this decision and recommend to continue exploring potential overlapping interests and synergies within the unit and to take advantage of the unique skill set and technology present in the group.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

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

EVALUATION

Overall assessment of the team

Thomas Wollert leads an established research group, well known in the field of autophagy and in vitro reconstitution of membrane-remodelling systems. The group has been able to bridge in vivo and in vitro experiments, filling an important niche in the field. In the last seven years, the group has shown very good to excellent productivity, while successfully moving from yeast as sole model system towards also mammalian systems to study autophagy in the context of neurodegenerative diseases, cancer and the replication of coronaviruses.

Strengths and possibilities linked to the context

The research team has mastered the in vitro reconstitution of membrane remodelling system with a focus on autophagy. The team leader's seminal Cell paper from 2014 has established the team leader as a strong player in the field, who is able to establish highly challenging biochemical and cell biological experiments to obtain novel insight into the mechanism of autophagy. The research uses various experimental techniques, including protein purification and in vivo experiments, and the team is one of the few in the world that is able to perform such sophisticated experiments. Retaining such a broad expertise, especially in light of continuous turnover of personnel, during a move between two different countries and during a pandemic. This toolset in the unique environment of this unit offers unique synergies and empowers the research to perform high-impact studies. Since 2017, the team had a very good output of research papers, with ten publications, out of which two were research papers with the team leader as senior author. One paper has been resubmitted after revision to Nature Cell Biology after an initial submission as a preprint in 2022. The team has succeeded in attracting competitive funding of in total around 780k Euro (Carnot Pasteur Microbes et Santé, Pasteur-Weizmann Research Program, ANR).

Weaknesses and risks linked to the context

In comparison to other teams in the research unit, the scientific output of the team has been somewhat lower, but still very good to excellent. We are aware that the in vitro reconstitution of complex intracellular behaviour is a highly challenging task that not only requires knowledge of all the biomolecules involved in a particular process, but also to have obtained them in their pure and active form. In addition, one has to establish experiments that reproduce the physiological conditions found in vivo such that the purified systems show similar behaviour as found in the living cell. At the same time, the assay has to provide experimental access to quantifiable properties of the reconstituted system. All these things are difficult to achieve and require not only detailed scholarship of current knowledge, but also a lot of perseverance and talent by the experimental scientist. Students and postdocs with these qualifications are typically hard to come by, which can seriously limit the progress of a project. At the same time, students and postdocs expect to have a publication after 3–4 years into the project. These challenges can somewhat explain the delay in publications.

Analysis of the team's trajectory

Compared to the time at the Max Planck Institute, the research group appears to have been somewhat less productive in the last seven years. The research team has arrived at Institut Pasteur in 2017, after the PI had run a very successful lab at the Max-Planck-Institute of Biochemistry in Martinsried, Germany. Moving a research lab is a huge effort and also risk, not only the equipment, but especially the scientific expertise and experimental knowledge, as the scientific staff decides to stay behind, in particular during a pandemic. However, the research group seems to have now set the ground for new major discoveries, providing their expertise in synthetic biology and in membrane biochemistry especially to the unit. This is already evident by the fruitful existing collaboration with the group of A. Subtil. The preliminary findings of the group using in situ cryo-electron tomography are exciting and we believe that this approach, in combination with cell biology and biochemical reconstitution experiments offers great opportunities for novel discoveries.

RECOMMENDATIONS TO THE TEAM

We recommend to strengthen and deepen collaborations with other members of the unit and take full advantage of their expertise in expertise in synthetic biology and in membrane biochemistry. We also suggest to split larger projects to consider splitting up larger projects to increase the number of publications per scientist in the group. This could not only secure a continuous publication output but would also be beneficial for the scientific careers. In light of the rather small group size, we expect it will be challenging to perform this broad range of experimental techniques on a top level.

Team 8: Imaging and Modelling Unit

Name of the supervisor: Christophe Zimmer

THEMES OF THE TEAM

The team combines experimental approaches with developments in computational imaging (in particular single molecule localisation microscopy), image analysis, and modelling to study the fine 3D organisation of the chromatin as well as the subcellular distribution of RNA molecules at the molecular level.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The main recommendation emerging from the last evaluation was to focus on a few projects rather than getting dispersed by following too many interesting projects. While the team participated in various collaborative projects, it followed this recommendation and focused on two main research topics related (i) to the development of single-molecule localisation microscopy for high-resolution imaging of chromatin architecture and (ii) to spatial transcriptomics projects.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**6**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	4
Doctorants	4
Sous-total personnels non permanents en activité	**9**
Total personnels	**15**

EVALUATION

Overall assessment of the team

The team's overall activities have been excellent to outstanding.
Its capacity to combine both experimental and computational expertise and thus create a multidisciplinary environment prone to the development of truly integrative projects has been impressive. This resulted in outstanding scientific production in major biological journals and in high national and international visibility in the field of biological imaging.
The team has had an active policy of sharing its developments with the community through the sharing of open-source software.

Strengths and possibilities linked to the context

The team's scientific production has been outstanding with 28 published articles, including twelve research articles with last author positions, most of them in high-standard biological journals (Nat Communications, Nat Biotechnol, Nat Methods, Genome Biol, EMBO J, NAR…).
The team has raised a number of funds to support its research (8 ANR fundings as a partner, 1 FRM and 1 ANR grant as coordinator). It has been very active in establishing partnerships with the industry, through SANOFI-funded projects as well as a joint CIFRE PhD. The team has also submitted one application for an international patent related to the reconstruction of images acquired by single-molecule localisation microscopy.

The team has attracted high-level collaborators from different backgrounds, training 7 PhD students and 7 postdocs over the evaluation period. All students and postdocs who left the lab obtained first-author publications.
The team has been involved in implementing AI-based methods since 2015 and has gained very valuable expertise in this rapidly expanding field. This expertise opens a number of opportunities, on both imaging and image analysis sides.

Weaknesses and risks linked to the context

Although the team has been overall well funded, most of the external grants were obtained in the context of collaborative projects led by other teams (8 ANR funding as a partner vs 1 FRM and 1 ANR grant as coordinator), limiting the capacity of the team to exploit its potential and develop long-term projects.
Although partnerships with the industry have been initiated (e.g. Sanofi joint projects), this could be improved given the expanding needs in digital image analysis and the recognised expertise of the team.
A major strength of the team is to be autonomous in performing truly interdisciplinary projects combining experimental and computational work. The lack of a permanent staff with expertise in experimental biology, however, requires regular hiring and puts the team at risk of losing expertise.

Analysis of the team's trajectory

Christophe Zimmer has just taken a professor position at the University of Würzburg (Germany). He will keep his affiliation with the Pasteur Institute and spend 20% of his time supervising a smaller research team working on the multicolour imaging of thick samples (Cell-ID consortium) and the development of image-based phenotyping methods for antimicrobial drug discovery. The team will also continue to provide imaging expertise and help in some other collaborative projects within Pasteur.

RECOMMENDATIONS TO THE TEAM

The team's multisite and multi-project trajectory appears quite challenging, so it is recommended that the team stays as focused as possible. The imaging strategy deployed for the Cell-ID consortium needs to be better defined.

Team 9: Membrane Traffic and Pathogenesis

Name of the supervisor: Chiara Zurzolo

THEMES OF THE TEAM

The laboratory of Chiara Zurzolo addresses basic aspects of membrane dynamics and trafficking, as well as protein trafficking, in the areas of neuronal pathophysiology and in other pathological situations.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous committee recognised the overall quality of research, the balance between research and administrative aspects, and the central place of the team within the department. No specific recommendations other than to follow the current trajectory have been made. In any case, in light of the present evaluation, the integration of this team into the Pasteur Institute is totally justified and beneficial for the overall 'cell biology research' aspects of the Institute.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**6**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	3
Doctorants	4
Sous-total personnels non permanents en activité	**8**
Total personnels	**14**

EVALUATION

Overall assessment of the team

The team has been very productive at all levels, including publications, communications, expertise, and grant applications. The use of cutting-edge technologies, such as cryo-electron tomography, also underlines the quality and diversity of the approaches. Moreover, the team has made a high number of fruitful internal collaborations within the department. Overall, the quality of research associated with the team is excellent to outstanding.

Strengths and possibilities linked to the context

The approaches are of top quality and biological concepts proposed by recent research in the lab definitively highlight the quality of the team. The team leader has been able to secure approximately 4M€ (from EU programs, ANR, FRM, INCa, etc.) over the last five years. The team should be commended for its professional approaches in every compartment of a research laboratory: lab meetings, student mentoring, promotions, technical approaches, diffusion, and – of course – publications (more than 40 published papers over the last evaluated period). This includes articles in high-profile journals such as Nature, Science Advances or PLos Biology. The integration of this team within the department is highly relevant, addressing simultaneously basic cell biology, neuronal biology, and pathology as well as side projects that align with cancer and infection.

Weaknesses and risks linked to the context

Very few minor weaknesses are identified. Considering the research (past and future) frame of the lab, it might be possible to give more responsibility to other researchers/PIs of the team within some specified/dedicated axes.

Analysis of the team's trajectory

The trajectory of the lab will address both mechanistic and pathophysiological aspects of membrane trafficking, 'tunnelling nanotubes' (TNTs), and organelles dynamics, which makes sense regarding the history of the lab. In particular, sub-projects about the roles of TNTs in viral infection and cancer progression, as well as cytoskeleton(s) implication in chemo-mechanical transduction are very smart and sound exciting. The team leader is an internationally recognised leader in the field and the present trajectory fully supports this statement.

RECOMMENDATIONS TO THE TEAM

Recommendations proposed here could only rely on superficial aspects. The size of the team is already quite big and the high number of PhD students and postdocs should be – as much as possible – proportionated with the ongoing and future projects. As said previously, sharing both research aspects and administrative management with other researchers/PIs of the team could help to secure a proper and efficient trajectory for the future.

CONDUCT OF THE INTERVIEWS

Dates

Start: 06 février 2024 à 9 h

End: 07 février 2024 à 18 h 30

Interview conducted : online

INTERVIEW SCHEDULE

Interview day 1: Tuesday 6th of February 2024

9 a.m. – 9:30 a.m. HCÉRES committee meeting
Closed-door meeting

9:35 a.m. – 9:40 a.m. HCÉRES rules and procedures by J. Dutrieux
Public session (all unit members)

9:40 a.m. – 10:40 a.m. Administrative and scientific presentation of the unit's achievements and future by S. Etienne-Manneville/A. Subtil
40 min presentation
20 min discussion
Public session (all unit members)

10:40 a.m. – 11 a.m. Committee debriefing and coffee break
Closed-door meeting

Teams audition #1 *Public session (15 min presentation + 15 min discussion)*			
Time	**Zoom link**	**Team Number**	**Presentation by**
11 a.m. – 11:30 a.m.	Same as unit presentation	5	A. Subtil
11:35 a.m. – 12:05 p.m.	Same as unit presentation	1	A. Echard
12:10 p.m. – 12:40 p.m.	Same as unit presentation	2	J. Enninga

12:40 p.m. – 1:40 p.m. Lunch break and committee debriefing
Closed-door meeting

Teams audition #2 *Public session (15 min presentation + 15 min discussion)*			
Time	**Zoom link**	**Team Number**	**Presentation by**
1:45 p.m. – 2:15 p.m.	Same as unit presentation	4	J-C. Olivo-Marin
2:20 p.m. – 2:50 p.m.	Same as unit presentation	8	C. Zimmer
2:55 p.m. – 3:25 p.m.	Same as unit presentation	6	T. Wai

4:20 p.m. – 4:40 p.m. Committee debriefing and coffee break
Closed-door meeting

Teams audition #3 *Public session (15 min presentation + 15 min discussion)*

Time	Zoom link	Team Number	Presentation by
4:45 p.m. – 5:15 p.m.	Same as unit presentation	7	T. Wollert
5:20 p.m. – 5:55 p.m.	Same as unit presentation	3	S. Etienne-Manneville
6 p.m. – 6:30 p.m.	Same as unit presentation	9	C. Zurzolo

6:30 p.m. – 6:45 p.m. Committee debriefing
Closed-door meeting
6:45 p.m. End of day 1 Interview

Interview day 2: Wednesday 7th of February 2024

8:45 a.m. – 9 a.m. HCÉRES committee meeting
Closed-door meeting

9 a.m. – 9:45 a.m. Meeting with ITAs *(in French)*
Closed-door meeting in the absence of hierarchical person

9:50 a.m. – 10:35 a.m. Meeting with Researchers
Closed-door meeting in the absence of hierarchical person

10:40 a.m. – 11:15 a.m.Meeting with PhD students and postdoctoral fellows
Closed-door meeting in the absence of hierarchical person

11:15 a.m. – 12:55 p.m. Committee debriefing and lunch break
Closed-door meeting
1 p.m. – 1:40 p.m. Meeting with institutions representatives
Closed-door meeting

2 p.m. – 2:45 p.m. Meeting with the unit direction
Closed-door meeting
2:50 p.m. – 6:30 p.m. Redaction of the final report
Closed-door meeting

6:30 p.m. End of the interview

PARTICULAR POINT TO BE MENTIONED

Not applicable

GENERAL OBSERVATIONS OF THE SUPERVISORS

The institution responsible for submitting the application, which is also responsible for coordinating the response for all the research unit's supervisory authorities, has not submitted any general comments

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