

EVALUATION REPORT OF THE UNIT  
Virologie

UNDER THE SUPERVISION OF THE  
FOLLOWING ESTABLISHMENTS AND  
ORGANISMS:

Institut Pasteur

Centre national de la recherche scientifique,  
CNRS

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**EVALUATION CAMPAIGN 2023-2024**  
GROUP D

Rapport publié le 06/06/2024



In the name of the expert committee<sup>1</sup> :

Michael Schindler Chairman of the committee

For the Hcéres<sup>2</sup> :

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

<b>Chairperson:</b>	Mr Michael Schindler University Hospital Tübingen Allemagne
	Ms Christine Goffinet LSTM, UK
	Ms Evelyne Manet, CIRI (representative of CNRS)
<b>Experts:</b>	Mr Yorgo Modis University of Cambridge UK
	Mr Antoine Touzé Université de Tours (representative of CNU)
	Mr Ruzek, Masaryk University, Brno, Czechia
	Ms Jennifer Molle, CRCL, Lyon

## HCÉRES REPRESENTATIVE

**Ms BARTOSCH Birke**

## REPRESENTATIVE(S) OF SUPERVISING INSTITUTIONS AND BODIES

Mrs Sylvie Guerder, CNRS  
Mr Patrick Trieu-Cuot, Institut Pasteur

## CHARACTERISATION OF THE UNIT

- Name: Virologie
- Acronym: Virologie
- Label and number: num
- 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 UMR3569 'Virology' is part of the Institut Pasteur Virology department. According to its name, the main topics are human pathogenic viruses and their animal hosts. Research questions are centred around the topics viral epidemiology and evolution, viral replication (anti)-viral immune and host responses (innate or adaptive) and strategies to control viral infection, i.e. vaccines and therapeutics. As a matter of fact, during the last mandate there was a strong shift to coronaviruses which is expected as the Institut Pasteur dedicates its research towards benefit of human health and the Institut Pasteur had some major breakthrough discoveries on this topic. Moreover, coronaviruses are embedded in the main 'zoo' of viruses investigated within the UMR3569, that are all within the focus of emerging and re-emerging viruses that were introduced into the human population as zoonotic spillover from animal hosts. This includes respiratory viruses that are spread from mammals, as for instance Influenza, as well as insect-borne viruses, aka arboviruses or more recently DNA viruses, for instance Mpox ('monkeypox'). Thereby, the unit covers nearly the whole range of highly relevant human pathogenic viruses and performs state-of-the art and cutting-edge research on them.

## HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The unit is embedded within the Institut Pasteur campus in central Paris, where it is distributed over several buildings. It was originally created in 2006. It received its current label UMR3569 in 2012 in the context of an AERES evaluation in 2011. Then, it was evaluated as part of the Virology department of the Institut Pasteur by the HCÉRES in 2017 and received approval for another mandate in 2018.

## RESEARCH ENVIRONMENT OF THE UNIT

Within the campus of the Institut Pasteur the unit is embedded in a vibrant research environment. It is part of LabEX 'IBEID' that has a focus on infectious diseases and the Equipex cryo-electron microscopy facility. As a UMR 'Unités Mixtes de Recherche' it has agreements with multiple stakeholders including the CNRS, Inserm, INRA, INRIA, Ecole Polytechnique and the CNAM and hence hosts research personnel from these institutions.

Furthermore, the unit is in strong cooperation with the local universities, the Université Paris Cité, Sorbonne Université, ENS/PSL, Paris-Saclay and is hence involved in teaching, welcomes incoming lecturers and participates in master and PhD programs. Institut Pasteur is also a partner of the Université Paris Cité and is thus a member of the IDEX obtained in March 2022 by this university. These partnerships allow the research teams of the campus to benefit from university doctoral contracts, mainly from Université Paris Cité but also from Sorbonne Université and Université Paris-Saclay.

Furthermore, all over Paris, there is a strong local and diverse research community covering nearly all aspects of biomedical science.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	10
Chargés de recherche et assimilés	17
Personnels d'appui à la recherche	42
<b>Sous-total personnels permanents en activité</b>	<b>74</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	5
Post-doctorants	14
Doctorants	16
<b>Sous-total personnels non permanents en activité</b>	<b>35</b>
<b>Total personnels</b>	<b>109</b>

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	24	41
CNRS	0	3	1
AUTRE	5	0	0
Total personnels	5	27	42

## GLOBAL ASSESSMENT

Overall, the unit's performance in the last evaluation period has been outstanding.

The evaluation of the unit reveals a highly productive and impactful research entity with worldwide visibility. Previous recommendations have been partially addressed, with progress and achievements in patent filings and public engagement activities. The unit has set ambitious scientific objectives, focusing on the study of emerging viruses and host immune responses. It benefits from a highly stimulating research environment in the larger context of the Paris biomedical research landscape and national as well as international collaborations. The unit's scientific reputation is, furthermore, underscored by its success in competitive calls for projects, including two ERC grants and numerous grants from organisations such as ANRS, ANR, NIH, LABEX, Wellcome Trust, Gates Foundation just to name a few. The budget ranged from 3.2 to 4.4 M€/year with a total amount of 20M€ over the reporting period, of which 85% came from external contracts.

It attracts top international early career researchers, with 35 defended PhD theses and eighteen post-doctoral students joining during the evaluation period. Half of the current PhD students and postdocs in the unit are of foreign origin. The unit's integration policies for new staff members contribute to its attractiveness and ensure a supportive research environment.

The unit demonstrates excellence in scientific production, with a high output of publications (>500) in prestigious journals including Nature and Science. The quality and quantity of publications are exceptional in relation to the resources and highlight the unit's research potential, with each team contributing significantly. Moreover, the unit adheres to principles of research integrity, ethics, and open science, with measures in place to ensure fair authorship and compliance with ethical standards.

The unit's research activities have a tangible impact on society, with interactions with the non-academic world and the development of products for cultural, economic, and social benefit. During the evaluation period, the unit filed 22 patents of which two were licensed. Industrial collaborations with companies like Janssen and Sanofi further enhance its societal relevance. Additionally, the unit actively engages with the general public through media interviews, communication events, and science and society seminars.

The trajectory focuses on continuing its research on emerging and re-emerging human pathogenic viruses. Despite challenges such as the retirement of key personnel, the unit remains well positioned to tackle virological challenges as they made strategic recruitment that complement their main research activities.

In summary, the unit exemplifies excellence in scientific research, resource utilisation, and societal engagement. Its achievements and trajectory position it as a leading international entity in the field of human pathogenic viruses, with significant contributions to virology and public health. This is not only exemplified, but highlighted by the numerous breakthrough publications in the context of the SARS-CoV-2 pandemic that made significant contributions to understand SARS-CoV-2 co-evolution with the immune system and the impact on viral transmission and neutralisation by the natural immune response, vaccines and therapeutic antibodies. This is a bona-fide example of how the unit accomplished its mission as leading research hub in virus-host interactions in an outstanding manner.

## DETAILED EVALUATION OF THE UNIT

### A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous evaluation in 2017 of the unit was done in the context of the whole Virology department of the Institute Pasteur. Hence, several of the previous recommendations are not unit specific or address topics that can only be managed in the context of the whole institute. More specific issues were partially addressed.

For instance, the unit does not comment if there is a structured process to improve the valorisation of results but notes that in the reporting period seventeen patents have been filed and some are licensed.

Similarly, public engagement and outreach activities were conducted, but no strategic communication plan was developed due to the pandemic. To improve collaboration and research between postdocs and PhD students and to support career development, several seminars have been implemented and students now organise monthly Virology clubs, invite external speakers and are actively involved in courses to gain teaching experience.

Unfortunately, more general career development strategies for group leaders or engineers are difficult if not impossible for the unit to develop as it is embedded in the larger context of the department at the Institute Pasteur and hence has to align with the overall strategy and management.

Nevertheless, new teams have been created and implemented.

### 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 objectives are excellent to outstanding.

##### Assessment on the unit's resources

The resources are outstanding.

##### Assessment on the functioning of the unit

The functioning is excellent to outstanding.

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

### Strengths and possibilities linked to the context

The objectives set itself by the unit were 'to develop the study of emerging viruses in the context of global warming, to uncover the mechanisms underlying viral dissemination, and to understand the innate responses of the host as well as the acquired immunity against viruses'.

The unit had the right expertise to fulfil these ambitious objectives: the various teams cover a large number of virus families among which emerging or re-emerging viruses that represent major threats for human populations worldwide. The interest of the teams covers all aspects of viral infection: from viral replication, host antiviral defence, molecular physiopathology to molecular epidemiology.

The approaches used to tackle these different aspects are multidisciplinary, including epidemiology, immunology, molecular biology, biochemical and structural biology, genetic and proteomic-based methods.

This variety of expertise has proven to be particularly efficient during the SARS-CoV-2 pandemic, with five teams being involved in the Institut Pasteur SARS-CoV-2 task force. Altogether, these teams produced major contributions to the characterisation of SARS-CoV-2, as well as to the comprehension of the immune response to infection, in highly recognised journals.

Concomitantly, very important results have also been generated on the other viruses of interest and in the field of antiviral immunity. Again, some of these discoveries have been published in high-quality journals.

### Weaknesses and risks linked to the context

The retirement of several PIs opens the risk of losing some expertise, especially in the study of respiratory viruses.

## *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 is embedded into the Virology department of the Institut Pasteur that comprises 23 teams. This provides a very stimulating environment.

The unit was home for several national and international reference centres and networks, including two National Reference Centers (NRC) and three WHO laboratories. The unit also benefits from the 'Réseau International des Instituts Pasteur et Instituts associés'. This rich network of laboratories gives the unit the opportunity to initiate many collaborations and to access a large variety of biological samples. This places the unit in an excellent position to quickly respond to threats from emerging viruses as was the case during the SARS-CoV2 pandemic.

The unit also has access to a great number of technological and platforms that are provided within the Institut Pasteur. These facilities allow the unit's teams, access to cutting-edge technologies as well as animal models. Moreover, several biobanks, including viruses and human samples, are accessible on site. Finally, the unit is part of the LabEx 'IBEID' focused on infectious diseases and associated with an Equipex that provides state-of-the-art cryo-electron microscopy.

The unit is associated with two doctoral schools: ED 562 Biologie (Sorbonne, Paris Cité (BioSPC) and ED 563 Médicament, Toxicologie, Chimie et Imagerie (MTCI) which allows a good recruitment of PhD students.

### Weaknesses and risks linked to the context

The Nanoimaging Facility is severely understaffed and urgently needs additional highly trained technicians or engineers to provide the necessary technical support.

Space constraints within the Institut Pasteur may restrict the future development of some of 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 UMR is associated with the virology department of the Institut Pasteur. As such, the UMR both complies to and benefits from the good practices and rules set up by the Institut Pasteur, in terms of human resources management, gender equality, safety, environment, ethical protocols and protection of data.

The Institut Pasteur is committed to the principles of the European Charter for Researchers and has drafted a human resources management strategy for research (HRS4R).

In January 2022, the Institut Pasteur has published a Gender Equality Plan (GEP) to help implementing actions in favour of equality, diversity and inclusion. Within the UMR, gender appears to be well balanced regarding PIs as well as group leaders (50% of the group leaders were women). This ratio is maintained with the creation of two new junior teams.

The Institut Pasteur has a general IT security policy based on international standards (ISO2700X). Measures to ensure the prevention and monitoring of environmental risks, have been implemented at the level of the Institut Pasteur. Biodiversity and sustainability are taken into account with specific measures which have been set up since November 2022. These measures include favouring trains over planes for journeys of less than 4 hours, lowering heating and air conditioning. Other projects aiming at implementing measures for biodiversity and sustainability are being developed. Finally, the Institut Pasteur has a crisis management system with a business continuity plan (BCP), that applies to the UMR.

Weaknesses and risks linked to the context

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## EVALUATION AREA 2: ATTRACTIVENESS

### Assessment on the attractiveness of the unit

The unit has an outstanding reputation and worldwide visibility. The staff support is excellent to outstanding, grant leverage outstanding and the quality of the available technology is outstanding.

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

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

The unit has an attractive scientific reputation first and foremost because of the quality of its research and its excellent environment within the Paris Institut Pasteur. The excellence of the UMR is attested by the great number of publications in the most highly recognised journals and the number of citations of their work. Hence, two of the team leaders were in the Clarivate list of highly cited scientists for years 2021 and 2022. The prestige of the unit is also attested by the number of prizes and distinction obtained both by senior scientists and young researchers such as Prix Duquesne (n=2), Lucien Tartois Award, elected EMBO member. Members of the unit participate in multiple steering bodies and are part of many evaluation panels and committees. UMR members belong to 23 different Scientific Societies or International Academies. Several members also have editorial responsibilities in various international journals. Finally, they have been involved in the organisation of ten international conferences including Keystone Symposia and ESWI Influenza Conferences. The reputation of the unit in the European and World research is also reflected by the unit being host for several international WHO reference Laboratories.

During the evaluation periods many PhD students have been trained, leading to the defence of 35 theses. Eighteen post-doctoral students have joined the UMR during the same period, demonstrating the attractiveness of the unit. Many former PhDs and postdocs trained in the UMR have become successful scientists in France or abroad.

Several members of the UMR are involved in teaching Virology at the Institut Pasteur (co-direction of two Institut Pasteur courses) as well as in various courses in France and abroad, i.e. the EMBO integrative structural biology course in 2022. This also participates to the reputation of the UMR in France and abroad.

The Virology department of Institut Pasteur, in which the UMR is embedded, provides a wide range of scientific animation, with twenty seminars per year, often given by researchers from abroad which strongly contributes to the national and international visibility of the department. There is also one-day thematic mini-conferences with up to half of speakers from the unit and the rest being invited speakers.

The unit is also attractive by the implementation of an active integration policy for new staff arriving in the UMR. There are mandatory e-learning/online courses on professional risks, information systems, security, etc. New staff can also follow various trainings focused on the use of scientific resources, electronic lab notebook, etc. An intercultural seminar aimed at facilitating exchanges between the multiple nationalities present on campus is organised on a yearly basis. PhD students not only have a thesis advisory committee, including at least two external researchers, that meets every year, but they also have a mentor outside the UMR. Post-docs also have



complementary support, with a yearly interview to discuss their project and perspectives. Finally, young researchers are invited to meet and have lunch with the speakers of the Virology department's seminars. They also have the opportunity to invite speakers.

During the evaluation period, the unit had outstanding record in the obtention of grants and contracts, both at the national and international level. At the international level, two PIs have obtained an ERC grant, one an EMBO young investigator program and one an HSFP grant. The UMR has four NIH contracts, one Wellcome Trust, several DARPA (Defense Advanced Research Agency) grants. At the national level, the Unit has obtained 38 ANR contracts as well as a great number of contracts from caritative associations or foundations such as ARC, FRM, ANRS, etc. (over 100 different contracts altogether). PhD students and postdocs have obtained fellowships from SIDACTION, Marie Curie, EU, EMBO, etc.

The unit is also attractive for the quality and number of equipment and technological expertise provided by the Institut Pasteur, through its department of technology. This department composed of many different Technological Platforms covers most of the needs of the Unit.

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

There does not seem to be an overall strategy in place how to manage the remaining team members upon departure/retirement of team leaders. This is especially concerning for group leaders within the teams.

## EVALUATION AREA 3: SCIENTIFIC PRODUCTION

### Assessment on the scientific production of the unit

Scientific production is outstanding both in quantity and quality.

- 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

Over the evaluation period, the unit has had an outstanding record of publications, both in quantity and quality. Altogether, the unit has published 503 scientific articles, many of them in high-profile journals such as Nature, Science, Cell, Cell Host & Microbe Immunity J. Exp. Med, PNAS, PLoS Biology, PLoS Pathogens, EMBO J., EMBO Reports, Nature Communications, Nature Microbiology, Science Advances, Elife, etc. Many of these publications have members of the unit in leading positions.

Members of the Unit have been invited to present their work in a great number of international conferences. The output of each team, although variable in quantity, is proportional to each individual team's size which varies greatly between junior teams and more experienced teams (from 7–8 team members to over 35). Thus, every team of the unit appears to be very productive.

Regarding research integrity, ethics and open science, the UMR has developed measures for open and FAIR science. The unit is well aware of predatory journals and supports open science. Many of their publications are in open access journals. The unit has established a policy for fair consideration of any significant contribution to be acknowledged in the list of authors.

The Unit complies to the appropriate ethical principles regarding the use of human biological samples, animal monitoring and welfare during experimentation. In this respect, the Institut Pasteur signed the GIRCOR transparency charter on the use of animals for scientific and regulatory purpose in France.

With respect to scientific integrity, the Institut Pasteur has created an independent 'scientific integrity and conciliation committee' to ensure application of the Institut Pasteur 'Scientific Integrity Charter' that also applies to the UMR. A 1.5 h lecture course on ethics, scientific conduct and plagiarism organised by the Institut Pasteur is mandatory in the bioinformatics program for PhD student. Moreover, the CNRS has a dedicated office for ethics and scientific integrity on campus that includes a referent for scientific integrity.

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

None were observed.

#### EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The contribution of research activities to society is excellent.

- 1/ The unit stands out for the quality and the amount of its interactions with the non-academic world.*
- 2/ The unit develops products for the cultural, economic and social world.*
- 3/ The unit shares its knowledge with the general public and takes part in debates in society.*

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

The UMR hosts National Reference Centers for respiratory viruses and for enteroviruses. The NRC/NIC hosted by the team van der Werf is also a WHO H5 reference laboratory for zoonotic influenza viruses and was designated among the first SARS-CoV-2 WHO referral laboratories and ECDC/EEA SARS-CoV-2 reference laboratory. As such, it contributed to numerous expert and advisory groups for national (DGS, SpF, HCSP, HAS, ANSM, ANRS-MIE, ANSES) and international (WHO, ECDC, ISIRV, ESWI, ISARIC, GISAID) bodies. Notably, Mrs van der Werf is a member of the Technical Advisory Group on Virus Evolution (TAG-VE) of the WHO, a member of the DSMB/DSMC for the clinical trials DISCOVERY and SolidAct and a member of the SAB of the ANRS-MIE.

Furthermore, the unit has provided in 2015 the first complete HTLV-1 epidemiological data (maps and tables) for the 203 world's countries. The unit has since then participated at the first global consultation by WHO (Tokyo 2019) on the epidemiological and clinical aspects of HTLV-1.

The unit filed 22 patents in the last period. For example, the current patenting of potential therapeutic antibodies against SARS-CoV-2 have been licensed to SpikIMM, a start-up that has been created by an IP member in the Immunology department. The UMR teams also have industrial contracts (with Janssen, Sanofi, Biomérieux, CEPI, SPIKIMM, Reviral, Egle Therapeutics, etc.).

The unit largely participates to dissemination of knowledge towards a large audience. Its members have communicated to the lay public (100 interviews in the media (TV, radio, written, social networks) or to communication events (e.g. Rotary Club International). Members of the UMR have coordinated scientifically or participated conferences such as 'Vaincre le virus' by Barthelemy Togo, Centre Georges Pompidou, 2017 and 'Organoïde-Pasteur' meetings between scientists & artists; 'Dans la bibliothèque de Pasteur avec Di Rosa' by Hervé Di Rosa. Over the evaluation period, scientists of the UMR members have organised eleven Science and Society seminars where philosophers, sociologists, historians and qualified people were invited to discuss topics related to the interactions between science and society with researchers and staff of Institut Pasteur. They are also responsible for the Pasteur Course 'Introduction to the relationships between science and society' created in 2016 and renewed every year. This course provides a basic training in philosophy, sociology, ethics of science and enables the participants to work on a specific issue at the interface between science and society (ethical questions related with research on vaccines, embryo genome editing, numerical twins, etc.). UMR members were responsible for the partnership, signed in 2021, between Institut Pasteur and the Utopiale de Nantes. This partnership has organised a Convention that allowed fifteen scientists from Institut Pasteur to participate in round tables and presentations in front of a very large audience (up to 100,000 admissions over the 4 days of the convention).

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

The unit has the potential to reinforce translational and industrial activities.

## ANALYSIS OF THE UNIT'S TRAJECTORY

The unit consequently proposes to continue research on emerging and re-emerging human pathogenic viruses as intensively conducted during the Covid pandemic and before. The work on different pathogens including arboviruses, coronaviruses, influenza and others will be embedded within overall topics that encompass the investigation of (i) viral epidemiology and evolution (ii) viral replication and pathogenesis (iii) host responses to infection and (iv) antiviral strategies/control strategies. While this is a broad spectrum of viruses and topics, it is realistic that the unit succeeds to tackle these tasks, as it has already performed remarkably in the various areas in the past. Furthermore, upon closing of several teams mainly due to the retirement of the group leaders in the past there was an establishment of two new teams that complements with the six remaining teams of the last evaluation period. The trajectory is an expected continuation of the outstanding success of the unit and builds on the core expertise of the teams.

## RECOMMENDATIONS TO THE UNIT

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

The unit should enter into dialogue with its supervising institutions to ensure proper staffing of the technological platforms and core facilities.

To prepare for the recent/future retirement of current PIs, strategies should be put into place that allow members of these groups to continue ongoing scientific projects.

### Recommendations regarding the Evaluation Area 2: Attractiveness

It is recommended to set up conditions that facilitate the recruitment of team leaders coming from outside IP/abroad.

### Recommendations regarding Evaluation Area 3: Scientific Production

The unit is encouraged to continue their outstanding scientific production.

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

The unit should reinforce translational and industrial activities.

## TEAM-BY-TEAM OR THEME ASSESSMENT

**Team 1:** Molecular Genetics of RNA Viruses  
 Name of the supervisor: Sylvie van der WERF

### THEMES OF THE TEAM

The activities of the Molecular Genetics of RNA viruses team are dedicated to respiratory viruses with focus on influenza viruses, coronaviruses, and to hepaciviruses. The research interests are also linked to the activities of the National Reference Center (NRC) for respiratory viruses and WHO National Influenza Center (Northern France) and WHO SARS and H5 reference laboratory associated to the team (NRC/NIC). During the past period, activities were centred on viral evolution and virus/host cell interactions including virus interactomics studies to evaluate the mechanisms involved in host restriction and host specificity as well as the impact on pathogenesis. Since 2020, with the COVID-19 pandemic, activities of the team have been largely dedicated to SARS-CoV-2 with major contribution to the national and international response.

### CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

- The subgroup studying hepaciviruses has published its findings on NS2 functioning and obtained new funding.
- The organisation of the team's future leadership remains unaddressed with the retirement of the PI and closure of the group. Continuation of the research lines on virus interactomics and hepacivirus/host interactions should be ensured.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	23,5
<b>Sous-total personnels permanents en activité</b>	<b>29,5</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	3
<b>Sous-total personnels non permanents en activité</b>	<b>4</b>
<b>Total personnels</b>	<b>33,5</b>

### EVALUATION

#### Overall assessment of the team

The overall assessment of the bilan of this team is outstanding.

#### Strengths and possibilities linked to the context

The team has made significant strides in advancing our understanding of influenza and SARS-CoV-2 viruses, with their discoveries being disseminated through over 150 scientific journal articles. Particularly noteworthy are their

investigations into the molecular drivers of genetic diversity and evolution of influenza viruses, exploration of virus-host proteome interfaces influencing influenza virus adaptation, studies on SARS-CoV-2 genetic evolution, examination of the interface between SARS-CoV-2 and human proteins, and the development of novel control measures against respiratory viruses.

The team is very well known and respected for their studies on influenza and more recently also SARS-CoV-2 research as well as profiling of virus/host interactions and hepatitis host cell interaction studies. The team is also hosting the WHO H5 reference laboratory for zoonotic influenza viruses and was one of the first SARS-CoV-2 reference laboratories. The team was involved in several expert and advisory groups for national (DGS, SpF, HCSP, HAS, ANSM, ANRS-MIE, ANSES) and international (WHO, ECDC, ISIRV, ESWI, ISARIC, GISAID) bodies.

The funding of the group was secured with two international contracts NIH 101k€ partners; ten European grants (EU-FP7, EU-Horizon 2020, ECDC/ECDC-HERA, etc. 2 as leaders 260k€; 13 national grants 483 k€ they were leaders on 7; 11 of those national grants were from ANR. Notably, the PI is a member of the Technical Advisory Group on Virus Evolution (TAG-VE) of the WHO, a member of the DSMB/DSMC for the clinical trials DISCOVERY and SolidAct and a member of the SAB of the ANRS-MIE. Recognition of the team both in the field of respiratory viruses and hepatitis is also highlighted by editorial responsibilities of the senior members for various journals (Eurosurveillance, Frontiers in Microbiology, Microbes and Infection), participation in organising committees of scientific events and international meetings (e.g. Journées Francophones de Virologie, ESWI International Conferences, International Symposium on Hepatitis C Virus and Related Viruses) and multiple invitations as chair or as speaker to international conferences. The René et Andrée Duquesne prize was awarded to Sylvie van der Werf in 2021. The team organised five international congress organisations (ESWI; International Conference Institut Pasteur-ANRS-MIE «COVID-19 : advances and remaining challenges, Preparedness, Prediction and Prevention of Emerging Zoonotic Viruses: Challenges and Opportunities, Château de Montvillargenne, Gouvieux, France).

The scientific productivity of the team is truly exceptional, having published 139 peer-reviewed articles (27 in broad scope journals such as Science, Nature, Nature Com, PNAS, EMBO J, Cell, etc.). Both the Principal Investigator (PI) and team members including PhD students and postdocs frequently serve as corresponding, leading authors, or first authors of these publications. Their research has been featured in highly respected journals such as Nature, Nature Biotechnology, Lancet Infectious Diseases, Nucleic Acids Research, and numerous others.

Additionally, the team has engaged in active collaboration with industrial partners, resulting in six industrial contracts totalling €194k. These collaborations involved partners such as Sanofi Microbiome, CEPI MV Covid, and EXP Virbac ENouf. seven patents have been obtained and one has been licensed. Thirty contracts with charities/foundations for 990 k€ were obtained. The team was leader on sixteen of those. Furthermore, the team has made significant societal contributions by leveraging their expertise to inform health policies and control measures. The team has also made influenza and SARS-CoV-2 isolates and sequences available to the scientific community. This was particularly crucial during the COVID-19 pandemic and more recently during avian influenza epizootics. Additionally, group members have been actively involved in teaching activities and have regularly communicated with the media (TV, radio, written), thereby enhancing public awareness and understanding of relevant scientific issues.

The team hosted 4 Masters and 9 PhD students over the evaluation period. Members teach in two UPCité graduate schools (EUR-AntiRes; EUR-1H-EID).

#### Weaknesses and risks linked to the context

None

#### Analysis of the team's trajectory

not applicable

### RECOMMENDATIONS TO THE TEAM

not applicable

**Team 2:** Epidemiology and Physiopathology of Oncogenic Viruses  
 Name of the supervisor: Antoine GESSAIN

## THEMES OF THE TEAM

The research of the EPVO team is dedicated to epidemiology, physiopathology, and immunology focusing mainly on retroviruses (Human T cell lymphotropic viruses – HTLVs and their simian counterpart STLVs, as well as simian foamy viruses – SFVs – and HIV), herpes viruses (HHV-8) and some emerging viruses, including Chikungunya, Zika and Monkeypox.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Concerning the main recommendation on scientific production and activities by the previous committee, this was clearly addressed with success with a new productive project focused on immunological studies on foamy viruses of zoonotic origin in humans. The team demonstrated the presence of potent neutralising Abs (nAbs) targeting the Env RBD (Plos Pathog. 2018), and have solved the SFV Env structure (Nat. Comm. 2023) that led to the identification on neutralising epitopes (Plos Pathogens 2023). A minor recommendation has been addressed by the publication of a comprehensive review on the molecular epidemiology, genetic variability and evolution of HTLV-1 (Retrovirology 2019).

Concerning the recommendations on scientific strategy and projects, the work conducted by PI, PhD and postdoctoral researchers on the SFV project (see supra) is a clear answer. Studies on HHV-8 transmission are still ongoing but MCPyV studies have been discontinued. Omics have been integrated in research projects (NGS, MS).

Overall, the team have taken into account the previous committee recommendations.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	2,5
<b>Sous-total personnels permanents en activité</b>	<b>9,5</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	2
<b>Sous-total personnels non permanents en activité</b>	<b>3</b>
<b>Total personnels</b>	<b>12,5</b>

## EVALUATION

### Overall assessment of the team

Overall, the assessment of this team is excellent. With excellent to outstanding for scientific production, a very good societal impact.

## Strengths and possibilities linked to the context

The studies performed in the team during the past years have been internationally recognised. Major achievements of the epidemiology group are mainly on HTLV-1 diversity and transmission in endemic countries (JID 2022, Retrovirology 2019). In addition to the results about the maternal transmission of HTLV-1 and some arboviruses (Viruses 2019, Frontiers Microbiol 2020, Viruses 2022), the physiopathology group demonstrated the impact of LTB4 and claudin 7 on cell to cell transmission of HTLV-1 (Nat Comm, 2017, Front Microbiol, 2021). The immunology group has evidenced and characterised anti-RBD neutralising antibodies in humans infected with the SFV zoonotic virus (Plos Pathog. 2018, Nat. Comm. 2023, Plos Pathogens 2023).

The overall production of the team comprises 76 publications including eight reviews (one on Monkeypox published in NEJM) and a book chapter and two genome announcements. Team members are first or last authors on 42 publications. Other publications resulted from the numerous productive collaborative studies with both French and foreign groups. The publications are mainly in journals of high prestige: Nature Communications, Clinical Infectious Diseases, PloS Pathogens, Journal of Infectious Diseases, Emerging Microbes and Infections, Blood Advances, PloS Tropical Neglected Diseases.

In the evaluated period, the academic reputation allowed the team to obtain sustained levels of funding (206 to 314 k€/year) with contracts at the European level (N=1, UE H2020 EVA-GLOBAL, leader), at the national level (N=19, ANRS, ANR, ANR-LBX FRM, LNCC, FRM), and at the regional level (N=2, Cancéropôle, Ville de Paris).

The team is highly active in training PhD students. The supervision potential of the team relies on five HDR. In the evaluated period, 7 theses have been defended and three are ongoing. Eight of the theses were or are conducted in link with ED 474 *Frontière de l'Innovation en Recherche et Education* the two others are linked to Cameroon. The thesis duration is frequently 4 years. PhD students published two to 4 papers in association with their thesis director as last author. Except one student with a still ongoing thesis, all have a first position paper. The journals are from very good to excellent in the field of virology or in generalist journals (Nat Comm).

Team leaders have participated in high-level evaluation committees (ANR Covid, Scientific Councils of IPs of Madagascar, Guadeloupe and French Guyana of the International Network).

Since the previous evaluation and based of its long history on retrovirology, the team has demonstrated his capacity to rapidly develop sound research on SFV and to continue excellent research on viral epidemiology. Additionally, the EPVO team has continued to have a clinical impact as expert laboratory on serological and viro-molecular aspects of HTLV-1/2 and HHV-8 infections and their associated diseases with several connections with hospital's departments and animal care facilities.

## Weaknesses and risks linked to the context

The team reports a limited valorisation activity (no patent, and interaction with companies) and a moderate dissemination activity to the 'grand public'.

## Analysis of the team's trajectory

The team trajectory is in direct line with the evaluated period. The structuration of the team will not be modified since it has proven to be productive in terms of (co) publications.

The team will continue ongoing projects on clinical and molecular epidemiology studies on HTLV-1. The first main objective is to identify the different modes of transmission and acquisition of HTLV-1 in central Africa (Gabon, Cameroon), the largest endemic area for HTLV-1. The team plans to identify in more detail the risk factors associated with HTLV-1 transmission. The team will benefit of a long-lasting collaborations at the local level. The second objective is to geographically enlarge the study of circulating HTLV-1 strains in both central Africa (extension to CAR, DRC and Nigeria) and South Asia. The access to samples from CAR, DRC and Nigeria is not disclosed. Additionally, molecular epidemiology studies will be conducted on new HTLV-2, 3, 4 strains addressing particularly NHP reservoirs. All these studies will benefit of the Pasteur local network in Yaoundé and the CIRMF in Gabon.

Based on a first report in 2020, epidemiological studies on the link between HTLV-1 and ATL will be continued. Clinical and epidemiological description of a series of more than 130 cases of ATL diagnosed and followed in Guyana since 1990 will be done. A prospective study to determine the incidence of ATL cases will also be conducted as a follow-up of the princeps study. The team will also continue in the frame of a PhD thesis on a collaboration with MNHN to study Monkeypox reservoir using ecological niche in silico modelling to confirm the suspected role of a tree squirrel. Additional studies based on comparative phylogeographic studies between the virus and its reservoir(s) – squirrels and rodents from central Africa will allow testing the hypothesis of host-virus co-evolution. Finally, ongoing studies on HHV-8 in Vanuatu and central Africa will be continued in collaboration



with Quintana-Murci's team. The team's program is huge but is sustained by a long-standing collaborative network which was shown in the past to be highly productive.

**The physiopathology subgroup's project echoes the project of the epidemiology group** in several points. The group plans to establish a PDX model of ATL in order to develop therapies against this aggressive cancer in collaboration with a group at Necker's hospital. Always on HTLV-1, the group plans to study differences in pathogenesis and persistence by characterising the function of all viral transcripts or alternative transcripts encoding accessory proteins. Studies on two accessory proteins for different genotypes are ongoing in collaboration with C Journo (ENS Lyon). The group will also study arboviruses – muscle cells interactions. These studies will be extended to synoviocytes and chondrocytes. Based on their experience with ZKV, the group will also continue the study of mechanisms of virus transmission by breast-feeding in the YFV model as they have previously done with ZKV.

**The immunology subgroup's** project is based on the recent successes on SFV neutralisation. The aim is to decipher the mode of action of SFV-specific neutralising Abs using human monoclonal nAb, tested in binding and functional assays, in relation to structural data (support from IBEo identify the host receptor essential for SFV entry into cells (collaboration with F. Rey's and A. Amara's teams). SFV co-infection with endemic viruses (SIV, HIV and HTLV-1) will be studied. This part of the project needs clarification particularly on methodology (epidemiological or experimental approach or both). Two funded studies on paediatric HIV will also be continued.

Overall, the team continues its ongoing projects and builds on its recent successes.

## RECOMMENDATIONS TO THE TEAM

The committee recommends continuing the excellent integrated research on HTLV-1 and SFV. Given the retirement of the current PI after the next contract, the team members should foresee and prepare their future trajectories.

**Team 3:** Structural Virology

Name of the supervisor: Félix REY

## THEMES OF THE TEAM

The overarching research theme for Team 3 is to understand cell-entry pathways and membrane fusion mechanisms of enveloped viruses, with a focus on flaviviruses, bunyaviruses, alphaviruses, herpesviruses. The team also study host immune responses to viral infection, with a focus on understanding the organisation and antigenicity of the class II surface glycoprotein layer of hantaviruses, nairoviruses, phenuiviruses and bunyaviruses using structural approaches. A third theme of identifying the neutralisation mechanism of human antibodies against viruses from each of the virus genera listed above.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations were to maintain the outstanding research trajectory and improve the gender balance of the team at the postdoctoral level.

The research trajectory has been maintained at the highest level.

The current gender balance is near parity and there are more women than men among the group leaders within the team.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	6
Personnels d'appui à la recherche	4,5
<b>Sous-total personnels permanents en activité</b>	<b>13,5</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	5
Doctorants	3
<b>Sous-total personnels non permanents en activité</b>	<b>8</b>
<b>Total personnels</b>	<b>21,5</b>

## EVALUATION

### Overall assessment of the team

This team is considered outstanding.

### Strengths and possibilities linked to the context

It is clear from the outstanding publication track record of team 3 that it has performed at the very highest international standard. The team's work on virus cell entry in the last few years has provided detailed pictures and invaluable mechanistic insights on how a wide variety of important RNA viruses deliver their genome into the cytosol. This work has had a great impact on the field. As a result, team 3 has gained international recognition as a leader in the field of structural virology. It is one of the top 'go-to' research teams for structural work on viral glycoproteins, allowing it to forge a large number of fruitful collaborations with groups across Europe and beyond. The group compares extremely favourably with others in the field in terms of scientific production with more than 100 publications from the team since 2017. Among these publications, a significant fraction of

key original research articles had team members other than the PI as key authors, for example *Sci. Transl. Med.* 2023, *Nat. Commun.* 2022, *EMBO Rep.* 2022 and *PLOS Biol* 2021.

The team has continued to attract considerable research funding, totalling approximately one million Euro per year from various sources including national projects (for example a total of 1.1M Euro from ANR), international organisations (for example: 271,000 Euro from DARPA and 1.07M Euro from ERC), and industry collaborations. The team secured multiple contracts, including a contract with Sanofi for vaccine research; a Wellcome Trust contract to study stabilised dengue virus antigens; and ANR contracts. Other team members obtained their own funding, including a postdoctoral fellowship from SIDACTION. Attractiveness is further evident by the number of Masters students (12), PhD students (6), and postdoctoral researchers (>30) who were part of the team since 2017. There was good gender balance among trainees and a significant fraction came from outside France. Various team members were invited to international conferences. A PhD student was awarded a prize from Fondation Bettancourt-Schueller in 2018 and obtained a tenure-track position at the MRC-LMB (Cambridge, UK). Two researchers also obtained faculty positions. The team leader is a member of prestigious scientific boards, including the EMBL SAB, and the Institut Pasteur Board of Directors. They are a member of the French Academy of Sciences and the Institut Pasteur Covid Task Force, demonstrating high-level recognition as a scientist and opinion leader.

One researcher in the team took part in teaching of three electron microscopy courses. The Team Leader taught at the Fundamental Virology course of Institut Pasteur, co-organised by one of the group leaders within the team. One researcher in the team organised eleven Science and Society seminars since 2017. They have also been responsible for the Pasteur Course 'Introduction to the relationships between science and society' since 2016.

## Weaknesses and risks linked to the context

Many of the new project proposed by this team and by Team 9 rely on cryo-EM and cryo-ET approaches, which requires highly specialised equipment and expertise. There is a risk of missing some of the proposed research objectives if the necessary equipment and technical support for these new and challenging techniques, specifically cryo-ET, are not built up and reliably maintained.

## Analysis of the team's trajectory

The team leader is a fully established and highly respected researcher of worldwide reputation. Based on his body of work and track record, he and his team have contributed outstanding research that is competitive with the best in the field. The team leader has demonstrated that he is an internationally competitive researcher in the area of structural virology, and there is a clear promise for continued future scientific productivity and professional development.

A previous major contribution from the team was the discovery that two important families of cell-cell fusion proteins, the HAP2 gamete fusion proteins and the nematode FF fusion proteins, have the same protein fold as class II virus envelope proteins. This established firm evolutionary and mechanistic links between families of proteins that catalyse virus cell entry, gamete fusion and epithelial syncytia formation in nematodes, families that had not previously been thought to be related. This discovery had far-reaching implications for our understanding of virus-host co-evolution. It also provided a new set of tools and approaches to study virus entry and eukaryotic membrane fusion processes.

The team's current research and proposed projects for the next five years focus on complementing tradition structural approaches with newly developed cryo-electron tomography (cryo-ET) approaches that allow virus structure to be studied in situ in the cellular context. The team is well positioned for this with cryo-ET equipment and expertise having been recently added at Institut Pasteur. This approach will allow the team to address the function of eukaryotic structural homologs of the viral proteins, which drive fundamental processes such as fertilisation, for which the molecular mechanisms remain incompletely understood. The team leader has secured EU funding to use AI to design new immunogens for key viral pathogens including the Crimean-Congo haemorrhagic fever virus, a BSL4 pathogen high in the WHO list of priorities for preparedness. Overall, the team seems on course to maintain its outstanding research trajectory.

From the strategic and administrative perspectives, the team leader has ensured the continuity of research established under his team by reorganising the work in themes, with three outstanding researchers appointed as group leaders by Institut Pasteur. These three groups, working next to the new unit team (team 9), will help ensure that high-level structural virology will be maintained on campus in the medium and long term.

## RECOMMENDATIONS TO THE TEAM

Make a plan for how to build up and maintain a world class cryo-EM and cryo-ET facility with the necessary technical support and reliability is required for the proposed projects over the next period of the UMR Unit. It came to light during the review that the Nanoimaging Facility is severely understaffed and urgently needs additional highly trained technicians or engineers to provide the necessary technical support.

The team is expected to maintain the outstanding scientific output and prepare for the team leader's retirement.

**Team 4:** Virus and Immunity

Name of the supervisor: Olivier SCHWARTZ

## THEMES OF THE TEAM

Over the evaluation period, the team has focused on investigations of HIV and coronaviruses, centering on fundamental research addressing cellular and viral membrane fusion, viral replication and virus/host interactions. This included mechanistic work on the formation and ISG-mediated perturbation of the syncytiotrophoblast; anti-HIV antibodies and the impact of both commensal and pathogenic bacteria on T-cell activation and HIV-1 infection. In the context of SARS-CoV-2, research topics included aspects of coronavirus tropism, cell-intrinsic innate immunity and humoral responses, including studies on the efficacy of anti-COVID vaccines and monoclonal antibody-based therapies.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Based on the experts' opinion that the team should put efforts in expanding its outreach to industry and other public outreach outputs, in the evaluation period the team worked with industrial partners on SARS-CoV-2, designing seroneutralisation assays that have been used to test the immunogenicity of candidate vaccines by Sanofi. They also cooperated with the start-up Spikimm to test the antiviral activity of therapeutic monoclonal antibodies which are currently in Phase I clinical trials. Members of the team have regularly communicated to the lay public by through more than 100 interviews in the media (TV, radio, written, social networks) or by participation to communication events. Team members coordinated or participated to Art & Science exhibitions or conferences, such as 'Vaincre le virus' by Barthelemy Toguou, Centre Georges Pompidou, 2017; 'Organoïde-Pasteur' meetings between scientists & artists; 'Dans la bibliothèque de Pasteur avec Di Rosa' by Hervé Di Rosa. Permanent Exhibition, Institut Pasteur, 2017. « Biodesign, La Fabrique du vivant » Centre Georges Pompidou, 2019 ; «

Micromonde : vivre avec les petits êtres » Musée du Quai Branly, 2022 ; « La Vallée », Fabrice Hyber, Fondation Cartier, 2023. Together, outreach to non-academic partners has clearly increased.

Another recommendation was to recruit/retain female researchers in higher positions. The current team includes two women among the five permanent scientists, so it seems that parity has been reached.

Finally, the experts were sceptical regarding the long-term outcome of the ZIKV project activities, and the team has discontinued these activities.

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

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

## EVALUATION

### Overall assessment of the team

The team's scientific assessment is outstanding.

## Strengths and possibilities linked to the context

The team has championed in generating major contributions to SARS-CoV-2, variants of concerns, their different sensitivity to antibodies and modes of cellular recognition of infection. At the same time, the team has managed to uphold research activities on HIV-1 and got not distracted from their genuine expertise. This strategy results in an important gain of expertise and a widening of the research portfolio and demonstrates that the team is able to apply their expertise to newly emerging viruses.

The success of the team is documented by the publication of 100 articles in leading journals (Nature, Science, Nat. Med, etc.), with 35 as lead authors with all team members contributing and filing of three patents (one licensed). Scientific outreach includes elements of art, where scientific pictures and images are translated in artistic illustrations for research journal covers and other publications. The team's work is based on intensive collaboration with a network of clinics and hospitals, which allowed the team to isolate different variants of concern at unprecedented pace.

The team holds several editorial responsibilities of senior members (Journal of Virology, Microbes and Infection), has reviewed hundreds of manuscripts and grant proposals, participated in organising committees of numerous scientific events, national and international meetings. The team members received multiple invitations as chairs or as speakers to international conferences. Prestigious prizes were awarded to junior and senior group members Prix L'Oréal « Women in Science » 2017, Prix jeune chercheur Académie des Sciences 2021, Prix René et Andrée Duquesne 2022, Prix de thèse de la Chancellerie 2022, Prix de thèse SFV, ANRS-MIE 2023. The team attracts a high number of Masters (12), PhD students (8) and post-doctoral researchers (10), who were part of the team over the 2017–2022 period. Recognition is further evidenced by its success in competitive calls for projects both at national and international levels, with funding granted over the period from numerous national (ANR, ANRS/ANRS-MIE, APHP, Fondation pour la Recherche Médicale (équipe labélisée), Institut Pasteur, Sidaction, Sanofi, Spikimm, Roche-Emulate...) and international (EU-FP7, EU-HERA) sources. In total 36 grants ranging from 4k to 390k Euro, including 4 industrial partnerships summing up to over 3.7 M€ were obtained.

## Weaknesses and risks linked to the context

Post-COVID19 funding fatigue, which is already manifesting itself and expected to increase soon, makes it necessary to either redirect research projects to other virus families and/or identify niches of research within coronavirology which have remained largely unexplored and for which funders will be convinced.

## Analysis of the team's trajectory

Already before the pandemic, the PI was a fully established and world-renown researcher of international reputation. His team managed to excel further by increasing research activities, now including several aspects of SARS-CoV-2 biology, tropism and humoral immunity. It is important to mention that, remarkably, these new outputs were of scientific excellence, despite the absence of a particular focus on coronavirology prior to 2020.

The team's proposed projects for the next five years focus on the expansion of SARS-CoV-2 and HIV-1 research, building on their previous achievements. The experts agree that inclusion of endemic seasonal coronaviruses causing common colds, HKU1, 229E, NL63 and OC43 which circulate worldwide is a viable strategy in order to make use of the expertise in the context of the pandemic, giving that these four viruses, despite not belonging to the highly pathogenic coronaviruses, cause an enormous economic loss in societies. The future study of MPOX, an emerging pathogen of potentially global importance in the future and where the team has already provided valuable contribution, has the potential to replace some SARS-CoV-2 activities for which funding might be more and more difficult to obtain in the future.

## RECOMMENDATIONS TO THE TEAM

The experts recommend to continue the very successful scientific trajectory of working on emerging viruses by applying scientific technologies and concepts established in the team, while at the same time intensifying HIV research.

**Team 5:** Viruses and RNA Interference

Name of the supervisor: Carla SALEH

## THEMES OF THE TEAM

The Viruses and RNAi unit focuses on vector biology and infectious diseases, particularly on understanding how insects maintain functional robustness during viral infections. Their research seeks to uncover the mechanisms that enable insects, as vectors of viruses, to remain persistently infected without experiencing harm. This stands in contrast to vertebrate hosts, where the same virus can lead to disease or mortality.

By investigating this phenomenon, the group aims to shed light on the factors contributing to the resilience of insect vectors to viral infections. Understanding these mechanisms could have implications for developing strategies to control vector-borne diseases and mitigate their impact on human health.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The committee's recommendations from the previous report have been duly noted and addressed by the team. Efforts have been made to maintain the publication of high-quality work while also focusing on increasing outreach and attracting more PhD students. Additionally, steps have been taken to strengthen interpersonal communication and foster teamwork within the group. The team remains committed to overcoming bureaucratic obstacles to ensure smooth operations.

Furthermore, the team continues to excel in enhancing its international visibility and advancing translational work.

## 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	5
<b>Sous-total personnels permanents en activité</b>	<b>6</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	4
Doctorants	2
<b>Sous-total personnels non permanents en activité</b>	<b>6</b>
<b>Total personnels</b>	<b>12</b>

## EVALUATION

### Overall assessment of the team

This team is assessed as excellent to outstanding.

### Strengths and possibilities linked to the context

The primary objective of the team is to elucidate how the insect immune system contributes to the organism's resilience during viral infections, a topic explored by only a select few researchers globally with implications for public health and vector-borne disease control. Notable discoveries during the evaluation period include the characterisation of ribosomal RNA (rRNA) sequences from 33 mosquito species worldwide, the demonstration of synergistic action among innate immune pathways in constraining RNA virus evolution in *Drosophila*, evidence supporting long-lasting transgenerational antiviral immunity in insects, and the identification of Dicer-2-

dependent generation of viral DNA from defective RNA viral genomes, which modulates antiviral immunity in insects. These findings represent significant contributions to the understanding of insect immune responses to viral infections.

The team utilises unique research models, likely offering novel insights into the field and providing a distinctive contribution to the scientific community's understanding of insect immunity and viral infections. These include *Drosophila* and mosquito models for investigation of virus-vector interactions.

Since 2017, the team has published a total of 22 papers; several papers in reputable journals such as *Nature Ecology and Evolution*, *Cell Host and Microbe*, and *Cell Reports*, with frequent involvement of the PI as corresponding author. However, the citation rate for these works remains relatively modest. The team demonstrates a commitment to open access publishing, including preprint server submissions, and prioritises storage and sharing of primary data. The team received numerous grants for a total of 3.2 M€ during the evaluation period (Marie Skłodowska-Curie Actions, DARPA, NIH, ERC, H2020, ANR, etc.).

The team also actively engaged in teaching and science popularisation initiatives. Examples of teaching activities are: Master Course Virology, École Normale Supérieure de Lyon, France ; Course Insects Vectors, Institut Pasteur, Paris, France; Course Multiple Roles of RNA, Institut Pasteur, Paris, France; Course Genome Analysis, Institut Pasteur, Paris, France; Master Course Virology, University of Strasbourg, France; Master Course Small RNAs, University of Buenos Aires, Argentina; Master Course Virology, École Normale Supérieure de Paris, France. The international visibility of the team is reflected by 4 out of the current five post-doctoral researchers being of foreign origin. The PI has been elected fellow of ASTMH, EMBO and received the Lucien Tartoise Award. The team has been implied in the organisation of three international congresses (Keystone, Biological functions of transposons helsinki, 1<sup>st</sup> conference of the French society of extracellular vesicles).

## Weaknesses and risks linked to the context

No significant weaknesses were identified.

## Analysis of the team's trajectory

The main projects planned for the next five years align seamlessly with the central research topic of viral emerging diseases and the control of viral diseases, which is the core focus of the UMR. These projects have been meticulously designed, leveraging previous data and projects conducted by the team. They represent a balance between ambitious goals and feasibility, indicating the potential to generate significant new insights and data. By tackling these projects, the group is poised to make important contributions to our understanding of viral diseases and their management, further solidifying their position at the forefront of this research field.

## RECOMMENDATIONS TO THE TEAM

Continue with this exciting line of research, publish in high-quality journals. Maybe, try to increase the number of publications, so every PhD student and postdoc will have a chance to publish a first-author paper.

To continue the excellent trajectory in research. It would be also good to intensify the international and interdisciplinary collaborations.

**Team 6:** RNA Biology and Influenza Viruses

Name of the supervisor: Nadia NAFFAKH

## THEMES OF THE TEAM

The team aims at understanding how the influenza A virus (IAV) genome is replicated, transported and assembled before its incorporation into progeny virions, all in close cooperation with host cell components. Research divides along two main lines, transcription and replication of viral genomic RNAs in the nucleus of infected cells and trafficking and assembly of newly synthesised viral genomic RNAs.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Not applicable, as the team was created during the last evaluation period.

## 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	1,5
<b>Sous-total personnels permanents en activité</b>	<b>3,5</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	2
Doctorants	1
<b>Sous-total personnels non permanents en activité</b>	<b>4</b>
<b>Total personnels</b>	<b>7,5</b>

## EVALUATION

### Overall assessment of the team

This team is considered excellent.

### Strengths and possibilities linked to the context

Through collaboration with structural biology teams, the team integrates cell-based and in vitro approaches to elucidate interactions between viral and cellular components. By developing innovative techniques, they aim to understand how IAV genomes reassortment, potentially leading to pandemic strains, offering insights crucial for developing anti-IAV therapies and improving pandemic risk assessment.

Some of the key scientific discoveries of the team showed involvement of the influenza viral polymerase and its subunit composition in transcription but also replication (Nat Commun 2024, PLoS Path 2019, 2022). Collaborative studies showed that the RED-SMU1 splicing complex is targeted by IAVs, which partially divert RED from its natural target mRNAs (NAR Genomics and Bioinformatics 2020) and structural analyses allowed identification of compounds that disrupt the RED-SMU1 complex, inhibit NS1 mRNA splicing and specifically inhibit IAV replication, while preserving cell viability (PNAS 2019). The team also developed a high-throughput droplet-based assay to study genetic reassortment of IAV by single-virus RNA sequencing (PNAS 2023).

The PI has participated/is participating to scientific committees (SAB of the Leibnitz Institute of Virology, Germany; SAB of the Institut de Biologie Intégrative de la Cellule, Gif-sur-Yvette ; Evaluation Committee of Institut Pasteur Scientists (COMESP – (co-chair in 2020–2021); Scientific Council of the Haut Conseil des Biotechnologies;



Scientific Committee on Select Agents at ANSES; Scientific Evaluation Committee BIHASC at INRA). She was a co-founder of the French CNRS GDR2073 ResaFlu and chaired the steering committee in 2020–2021. The PI and other team members have regularly served as experts for national and international funding agencies, as members of PhD and HDR juries as well as PhD advisory boards. The PI was awarded the 2018 'Prix Jacques, Georges et Elias Canetti', by the Scientific Council of Institut Pasteur and the 2019 'Prime d'Encadrement et de Recherche' by the CNRS.

Over the 2017–2022 period, the RBIV team has attracted two Master students, three PhD students and five post-docs including from abroad (2 PhDs and 3 post-docs). The team obtained project funding from both national (several ANR grants, DIM One Health 2.0, Institut Pasteur Self-Evaluation Document for Research Units 2023–2024 Evaluation campaign – Group D Research Evaluation Department 55 COVID-19 Task Force) and international (HFSP, 163K€) sources, a number of which as coordinator (ANR, HFSP, COVID-19 Task Force). The total amount of funding sums up to close to 1.6 M€.

During the 2017–2022 period, the team produced sixteen original publications including in high-profile journals (Nature, Nat Commun, PNAS), four review articles (Annual Reviews Biochem, Trends in Microbiology, PLoS Pathogens) and one method article. The PhD students and post-docs were (co)-first authors of ten articles (Nat Commun, PNAS, PLoS Pathogens) and senior researchers of the team were (co)-last authors of eleven publications. The team mentions that their scientific production on influenza viruses has been hampered with the COVID-19 pandemic. Some of their activities have been redirected to SARS-CoV-2 to contribute to the Institut Pasteur COVID19 Task Force.

Outreach activities (clinical partners, industrial partners and society) are in development but not yet implemented. However, two patents have been filed. The major outreach activity has been to help academic refugees to find their way in the French research ecosystem, notably through mentorship of recipients of the programme PAUSE (<https://www.programmepause.fr/en/>), and to host high-school students for short internships in the lab, with the participation of the entire team.

## Weaknesses and risks linked to the context

Outreach activities (society) and interactions with clinical and/or industrial partners remain to be implemented.

## Analysis of the team's trajectory

Funding is in place for current projects but not beyond 2025, with grant applications ongoing.

The team has done scientifically very well in the research field of influenza virus replication such as the influenza viral polymerase's role in transcription and replication, the targeting of the RED-SMU1 splicing complex by IAVs, development of compounds disrupting this complex to inhibit IAV replication, and the creation of a droplet-based assay for studying genetic reassortment of IAV. The main projects planned for the next five years align well with these central research topics of influenza virus replication.

## RECOMMENDATIONS TO THE TEAM

Outreach activities (society) and interactions with clinical and/or industrial partners should be implemented. The topic of pandemic preparedness in the context of influenza should offer multiple opportunities for intensified outreach activities.

**Team 7:** Virus Sensing and Signalling

Name of the supervisor: Nolwenn JOUVENET

## THEMES OF THE TEAM

Over the evaluation period, the team has focused on investigations of cell-intrinsic restriction and modes of sensing viral infections by + stranded viruses (mainly mosquito-borne flaviviruses and SARS-CoV-2). This main focus is complemented by activities related to the detection and characterisation of circulating polioviruses in Central African Republic, Madagascar and Algeria.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

not applicable as created during the last evaluation period.

## 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	3,5
<b>Sous-total personnels permanents en activité</b>	<b>5,5</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	2
<b>Sous-total personnels non permanents en activité</b>	<b>4</b>
<b>Total personnels</b>	<b>9,5</b>

## EVALUATION

### Overall assessment of the team

This team is considered excellent with a highly promising trajectory.

### Strengths and possibilities linked to the context

Starting off from their expertise in cell-intrinsic innate immunity and sensing of virus infections, the team managed to make very valuable contribution to SARS-CoV-2, including discovery of SARS-CoV-2-derived miRNA that circumvents the expression of IFN-stimulated genes (EMBO Reports, 2022) and correlation of control of viral replication with IFN responses (Journal of Virology, 2022), demonstrating their ability to apply their knowledge in the context of a new emerging virus. Their work on restriction and sensing of flaviviruses (ZIKV, YFV), and the peculiarity of the bat species in responding to virus infections, in total represents a multifaceted, yet complementary area of fundamental research. The latter is accompanied by a more applied research arm on enteroviruses, which contains discovery and characterisation of polio- and non-polio enteroviruses in several African nations. In principle, this mix of basic and more epidemiological research of emerging RNA viruses is a strength of the team.

The team attracts a high number of trainees (10), PhD students (7) and postdocs (4). Several team members are heavily involved in teaching (e.g. co-direction of a ten-week Virology Master class that hosts 30 students per year and welcomes over 90 virologists from all over Europe for invited lectures). The team contributes to WHO activities (as member of the WHO Global Polio Laboratory Network and as WHO Collaborating Centre) and to

the activities of the National Reference Center for Enteroviruses, which informs health policies and control measures on poliovirus and other enteroviruses emergence and outbreak. The team is a member of the French National Certification Committee for Poliomyelitis.

The team participates in organising committees of scientific events (e.g. Journées Francophones de Virologie), team leaders received multiple invitations as chair/speaker to national and international conferences (e.g. Journées Francophones de Virologie, Italian Society for Virology), to deliver talks in France (Université de Tours, Institut Cochin, Institut Curie, University of Montpellier, etc) and abroad (HKU-Pasteur Research Pole, Hong Kong; Leibniz Institute of Virology, Germany; University of Saskatchewan, Canada; Surrey University, UK; Ohio State University, USA; Karolinska Institut, Sweden; etc.), to be part of PhD and 'HDR' juries (over 30 in the past five years), and to be a member of recruiting committees for permanent researchers in academia. They were members of thesis advisory boards (> 20), received invitations to review national and international grants (ANR, ANRS, ANRS-MIE, ANR, IRBA, Finovi, Israel Science Foundation, Medical Research Council UK, EMBO short/long-term fellowships, etc.), and manuscripts for PloS Pathogens, Cell Reports, Cell, Nature Microbiology, JVI, Nature Communications, etc.

The team has numerous national (UMR Virologie, Ecole Vétérinaire de Maisons-Alfort; Institut Curie, etc.) and international collaborations (University of Saskatchewan, Canada; Pirbright Institute, the UK; Institute of Virology, Charité Universitätsmedizin Berlin, Germany, etc.).

In the evaluation period, 53 papers were published by this relatively small team in journals including e.g. EMBO Reports, NJP Vaccines, Nat Commun, Science, Lancet ID, Trends in Immunology. All PhD students published at least one first author paper, indicating that nobody is left behind in this team.

The team obtained funding from competitive calls from numerous national, European and international agencies (mainly Institut Pasteur, ANR, ANR Flash COVID-19, ANRS, DIM-1-Heath, EVA-GLOBAL, EU Horizon 2020, Boehringer Ingelheim Fonds, EMBO and Bill & Melinda Gates Foundation) (1.2 M€ in total) most of which as coordinator and with three ANR grants running until 2024 or 2025.

## Weaknesses and risks linked to the context

None identified.

## Analysis of the team's trajectory

Overall, the team's trajectory appears steep and successful. Despite size restriction imposed on the number of team members, they generated an impressive amount of high quality output.

The team's proposed projects for the next five years seem to pursue similar goals like in the past (successful) evaluation period, with no big changes regarding the pathogens of interest and methodological approaches. In the enterovirus research project arm, more fundamental research will be integrated, which the experts agree is a good strategy and may complement the other activities of the team in the context of flavivirus research.

## RECOMMENDATIONS TO THE TEAM

Given the broad expertise being present in the team, continue to collaboratively study research areas across flavi-polioviruses.

**Team 8:** Advanced Molecular Virology  
 Name of the supervisor: Francesca DI NUNZIO

## THEMES OF THE TEAM

The team works on spatiotemporal events governing retroviral reverse transcription (RT), in particular HIV-1. They previously found that RT can take place in membraneless organelles (MLOs). However, mechanisms governing MLO formation are largely unknown even though these compartments emerge as important for a variety of pathogens. Overall, the team is interested in determining how HIV-1 induces MLOs, the relevance of MLOs for the viral cycle and the role of MLOs in the context of other infections.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

not applicable as recently created

## 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	0
Personnels d'appui à la recherche	0
<b>Sous-total personnels permanents en activité</b>	<b>0</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	0
<b>Sous-total personnels non permanents en activité</b>	<b>0</b>
<b>Total personnels</b>	<b>0</b>

## EVALUATION

### Overall assessment of the team

The trajectory of this team is excellent to outstanding.

### Strengths and possibilities linked to the context

not applicable

### Weaknesses and risks linked to the context

not applicable

### Analysis of the team's trajectory

The previous track record of this team, even not part of the unit in the last mandate, is very impressive with new findings that change the dogma of the spatiotemporal order of HIV-1 reverse transcription. They contributed key findings that established reverse transcription not to take place solely in the cytoplasm but in the nucleus in membraneless organelles.

The project plan is ambitious and challenging but overall convincing and exciting. The team suggests to study MLOs in the context of HIV-1 replication and persistence building up on previous expertise in the team. In three WPs they aim to decipher virus-host interactions that govern establishment of MLOs by a process called liquid-liquid-phase separation (LLPS). They will analyse if and how MLOs are involved in regulation of viral replication and latency and finally want to translate their findings to preclinical models. This last part is not entirely clear in terms of feasibility.

Nevertheless, the project has the potential to come up with new concepts concerning LLPS and establishment of MLOs and their impact in viral infections.

## RECOMMENDATIONS TO THE TEAM

Intergrate into the unit and translate your findings to other viral infections.

**Team 9:** Structural Biology of Infectious Diseases

Name of the supervisor: Pablo GUARDADO-CALVO

## THEMES OF THE TEAM

The research focus of this newly formed independent team is to understand the cell-entry mechanisms of poxviruses using structural approaches. The first key aim is to determine the structure of the fusion complex by cryo-EM. The second uses state-of-the-art cryo-EM tomography (cryo-ET) to study the ultrastructure of proteins on the outer surface of poxviruses. Structural studies will be complemented with functional validation in collaboration with an international leader in the poxvirology field.

The team also collaborates with team 3 to study glycoproteins and cell-entry mechanisms of bunyaviruses.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Not applicable as recently created.

## 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	0
Personnels d'appui à la recherche	0
<b>Sous-total personnels permanents en activité</b>	<b>0</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	0
<b>Sous-total personnels non permanents en activité</b>	<b>0</b>
<b>Total personnels</b>	<b>0</b>

## EVALUATION

### Overall assessment of the team

With a promising research plan, a sound and worthy research output, but a limited number of publications as senior author relative to the team leader's career stage, the team is considered very good with the potential to develop an excellent research program.

### Strengths and possibilities linked to the context

not applicable

### Weaknesses and risks linked to the context

not applicable

### Analysis of the team's trajectory

Since joining the Unit as part of the Structural Virology Unit in 2015, The PI of team 9 co-authored sixteen original research articles and was listed as an inventor on three patent applications. He was co-corresponding author on two of these articles and co-first author on one article. He has not yet published any research articles as sole

corresponding author and only one as last author (Sci Transl Med. 2023). His most important contributions were two structural studies on glycoproteins from Rift Valley Fever virus (RVFV) and hantaviruses, respectively, using a combination of X-ray crystallography and cryo-electron tomography (cryo-ET).

In both of the team leader's papers as corresponding author, structural and biochemical data provide a detailed understanding of how viruses assemble and how they drive the fusion of the virus membrane to the host cell membrane. The structures detailed in these studies are promising targets for antiviral therapies. A consistent pattern through the work from the Team Leader's previous work is that protein crystallography data are rigorously used to gain detailed insights on the self-assembly and cell-entry mechanisms of enveloped viruses. He has contributed to many collaborative studies that employ multidisciplinary approaches, combining structural biology, biochemical assays, and cell-based approaches. The practical applications and translational potential of the data are carefully addressed. The structural data and analysis are consistently of high quality in the team leader's work. Overall, the team leader has demonstrated a very high level of scholarship and professionalism in his academic research.

The team leader's proposed project for the research period is to study the membrane fusion protein complex of poxviruses. The glycoprotein assembly governing membrane fusion in poxviruses is much larger and more complex than in other virus families. The team leader proposes to use cryo-EM and cryo-ET as the main structural approaches. Cryo-ET is a powerful new approach, but it is challenging and low-throughput. The team leader has recruited a world expert in poxvirology from the Univ. of Birmingham as his collaborator. Overall, the proposal is timely, exciting, and will be highly impactful if successful. However, it is also highly ambitious and technically challenging. Success will be dependent on availability of technical support and expertise at the electron microscopy facility of Institut Pasteur.

Based on his body of work and dossier, the team leader has contributed internationally competitive research at every stage of his career so far. Although his research output to date as a senior author is limited, he is on a promising trajectory. He has been successful in securing funding from the national and private sectors. He has put together an exciting but technically challenging proposal for the next five years.

## RECOMMENDATIONS TO THE TEAM

One of two aims proposed by this team and by team 9 rely on cryo-EM and cryo-ET approaches, which required highly specialised equipment and expertise. There is a risk of missing some of the proposed research objective if the necessary equipment and technical support for these new and challenging techniques, specifically cryo-ET, are not built up and reliably maintained.

It came to light during the review that the Nanoimaging Facility is severely understaffed and urgently needs additional highly trained technician or engineers to provide the necessary technical support.

The PI needs to carefully refocus his research themes given the limited resources (space/personnel) available.

**Team 10:** Viral Populations and Pathogenesis

Name of the supervisor: Marco VIGNUZZI

## THEMES OF THE TEAM

This team's primary focus revolved around monitoring and predicting the evolution of viruses by integrating virology, big data analytics, and evolutionary scientific approaches. Their research targeted medically significant and economically impactful RNA viruses, encompassing enteroviruses (such as Enterovirus 71, poliovirus, coxsackievirus, and rhinovirus), alphaviruses (including chikungunya, O'nyong'nyong, and Mayaro), flaviviruses (such as Zika, dengue, West Nile, Yellow fever, and Usutu), influenza A virus, and SARS-CoV-2. Additionally, they employed a combination of experimental evolution and computational methods to develop innovative antiviral strategies.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No information provided

## 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	0
Personnels d'appui à la recherche	0
<b>Sous-total personnels permanents en activité</b>	<b>0</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	0
<b>Sous-total personnels non permanents en activité</b>	<b>0</b>
<b>Total personnels</b>	<b>0</b>

## EVALUATION

### Overall assessment of the team

The bilan of this team is outstanding.

### Strengths and possibilities linked to the context

In 2022, Dr. Vignuzzi relocated his laboratory away from France. The productivity of the team was exceptional during the evaluation period (51 publications). They authored numerous papers in top-tier journals, including Nature, Cell Host and Microbe Nature Microbiology, Cell, Science, Nature Communications, among others, with Dr. Vignuzzi frequently serving as the corresponding author.

The lab received outstanding external funding from both local and international sources, including significant grants and participation in large scientific consortia. Seven grants with total budget with more than 34M Euro.

Additionally, the team submitted three patent applications, with Dr. Vignuzzi playing a pivotal role, showcasing the practical application of their research findings. The patents included following discoveries: Activated reporter protein for the detection of infection in a biological sample; Defective Interfering Viral Genomes; and RNA virus attenuation by alteration of mutational robustness and sequence space.



The research conducted by the team obtained remarkable visibility, not only through publications in prestigious journals but also due to Dr. Vignuzzi's active engagement on social media platforms, where he effectively popularised his scientific work and virology in general.

Key discoveries made during the evaluation period included the identification of defective viral genomes as therapeutic interfering particles against flavivirus infections in both mammalian and mosquito hosts. The team also made significant contributions to SARS-CoV-2 research, such as mapping protein interactions to identify targets for drug repurposing, characterising the global phosphorylation landscape of SARS-CoV-2, and uncovering the Dicer-2-dependent generation of viral DNA from defective genomes of RNA viruses, which modulates antiviral immunity in insects. These discoveries highlight the impactful and multifaceted nature of the team's research endeavours.

### Weaknesses and risks linked to the context

One potential weakness that could be noted is the broad focus of the research undertaken by Dr. Vignuzzi's team. While addressing a wide range of topics can lead to diverse insights, it may also result in less depth of analysis in certain areas. However, aside from this consideration, no other significant weaknesses were identified in the evaluation of their research activities.

### Analysis of the team's trajectory

not applicable

## RECOMMENDATIONS TO THE TEAM

not applicable

## CONDUCT OF THE INTERVIEWS

### Dates

**Start:** 07 mars 2024 à 8 h

**End:** 08 mars 2024 à 19h00

**Interview conducted: on-site or online**

### INTERVIEW SCHEDULE

March 7th

8:50-9:00 HCÉRES Rules and procedures  
 9:00-10:00 Administrative and Scientific presentation of the Unit  
 10:00-10:20 Debriefing committee (closed-door meeting)  
 10:20-10:45 Team 'Virus Sensing and Signalling'  
 10:45-11:25 Team 'Epidemiology and Physiopathology of Oncogenic Viruses'  
 11:25-11:50 Team 'Structural Biology of Infectious Diseases'  
 11:50-1:20 p.m. Debriefing committee and lunch break (closed-door meeting)  
 1:20 p.m.-2 p.m. Team 'Virus Sensing and Signalling'  
 2 p.m.-2:40 p.m. Team 'RNA Biology and Influenza Viruses'  
 2:40 p.m.-3:10 p.m. Debriefing committee (closed-door meeting)  
 3:10 p.m.-3:50 p.m. Team 'Structural Virology'  
 3:50 p.m.-4:30 p.m. Team 'Viruses and RNA Interference'  
 4:30 p.m.-5 p.m. Debriefing committee (closed-door meeting)  
 5 p.m.-5:40 p.m. Team 'Virus and Immunity'  
 5:40 p.m.-6:05 p.m. Team 'Molecular Genetics of RNA Viruses'

March 8th

9:00-9:20 Debriefing committee (closed-door meeting)  
 9:20-10:00 Meeting with ITAs (in French)  
 10:00-10:40 Meeting with researchers  
 10:40-11:20 Meeting with post-docs and students  
 11:20-11:40 Debriefing committee (closed-door meeting)  
 11:40-12:20 Meeting with institution representatives (closed-door meeting)  
 12:20-1:30 p.m. Lunch Break  
 1:30 p.m.-2:15 p.m. Meeting with the Management Team of the Unit (closed-door meeting)  
 2:15 p.m.-6 p.m. Redaction of the final report (closed-door meeting)

### PARTICULAR POINT TO BE MENTIONED

Pr Paul Diggard, Roslin Institut, Edinburgh, UK originally assigned as expert to the committee had to withdraw from the expertise for personal reasons.

### 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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