

EVALUATION REPORT OF THE UNIT
GEMS – Génomique évolutive, modélisation et
santé

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Institut Pasteur Paris,
Centre national de la recherche scientifique –
CNRS

EVALUATION CAMPAIGN 2023-2024
GROUP D

Rapport publié le 03/04/2024



In the name of the expert committee¹ :

Marcus Thomas Pius Gilbert, Chairman of the committee

For the Hcéres² :

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 President of Hcéres.

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

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

MEMBERS OF THE EXPERT COMMITTEE

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Mr François Criscuolo. CNRS. Directeur Adjoint Scientifique de l'Institut Ecologie et Environnement
Mr Patrick Trieu-Cot. Institut Pasteur

CHARACTERISATION OF THE UNIT

- Name: Génomique évolutive, modélisation et santé
- Acronym: GEMS
- Label and number: UMR 2000
- Composition of the executive team: Lluís QUINTANA-MURCI

SCIENTIFIC PANELS OF THE UNIT

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

THEMES OF THE UNIT

UMR 2000 consisted of 88 staff at the end of 2022, distributed among seven research teams all physically based at the Institut Pasteur, directed by Lluís QUINTANA-MURCI. The unit was created with a unified vision of applying population and evolutionary biology approaches to the study of infectious diseases, from the perspective of the biological diversity of mammal and insect vector hosts and their infectious agents. Common to these areas are a focus on adaptation, interactions between the host and infectious agents, and the study of population dynamics, and a use of diverse tools including genomics, post-genomic approaches, bioinformatics, statistics and modelling. An additional common goal is the translation of the findings through collaboration with a diverse set of parties for use in mitigating the impacts of infectious diseases on human health.

The seven research teams and their leaders are as follows.

HEG – Human Evolutionary Genomics (Lluís QUINTANA-MURCI), studying the genetic and evolutionary factors related to human disease susceptibility

IVI – Insect-Virus Interactions (Louis LAMBRECHTS), studying mechanisms of arbovirus transmission between mosquitoes and humans

EEAP – Ecology and Emergence of Arthropod-borne Pathogens (Anavaj AAKUNTABHAI), studying the pathogenesis of arboviruses (dengue) and vaccine development

MMID – Mathematical Modelling of Infectious Diseases (Simon CAUCHEMEZ), developing and applying statistical methods and mathematical models to study drivers and dynamics of outbreaks

MP – Microbial Paleogenomics (Nicolas RASCOVAN), studying how human pathogens and commensal microbes emerge and spread and evolve over human history, with a particular focus on South America

GGIV – (Kenneth VERNICK), characterising host-pathogen interactions during pathogen infection of mosquitoes.

MM – (Françoise DROMER), profiling invasive fungal infections in France

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

UMR 2000 was formed in January 2018, principally deriving from the prior unit URA3012 'Hosts, vectors and infectious agents: Biology and dynamics'. This prior unit was created on 01/01/2007. In August 2014 the management of URA3012 was taken over by Lluís QUINTANA-MURCI, who has directed UMR2000 since its creation. Initially consisting of six research teams, the unit was expanded to seven in 2020 with the creation of the Microbial Palaeogenomics team. While each of the different units have a distinct research focus, their research is united with regards to an ultimate mission that they describe as to 'Explore genetic and phenotypic diversity of organisms, across a range of complexity, their interactions and evolutionary patterns in the context of ecology, health and infectious disease'.

The unit is affiliated with INEE (primary) and INSB (secondary) under the scope of CNRS committee 29, and is physically based at the Institut Pasteur Paris Campus, distributed among four buildings. HEG, IVI, EEAP, and MMID teams are based in the Jacob building; MP in the Yersin building; GGIV team in the Sergent building and the MM team is based in the Duclaux building.

RESEARCH ENVIRONMENT OF THE UNIT

The seven research teams of UMR2000 are affiliated to five scientific departments of the Pasteur Institute. The HEG and MP teams are part of Genomes and Genetics; the EEAP and MMID teams are part of Global Health; the IVI team is part of Virology; the GGIV team is part of Parasites and Insect Vectors; and the MM team is part of Mycology.

Other key affiliations include the following.

HEG co-leads, and EEAP and MM are part of, the LabEx Milieu Interieur program, that is exploring what drives immune variation and disease risk in humans.

Six of the teams (all except MP) belong to the LabEx Integrative Biology of Emerging Infectious Diseases, that while based at the IP campus, involve partnership with Institut Cochin, Hôpital Necker, Hôpital Georges Pompidou,

Santé publique France, École Nationale Vétérinaire de Maisons-Alfort and Agence Nationale de Sécurité Sanitaire de l'Alimentation, de l'Environnement et du Travail. The aim of this program is to develop a structure to anticipate and tackle emerging infectious diseases

Three of the groups HEG, MMID, GGIV belong to Institut Carnot Pasteur Microbes & Santé, which exists to research applications and transferring technological solutions to industry.

Three of the teams, HEG, MMID, EEAP belong to Institut Convergence for the study of Emergence of Pathology through Individuals and Populations, that aims to develop a core structure to mobilise data resources, numerical sciences, and fundamental experimental biology in a range of health issues.

The MM hosts the French National Reference Center for Invasive Mycoses which interacts with Santé publique France to investigate the emergence of new pathogens or outbreaks of rare fungi.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	6
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	8
Chargés de recherche et assimilés	8
Personnels d'appui à la recherche	33
Sous-total personnels permanents en activité	56
Enseignants-chercheurs et chercheurs non permanents et assimilés	11
Personnels d'appui non permanents	0
Post-doctorants	18
Doctorants	11
Sous-total personnels non permanents en activité	40
Total personnels	96

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

Nom de l'employeur	EC	C	PAR
INST PASTEUR PARIS	1	12	32
AUTRES	6	1	0
CNRS	0	2	1
Total personnels	7	15	33

GLOBAL ASSESSMENT

The global performance of the GEMS Unit is outstanding. During the evaluation period, they performed state-of-the-art research that draws on a wide range of skills, with a principal focus on applying population and evolutionary biology to the study of infectious diseases and their consequences on their hosts. As such this overall objective aligns well with the general goals of their two supervising bodies, i.e. the Institut Pasteur and the CNRS Institute of Ecology and Environment.

Through the application of their methods to a wide range of study systems, from ancient and modern humans, to invertebrate vectors, to bacterial, viral and fungal pathogens, and thanks to the outstanding, and without doubt world-class quality of the scientific as well as administrative resources available to the unit, the scientific outcomes of the unit's seven teams are outstanding. For example, in the assessed period they published 462 papers, four books and four chapters spanning areas as diverse as population genetics, evolutionary biology, and health and disease biology. In addition to publishing in the most well-read discipline-specific journals (e.g. *Molecular Biology & Evolution*, *Nature Medicine*, *PLoS Pathogens*), they have also published 44 research articles in the very best journals (e.g. multiple papers in *Cell*, *Nature*, *Science*). Naturally, such a wealth of high-profile research means it is challenging to identify any singular highlight. However key representative papers that embody the depth, cutting-edge, and outstanding nature of their research include Choin et al.'s (2022) paper in *Nature* revealing new insights into the peopling and subsequent adaptation of Oceania, Aubry, et al.'s (2020) paper in *Science* revealing the genetic basis of Zika susceptibility of invasive *Aedes aegypti* populations, and of very local relevance, Salje et al.'s (2020) paper in *Science* that provided detailed insights into the burden of SARS-CoV-2 in France are excellent examples.

Additional evidence of the quality of their research is evidenced through their attraction of over 19 M€ in external funding, representing both French and International sources, including two ERC StG awards to the more junior members. The attractiveness of the unit is also clearly attested through the number of awards and honours gained by their staff, including elections to the Academy of Sciences as well as the CNRS Bronze medal, appointment at the Collège de France, and participation in the COVID-19 Scientific Committee that advised the French government.

The functioning of the unit is excellent. Each of the constituent teams performed collaborations with at least one other team, with 5% of the published papers (22) resulted from inter-team collaborations – a figure that is anticipated to increase in light of upcoming changes in the unit structure following the retirement of two team leaders and the inclusion of a new team.

Despite at heart being a unit whose focus is on evolutionary biology, team members have not neglected the broader contribution to society, at a level that can overall be described as outstanding. From the more applied context, this includes an excellent contribution focused on the development of dengue virus vaccines, as well as outstanding contributions in both France and abroad to teaching, outreach, collaborating with health departments and teams and playing a major role in the mapping and building of a public understanding of the COVID-19 pandemic.

In conclusion, the Unit is an outstanding example of the best science being performed by a diverse and energetic team, and is a credit to both the Institut Pasteur and the CNRS.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The unit has not previously been assessed in its current structure – rather the previous report was at the level of the Department of Genomics and Genetics. Thus only some of the recommendations raised were relevant, and these have been identified by UMR 2000 to relate to three areas:

- (i) improving the transfer of knowledge with regards to commercial/industrial activities,
- (ii) Addressing the gender balance skew
- (iii) and more emphasis on societal impact.

Comments on the three points follow.

Improved transfer of knowledge/commercialisation – Relatively little action has been taken in this context, with only ca 0.8% of their income derived from such activities. UMR 2000 make the valid argument that this relates to their principal focus on basic science and that commercialisation lies outside of their key focus.

Gender balance skew – UMR 2000 have taken considerable steps to help address this, for example introduction of equality and diversity policy in all units. This has resulted in a balanced result at the overall staff level. Nevertheless the unit notes that some imbalance exists at the postdoctoral level (43%) and significant imbalance exists at the level of team leaders (only 1/7 are female). As it stands, this latter ratio will worsen in the near future, given the retirement of two of the team leaders (Françoise DROMER (MM team leader) and Kenneth VERNICK (GGIV team leader). UMR 2000 state the intention of hiring a new team leader in the near future (Etienne SIMON-LORIERE), which will therefore bring the team leader ratio to 6 males and 0 females). On the positive side, one I/II junior scientist was awarded both a L'Oreal UNESCO award for Women in Science and ERC StG grant recently, and it is anticipated she will be poised to enter a leadership role in the near future.

Emphasis on importance of societal impact – UMR2000 have taken significant actions in this regard, in particular through overall expanding public engagement activities, and involving more junior team members in the process. Principally this has been achieved through teaching, websites, radio and TV interviews, popular science, podcasts, outreach to primary and high schools. Furthermore, the unit's dedicated webpage about the relevance of their research to the SARS-COV-2 pandemic was timely and a useful resource over the past years.

B – EVALUATION AREAS

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

Assessment on the scientific objectives of the unit

The overall assessment on the scientific objectives of the unit is outstanding. The unit is leading research at the forefront of population and evolutionary biology to better understand infectious diseases. The unit research plays a very important role in advising public health organisations concerning infectious diseases as demonstrated during the COVID pandemic for instance.

Assessment on the unit's resources

The overall assessment on the unit's resources is outstanding. The unit benefits from the unique environment proposed by the Pasteur Institute, in terms of space, equipment, human resources, administrative assistance and scientific environment. Over the period the unit teams manages to secure a high level of funding to pursue their scientific objectives.

Assessment on the functioning of the unit

The overall assessment on the functioning of the unit is excellent. While the overall gender balance in the unit is 50%, there is a lack of women with high responsibilities. The human resource management is excellent with a high level of progression of the staff and an easy access to training. In terms of ethics, the units follows regulation policies such as Nagoya protocol and the declaration of Helsinki. The unit is also involved in controlling and reducing the environmental impact of its research.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The main objective of GEMS is to decipher how infectious diseases spread spatially and temporally, taking into account the biological diversity of hosts and infectious agents. This major objective is in agreement with the general goals of both the Institut Pasteur and the CNRS institute of ecology and environment, the two major supervising bodies of GEMS. Regarding the recent pandemic, and spread of infectious diseases, it seems obvious that the scientific objectives of GEMS are in line with global needs for public health.

While the seven teams of GEMS have diverse and specific research interest, they all set scientific objectives which aim at improving human health. To do so, several teams are working closely with public health agencies or local communities: EEAP, MMID, MP and MM for instance.

These common goals among the teams can also be illustrated by collaborations within the unit, producing 22 articles published in scientific review over the 2017–2022 period involving several teams of the unit.

Finally, the relevance of the research objectives of the unit is confirmed by the very high amount of publications produced during the evaluated period with 462 papers, four books and four chapters.

Weaknesses and risks linked to the context

No particular weaknesses are notes in terms of scientific objectives.

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 part of the Institut Pasteur and thus benefits from its resources in terms of Human Resources, more than 80% of the permanent personnel present during the 2017–2022 period were recruited by the Institut Pasteur. Additionally, the ratio of ITA/researcher per team is pretty unique. As part of Institut Pasteur, the unit also benefits from the scientific environment with the involvement of all the teams in different transversal structures and centers, such as: The LabEx 'Milieu Intérieur' co-headed by the HEG team, the LabEx IBEID which involves 6 of the unit teams, the 'Institut Carnot Pasteur Microbes & Santé' which includes the HEG, MMID and GGIV teams, the INCEPTION project which includes the HEG, MMID and EEAP teams, and the 'French National Reference Center for Invasive Mycoses' which is hosted by the MM team. Finally, the unit has access to a wide range of technological tools, expertise and development such as 'omics, imaging, cell sorting and phenotyping, microfluidics, 3D cell culture, etc., and to multiple online resources through the 'Scientific Resource Center'.

Weaknesses and risks linked to the context

The actual and future repartition of the unit teams in separate buildings of the Pasteur institute could be an obstacle to facilitate the inter team interactions.

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

As part of the Institut Pasteur, the unit is committed to the European Charter for researchers which aims at improving recruitment practices, employment and working conditions, facilitating mobility, and developing career prospects. The unit is following the Gender Equality Plan implemented by the Institut Pasteur, to tackle gender inequalities and imbalances in research. In this context the teams of the unit prioritise diversity and gender balance among their staff.

Concerning ethics, the unit policy complies with the Nagoya protocol for field collection of biological samples, and has set a data management plan for data storage and sharing. For genetic studies, the unit follows ethical principles complying with Declaration of Helsinki, European directives and international declarations on human genetics data. The teams developing computational analysis are distributing their codes online to ensure they are freely available, and most of the teams are releasing their publications early as preprints, to ensure easy access to their results. Experiments with live infectious agents or genetically modified mosquitoes are following strict protocols to ensure containments and personal protection.

The unit also follows the Institute Pasteur Policies to prevent environmental risks. It implies regular controls on the water use, promotion of more sustainable mobility and energy sobriety, procedures for waste management, a prevention and eco-design plan to reduce the use of unrennewable resources, improvement of the biodiversity, etc.

Weaknesses and risks linked to the context

Despite the implementation of policy of gender balance, the number of women in leadership positions is still low, with only one woman among the seven team leaders during the period assessed period. For the new period, there will be no female team leaders at all in the unit. This gender imbalance was also noticed in the previous evaluation.

With the accumulation of structures (Pasteur Institutes Pasteur departments and CNRS unit), it seems that there is not a real feeling of belonging to the unit. A major part of the staff report that they do not really know people who work in teams other than their own one in the unit, or how to handle conflictual situations at the unit level. It could be beneficial at different levels to promote more cohesion and mediation at the level of the unit.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The overall assessment of attractiveness of the unit is outstanding. The teams of the unit are well known both nationally and internationally for their contributions to the understanding of the genetic and immunological factors influencing the susceptibility to infectious diseases, the transmission dynamics of viruses and the development of vaccines and treatments for these diseases. The attractiveness of the unit is attested from the numerous awards and honors such as the election at the Academy of Sciences, or the CNRS bronze medal and competitive grants such as ANR and ERC grants obtained by the members of the units during the evaluation period.

- 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 scientific reputation of the unit is attested by the achievements of the different teams and the awards received by their leader, like the appointment as Professor at the Collège de France and election at the French Academy of Sciences in 2019, the CNRS Bronze Medal in 2018, the Duquesne Prize in 2017, the Thérèse Lebrasseur Prize in 2017. In addition, the unit participates in the organisation of various academic training programs (more than 8 weeks per year) and all team leaders regularly give lectures at national and international courses.

The unit is using a convincing procedure for the integration of incoming staff. The attractiveness of the unit is attested by the recruitment of seven permanent researchers during the evaluation period (2 CR CNRS and 5 CR Pasteur) as well as the number of postdocs (54), PhDs (35) and interns (30) trained during the evaluation period.

The acquisition of around 19M€ by the unit during 2017–2022 is impressive, and consistent across time (3M€ per year). It is remarkable that almost 80% of these funds are obtained from competitive calls including international grants outside Europe (NIH, EMBO), two ERC Starting Grants and numerous ANR grants.

The funding of new equipment is discussed at the scale of the Pasteur Institute with the Technology Directorate and the scientific departments to ensure a fair distribution. Replacement or repair of out of order equipment is discussed regularly five times a year within a rejuvenation committee.

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

The gender bias among the team leaders is potentially altering the attractiveness of the unit for women in science. Perhaps a more explicit presentation of the strategy used for the recruitment of new team members and new teams in the unit could improve the functioning of the unit and make it more attractive.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The overall assessment of the scientific production is outstanding. The Unit has produced a significant and sustained body of scientific research between 2017 and 2022. This includes 462 peer-reviewed articles, one book, and four book chapters. A healthy proportion of publications were impactful and often published in the most prestigious scientific journals. The work spans several research areas including population genetics, evolutionary biology, health ecology, and infectious disease biology. The unit has adequate procedures in place as concerns research ethics, open science and best scientific practice.

- 1/ The scientific production of the unit meets quality criteria.*
- 2/ The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.*
- 3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.*

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

The unit produced 462 publications in the period consisting of 2017–2022. Even though the unit is fairly large, with over 250 members of staff, including 52 doctoral students, this nevertheless represents a healthy scientific output. This includes high-profile publications, including two in *Cell*, three in *Nature* and eight in *Science*. Furthermore, the publication output has increased significantly during the period evaluated (2017–2022), with an overall doubling of the number of publications yearly, from 36 in 2017 to 77 in 2022. This positive trend did not come at the cost of reduced quality. There is a fairly good balance of publication between research teams. All teams have been scientifically productive over the period evaluated.

Some particularly impactful work was performed on SARS-CoV-2, including probably the best study age-specific mortality of COVID-19, as well as a study exploring genetics manipulation of mosquitoes to control arboviruses, and important contribution to human evolutionary genetics.

The work complies with the principles of research integrity, ethics and open science, and the unit has place adequate safeguards and protocols to ensure best scientific practice in science, in terms of reproducibility transparency and ethics.

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

The unit has considerable research breadth with expertise in several fields of research. There may be a missed opportunity to perform interdisciplinary research at the interface of those themes (e.g. integrating human and pathogen genetics in single projects).

The unit seems to function primarily as a collective of largely independent teams. There may be potential to develop further synergies between research themes and field covered by the unit.

It is not obvious from the self-assessment document, to what extent the unit is involved in the generation of methods and software that can be applied by other researchers.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The overall assessment on the contribution of research activities to society is outstanding. The unit is involved in knowledge dissemination giving regular lectures to 'Collège de France' or participating to actions like 'Apprentis chercheurs'. The unit work has the major societal through interactions with various public health agencies, or the government to help improve public health, as experienced during the COVID pandemic. The unit is also strongly involved in the V4C start-up which aims at producing vaccines against dengue.

- 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

Several teams of the unit have partnerships with the non-academic world. For instance, the EEAP team work with local public health teams and Departments of Health at the central level. The MMID team work with public health agencies during epidemics. For instance, during the COVID-19 pandemic this team played an important role to support the French government policies producing more than 140 reports and publications. The MM team hosts the National Reference for Invasive Mycoses, and works with Santé Publique France in this respect.

In particular, the EEAP team which has previously developed patents for vaccines against Zika and Dengue virus, participated in 2020 to the creation of the start-up V4C: Vaccine For Communities. This company aims at developing a paediatric vaccine against dengue and to launch clinical trials to make it accessible.

The unit is involved in the field of research dissemination to general public. For instance, the HEG team participates in radio or TV interviews, teaching at the Collège de France, or in activities in primary and high schools. The IVI team is involved in the Apprentis Chercheurs program. The EEAP team works with communities to understand their practices about dengue and involve schools and school children in citizen science projects. The MMID team has constructed a dedicated webpage to present their research on COVID-19 to the general public. Even if research dissemination and valorisation represent only 10% of the unit profile, the societal impact of its actions is very high.

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

No particular weakness is noted in this field.

ANALYSIS OF THE UNIT'S TRAJECTORY

The unit is relatively dynamic, given both the retirement of two team leaders (VERNICK and DROMER), as well as the future inclusion of a new team (SIMON-LORIERE). While naturally the retirement has resulted in the termination of research in two areas, given SIMON-LORIERE's prior collaborations with certain teams in the Unit, overall it is to be expected that this future configuration will serve to bind the teams closer together. This in turn should serve to increase the overall feeling that the Unit is a unified research body – something that will help ameliorate the concerns raised by staff at the lower levels of the Unit that they do not identify particularly strongly as part of a Unit. Additionally, while it is unfortunate that the retirement of DROMER serves to remove the single female team leader, the presence of several high-profile female junior staff, who are actively building their own groups can be hoped to ultimately ameliorate this challenge. An additional change in the next period relates to the handing over of the Unit's leadership, from QUINTANA-MURCI to LAMBRECHTS. Although this could in theory result in major consequences to the structure and functioning of the Unit, it is the committee's impression that there is considerable overlap between the management philosophies of both researchers, both regards to what scientific topics are relevant to the Unit, but also how to balance for example meeting research goals with empowering the scientific development of their staff. As a result of this, and conversations had with LAMBRECHTS during the evaluations relating to concrete solutions to some of the challenges the Unit faces, it seems likely that the Unit's success will not only continue, but grow.

RECOMMENDATIONS TO THE UNIT

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

The committee recommends that the Unit apply effort aimed at creating an improved feeling of belonging among the personnel within the Unit. For instance, the Unit could encourage students and post-docs, and the PAR to organise dedicated social/scientific events for their groups. The committee also recommends that the Unit ensure that their monthly meeting transitions to in person as opposed to the online mode used now, to allow unit staff to meet and to have more interactions.

The committee also recommends major efforts are taken to improve the gender balance at the level of the team leader positions. Supplementary efforts should be engaged to recruit women for the new teams to join the unit.

Finally, the committee suggests that the unit considers a discussion with the Pasteur Institut to promote the creation of an ancient DNA laboratory, to facilitate the access, and improve efficiency both at the level of the unit and the institute.

Recommendations regarding the Evaluation Area 2: Attractiveness

The only point that the committee would like to reinforce to improve attractiveness of the unit is to strengthen again the policy to recruit more women at leading position.

Recommendations regarding Evaluation Area 3: Scientific Production

It is clear that overall the scientific production of the Unit is world class. Nevertheless, given that only about 5% of the published papers in the evaluated period involved the participation of more than one team, the committee recommends that the team leaders take steps to initiate more inter-team projects in the next period, so as to validate their grouping together as a Unit. Additionally, while the committee also accepts that the focus of the unit is fundamentally related to the study of basic evolutionary questions, any future attempts to translate additional findings to the applied context can only serve to boost the Unit, not only through the acquisition of additional resources, but also to elevate their reputation in the international research community.

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

The committee has no specific recommendations to the unit concerning this area.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Human Evolutionary Genetics (HEG)
 Name of the supervisor: Lluís QUINTANA-MURCI

THEMES OF THE TEAM

The team's principal aim is to characterise the impact of demographic and selective forces on the patterns of genome variation at the population level. This is done by first, exploring the demographic parameters characterising human populations, mainly African hunter-gatherers and farmer groups, as well as Pacific populations. Secondly, by exploring the action of selection on human genome diversity. Thirdly, characterise the contribution of genetic, epigenetic, and environmental factors to immune response variation, with a major goal of mapping genetic determinants of gene expression variation following immune activation.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report raised three recommendations directly relating to this team. The first was a fuller adoption of social media to disseminate the team's work. In this regard the team has been active at the level of different staff members, and notably they should be commended on the development of a detailed strategy for the results to the local communities.

The second was exploration of the data generated, e.g. that on immunomodulation, in therapeutic approaches. This has received little attention in the assessed period, which could reflect the team's principal focus on basic research. Nevertheless, it remains an interesting option to consider.

The third was whether the groups reliance on big data would be challenged by in house limitations of infrastructure (data generation or computational). This does not seem to have become an issue, thanks to investments in e.g. computational infrastructure at both the Institut Pasteur level, as well as locally in 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	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	9
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	4
Doctorants	2
Sous-total personnels non permanents en activité	8
Total personnels	17

EVALUATION

Overall assessment of the team

The overall assessment of the team is outstanding. Their scientific production is outstanding, including work published in the most influential journals in their areas (Science, Nature, etc.). The team's visibility is outstanding at the national and international level, as evidenced through grants and awards gained, but also outreach activities including standard media and teaching at the University and College de France, creation of MOOC, books, etc. The team's socio-economic transfer activities are excellent given the context that they work in a fundamental research area.

Strengths and possibilities linked to the context

The team is formed by seventeen people (11 nationalities), eight of which are non-permanent (4 postdocs, 2 PhDs), representing a broad range of complementary expertise including experimental scientists and computational biologists, who both develop new, and use state of the art, techniques. Notably in light of their data-driven research they also have one data engineer who is critical for data management as well as appropriate storage, dissemination to others, etc. As such they have developed a Data Management Plan describing for each project the management and lifecycles of the data generated. They have also developed a detailed strategy for sampling and dissemination of human data ensuring ethical compliance and consent at all levels, and embracing knowledge transfer to, and capacity building in local partners.

The team has had an excellent productivity in the period, consisting of 63 original articles as well as seventeen reviews and comments, three books, three book chapters. These include papers that the team has lead in the most influential journals in their areas, including *Science*, *Nature*, *Current Biology*, *PNAS*, *Nature Immunology*, *Nature Ecology and Evolution*, *Nature Communications*, etc.), and include several major reviews led by the team. Their diverse research derives from collaborations at different scales, including intra laboratory and Institute, but also international (teams representing 45 countries). Funding this productivity relies on an excellent grant success, with 3.753k € raised. These include 4 National Research Agency grants as coordinator, as well as grants from FRM, FdF, FA, National Geographic society. The team has also participated in one EU funded consortium, the COVID-19 Human Genetic Effort, and the Chan Zuckerberg initiative collaboration on African Ancestry Immune Cell Atlas. The team has also co-led LabEx Milieu Interieur consortium (2011–2024).

The team is committed to outreach and development of the next generation. They perform considerable dissemination including TV, radio, College de France lectures, popular science articles, and even a book in French with Spanish and English translations. Two team members have also been involved in primary and secondary school outreach. Beyond the conventional media appearances, this includes at the team level enforcing a rule of at least one major first authorship for PhD students and Postdocs, the encouragement of junior scientists to obtain their own funding and lead their own projects, and the mandating of attendance of one international conference per year. Overall six PhD students and twelve postdocs have been trained in the evaluation period, with most subsequently entering tenure track academic or industry positions. At the wider level the team is active in teaching and training in population genomics, evolutionary genetics, genetic epidemiology, organising three courses (at IP, Collège de France, Université Paris Cité) and a MOOC in evolutionary genetics that has attracted 2252 learners from 87 countries.

Weaknesses and risks linked to the context

While the team has no major weaknesses, several considerations can be raised that can be linked to their success at creating new research projects, sample collecting, data generation, and indeed training of the next generation of researchers.

Given their reliance on human bio-samples, there is a natural risk related to local or global modifications in laws relating to the collection, storage and use of samples. Thus, while the team has taken all the necessary steps needed to ensure that current samples were obtained following all guidelines, they will need to ensure they maintain a close watch on developments in relevant legal frameworks pertaining to these samples. Similarly potential risk exists with regards to the security of human data – to ensure it is not obtained and thus abused by parties who should not have it. In this regard a major benefit relates to the team's data scientist, as well as the clear thought that has been put into their data management plan.

Other considerations that could be perceived as a potential weakness include the following. Firstly, given the high status and scientific reputation of the team leader (not least his Professorship and Chair in Human Genomics and Evolution at the Collège de France and French Academy of Sciences), a natural risk is that the excellence of those working under him in the team may be overlooked by external parties, seeing them as an extension of the leader rather than an excellent scientist in their own right. A second one relates to the team's diversity – while excellent to see eleven nationalities represented, it is not clear if any represent the regions of scientific focus, the inclusion of which would be both of relevance with regards to knowledge transfer but help future-proof research on those populations. The third relates to the recommendation of the prior reports and the team's minimal focus on valorisation of the findings. While it should be appreciated that it is not the role of all teams to include applied research elements, ultimately doing so would not only benefit society, but could open interesting and relevant research funding streams.

Analysis of the team's trajectory

The team outlines three major research areas that are rooted in their current expertise, yet represent natural expansions into new research areas through incorporation of new datasets and tools. Two of these involve expansion of their interest in the neglected human populations of remote Oceania and the Amazonian rainforest, and relate to the integration of genetic, epigenetic and accessory data (e.g. indicators of immune response). The data generated will be relevant for deciphering how demography has shaped the populations in light of extreme demographic, environmental, and pathogen exposure, thus reveal more about both human evolution but also how our genome is shaped, and how we in turn shape our pathogens. These studies are state of the art, well planned, and rely on access to unique datasets, and thus likely to be able to attract considerable

interest from not only research funders, but the scientific community and the general public. The latter is ensured thanks to the well-developed sampling and dissemination plans already in place in the team.

The third project involves state-of-the-art single cell approaches to study population variation in immune responses to RNA viruses, with a key focus on how ancient admixture and natural selection have impacted immune response variation to SARS-CoV-2 and RNA viruses more generally. Here the combination of scRNA-seq and sn-ATAC-seq on experimental data with the population genetic and other evolutionary analyses that the team are known for is fascinating and will if successful attract considerable attention.

Overall given these plans plus the team's existing laboratory a computational resources, their active roles in teaching and dissemination, other initiatives, and their track record in producing valued Postdocs and PhDs, indicates they will continue to sit at the forefront of human evolutionary genomics.

RECOMMENDATIONS TO THE TEAM

Overall the team's performance is excellent, and few weaknesses can be raised that are a serious challenge to their progress. Naturally given the team's intended future focus on continuing to work with datasets generated from non-European human populations, it will be critical that they closely monitor any development in the legal and/or ethical frameworks relevant to their work, as well as ensure their safety of their sensitive human data. While the team already has excellent capacity building in place so as to transfer knowledge back to the communities with whom they work, the team is encouraged to find ways to include participation of scientists from such communities directly within the team. Also at the local level, any additional actions that can be taken to ensure that excellence profile of team leaders is not missed/diminished in light of the excellence of the leader should be considered. Lastly, the team is encouraged to reassess whether any of their results can be commercially leveraged on, either directly or in collaboration with other entities.

Team 2: Insect-Virus Interactions (IVI)

Name of the supervisor: Louis LAMBRECHTS

THEMES OF THE TEAM

The team's aim is to investigate the mechanisms underlying the transmission of arthropod-borne viruses (arboviruses) among humans by mosquitoes. Their general strategy involves interrogating natural variation in mosquito vectorial capacity to elucidate the underlying mechanisms, employing an integrative approach that combines genomics, quantitative genetics, and evolutionary biology methods.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Very few recommendations had been formulated during the previous evaluation. It mainly involved encouraging the team to secure research projects as the principal investigator. This aspect has been largely achieved with several competitive projects led by different team members.

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	6
Sous-total personnels permanents en activité	8
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	3
Doctorants	2
Sous-total personnels non permanents en activité	5
Total personnels	13

EVALUATION

Overall assessment of the team

The overall assessment of the team is outstanding. IVI team has garnered international recognition in the field of mosquito arbovirology and has significantly contributed to understanding the emergence of zoonotic viruses, particularly the Zika virus, in human populations. The team's scientific excellence is further highlighted by securing highly competitive funding, including an ERC Starting Grant, and receiving prestigious honors such as the bronze medal from CNRS.

Strengths and possibilities linked to the context

The team enjoys national and international recognition in the field of mosquito arbovirology. One of the strengths of this team lies in its ability to address scientific questions through the use of biologically realistic models (field mosquitoes & low-passage viral strains) combined with innovative approaches.

The IVI team has a strong publication record, with 56 peer-reviewed articles published from 2017 to 2022. Notably, they have demonstrated an increasing trend in the quality of their publications, including leadership roles in prestigious journals such as Science, Current Biology, Nature Communications, and PLoS Biology between 2020 and 2022. Most of their publications are primary research articles (48), complemented by opinion papers and reviews (8) in respected scientific outlets like Trends in Immunology and Cell Host & Microbe. The team's research contributions are led by both the team leader (25 research articles as senior author), and junior permanent scientists (6 publications as lead author).

One of the studies of the IVI team provides a significant contribution to understanding the emergence of zoonotic viruses in the human population. This research reveals that *A. aegypti*, a major arbovirus vector, specialised in biting humans and also enhanced its ability to acquire and transmit the Zika virus. This discovery highlights the role of vector evolution in arbovirus emergence, making it a major study (Aubry et al., Science 2020). Another study illuminates a critical aspect of Zika virus research, demonstrating that recent African strains possess a significantly higher transmission capacity and greater fetal pathogenicity in comparison to their Asian counterparts. This groundbreaking finding not only deepens our understanding of Zika virus dynamics but also underscores the urgency of monitoring and addressing the potential epidemic threat posed by African Zika strains. The implications of this study cannot be overstated, as it highlights the need for vigilant public health surveillance and further research to mitigate the risks associated with these strains, making it a seminal work (Aubry et al., Nature Comm 2021).

In addition to the outstanding scientific production, the team has secured highly competitive funding, including an ERC Starting Grant and four ANR grants (1 JCJC & 3 PRC). During the evaluation period, the team managed to raise close to 4.5 M€ in research grants, with more than 80% of the funding coming from external sources, which is excellent.

During the period, five postdoctoral researchers secured positions in academia, either as faculty members or research engineers, underscoring the exceptional track record of the IVI team. The team's attractiveness is also attested by the recruitment of two junior CNRS researchers in recent years. Furthermore, several team members have received prestigious honors, including the bronze medal from CNRS. These achievements underscore the team's excellence.

Weaknesses and risks linked to the context

A minor aspect that could be improved is the limited number of researchers holding a Habilitation à Diriger les Recherches (HDR) qualification, which is currently quite limited.

Analysis of the team's trajectory

The IVI team's research program for the next five years aims to investigate mosquito-arbovirus interactions, focusing on mosquito genetics, viral genetics, host-mosquito-virus interface, and infected mosquito behaviour to understand the molecular mechanisms underlying natural variation in arbovirus transmission. It is a continuation of the ongoing work of the team and is divided into four projects with relevant and original research questions.

The first project aims to establish a genetic panel of inbred lines for *Ae. aegypti* to investigate the genetic and non-genetic components of microbiota and vectorial capacity. This panel will facilitate quantitative genetic analyses, identify genetic factors related to microbiota and vectorial capacity, and serve as a valuable resource for the research community.

The second project aims to uncover the genetic factors influencing ZIKV transmissibility by creating hybrid viruses from high-transmissibility African ZIKV (Senegal_2011) and low-transmissibility Asian ZIKV (Thailand_2014) strains, followed by testing their transmission in mosquitoes and mice. This research seeks to understand why African ZIKV strains are more transmissible by mosquitoes than Asian strains, offering insights into ZIKV infection mechanisms and aiding the development of prevention strategies and vaccine candidates.

The third project aims to characterise the inhibitory effect of HDL and LDL on DENV acquisition by *Ae. aegypti* mosquitoes. Understanding how blood metabolites affect mosquito infection may lead to strategies for reducing DENV transmission and assessing the impact of drugs on transmission. This research involves confirming the effect of lipoproteins on DENV acquisition, investigating their impact on mosquito physiology using 'omics' technologies, and exploring the functional role of mosquito genes and microbiota in lipoprotein-mediated effects on DENV infectiousness. This project is a good example of an inter-team project within the unit.

The fourth project aims to (i) characterise the long-term effects of arbovirus infection on *Ae. aegypti* activity patterns, (ii) assess the impact of arbovirus infection on host-seeking behaviour, and (iii) model the flight-based behaviours of infected mosquitoes in response to host cues. This involves developing novel behavioural assays, utilising custom-built hardware and computer vision techniques, followed by statistical modelling to understand the influence of arbovirus infection on mosquito behaviour.

The team's expertise, infrastructure, and the fact that most of the projects are already funded guarantee their success.

RECOMMENDATIONS TO THE TEAM

The team's success and strong recognition in its area of expertise make it highly advisable to continue along this path.

Team 3: Ecology and Emergence of Arthropod-borne Pathogens (EEAP)

Name of the supervisor: Anavaj SAKUNTABHAI

THEMES OF THE TEAM

The team focuses on the study of the pathogenicity and the control of dengue. The first axis of the team is the development of a vaccine based on T-cell associated protective immunity. The second axis is the study of dengue disease pathogenesis and the physiological and immunological determinants leading to classical fever or severe dengue. The third axis focuses on vector control through the auto-dissemination of pyroproxyfen against *Ae. aegyptii*, while the team's expertise in arthropod-borne pathogens extends to various tick-borne diseases and malaria.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous evaluation of the team (formerly Functional Genetics of Infectious Diseases team) led to several recommendations. The first one highlighted that few high-impact studies were actually led by the team. In this regard the team successfully obtained EU funding to lead a consortium to tackle the major lacunae in our understanding of dengue. In addition, the team coordinates a large NIH-funded consortium to study the transmission, adaptation of RNA viruses in South-east Asia and West/Central Africa.

Second, the previous evaluation noted the variation among team members with regards to leadership and the reputation. All the permanent researchers of the team develop their own research projects, obtain specific fundings and supervise students. These projects extend the scope of the expertise of the team to other arthropode-borne pathogens like tick-borne diseases and malaria.

Third, a relative lack of involvement in interaction with the social, economic and cultural environment. The field work on dengue, however, yields multiple interactions with local public health services and has a direct impact on local communities, in particular in the Philippines. The extension of the unit with Japan may also offer interesting opportunities for multidisciplinary collaborations with economists and social scientists in Tokyo.

Fourth, training through research should be expanded at the PhD level, and students should publish more as first author. In this respect, six students obtained a PhD since 2017 and published at least one publication as first author.

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	4
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	9
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	1
Sous-total personnels non permanents en activité	3
Total personnels	12

EVALUATION

Overall assessment of the team

The overall assessment of the team is excellent. The team visibility is remarkable with the obtention of 24 national and international grants since 2017. The team is involved in many overseas projects including the NIH PICREID consortium in Senegal, Cameroon and Cambodia, as well as a clinical trial in Philippines. The outreach activities are excellent in particular towards local communities affected by arthropod-borne diseases. The socio-economic transfer is outstanding as team's research impacts directly local societies and has implications for local public health. The implication of the team in the development of a new dengue vaccine with ModeRNA may have important implications for the control of dengue.

Strengths and possibilities linked to the context

The team is renowned for its expertise at the interface between epidemiology and immunology of dengue. A strength of the team is the scientific network of collaborations developed and maintained over years with several different countries (Senegal, Cameroon and Cambodia, Philippines, Japan). The team has developed an efficient management plan and a rigorous procedural approach to handle data involving human participants from these different countries.

The scientific production refers to 85 publications since 2017 and one co-edited book on public-health and public policy. During the period, eight articles were signed by the team leader as last author in specialised journals, among which two in PLoS Neglected Tropical Dis and one in Frontiers in Immunology.

The team has a high success rate in its ability to fund its research projects, obtaining 24 grants since 2017 (between 347k€ and 581k€ each year): 2/3 of the resources are obtained from national grants, 30% from international grants and 2% from valorisation of the research. The team is involved in many overseas projects including the NIH PICREID consortium in Senegal, Cameroon and Cambodia as well as a clinical trial in the Philippines. In particular, the team is leading the NIH-funded PICREID consortium which involves many different countries across different continents. This kind of consortium is key for the development of more efficient strategies against emerging diseases. The expertise in the study of dengue virus may lead to the development of a new vaccine in the near future which would be a major breakthrough.

Beyond the study of dengue, other projects are emerging on the study of the epidemiology of other arthropod-borne pathogens such as tick-borne diseases and malaria. Besides, several ongoing projects are developing in collaboration with other teams of the unit (MMI and IVI).

Weaknesses and risks linked to the context

Teaching through research and PhD supervision could be increased. The diversity of projects developed within the team is perhaps affecting its productivity. But the committee recognises the ability of the team to generate and coordinate a multiplicity of international collaborations.

Analysis of the team's trajectory

The team highlights four axes of research within the context of emerging RNA viruses. First, the consolidation of the PICREID network funded by the NIH which aims to improve the capacity to respond rapidly and effectively to outbreaks using an intercontinental one-health approach and the establishment of Infectious Disease Center in south-east Asia as well as west/central Africa. In particular, the team is involved in enhancing surveillance and detection of unknown RNA viruses with potential spillover to humans, and understanding transmission dynamics of endemic RNA viruses with high risk of outbreak. Interestingly, this is an opportunity of interactions with the MMID team which is also involved in this network.

Second, the team is aiming to renew the joint Franco-Japanese unit with Kyoto University to study the tick metabolome across different environments to evaluate how different ecosystems may affect vector competence. In addition, the team wants to develop new markers to monitor the risk of exposition to ticks in both humans and animals.

Third, the team plans to study the influence of plasma lipoproteins present in the human blood on the acquisition of dengue virus by mosquitoes. They will combine metagenomics, transcriptomics and metabolomics approaches as well as functional validation of candidate genes with experiments. This axis will be great opportunity to collaborate with the IVI team on the development of novel transmission-blocking strategies.

Fourth, the team wants to carry on its work on the development of an mRNA dengue vaccine eliciting a T cell response against the four DENV serotypes. A development plan of the vaccine has been designed and a start-up was created in 2022. If successful, this new vaccine could be used as stand alone or in combination to improve the protection of naive individuals against the virus. In addition, the team wants to get involve in the battle against CCHF via the development of T cell epitope mapping and sequencing. This new line of research seems in line with the overall aim of the team.

RECOMMENDATIONS TO THE TEAM

The EEAP team is a key element of the GEMS unit because it plays a central role in many international collaborations on the epidemiology of arthropod-borne diseases. The only recommendation of the committee is to transfer this expertise to young researchers and to increase the supervision of PhD students in the future.

Team 4: Mathematical Modelling of Infectious Diseases (MMID)

Name of the supervisor: Simon CAUCHEMEZ

THEMES OF THE TEAM

The MMID team has used mathematical modelling to understand the transmission dynamics of infectious diseases such as influenza and COVID-19. Their research has helped inform public health policies and interventions aimed at controlling the spread of these diseases.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

NA: MMID is a new team

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
Sous-total personnels permanents en activité	6
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	3
Doctorants	2
Sous-total personnels non permanents en activité	7
Total personnels	13

EVALUATION

Overall assessment of the team

The overall assessment of the team is outstanding. The team has produced numerous high-level publications. It has raised significant funds and played an important role in the socio-economic fabric during the pandemic.

Strengths and possibilities linked to the context

The team is formed by ten people (4 permanents, one DR (promoted PR 1/4/2023), three postdocs, two PhD students and 4 engineers), without any CR since the departure of Salje Henrik (Cambridge). The team includes 4 IR, which is a very good point. There is only one HDR in the team. The MMID team utilises the High-Performance Computer Cluster at Institut Pasteur, which includes a dedicated partition for the team (5 nodes, each with 96 CPUs) for effective scientific programming.

The team has an outstanding productivity in the period, consisting of 110 articles. These include papers that the team has led to the most influential journals, including Science, Nature Communications, NEJM. The production appears to be very high in quality reviews.

The team has an excellent grant success with fourteen research contracts for a total budget of about 3 M€. These funds including contracts from the European Union (contribution to 4 European consortium: ZIKAlliance, RECOVER, VEO and DURABLE), US funding (NIH, DARPA) and French funders (ANR, ANRS-MIE, AXA-RF, Santé Publique France as well as private donors). Half of the grants come from international funding: 980k€ with international fundings (no UE), 470k€ with UE fundings, 670k€ with PIA fundings, 730k€ with associative fundings.

The leader was nominated as a member of the COVID-19 Scientific Committee advising the French government at the start of the pandemic, and is now a member of COVARs, the new scientific committee

supporting the French Government. He was nominated Chevalier de l'Ordre National de la Légion d'Honneur (Knight of the French Legion of Honor) in 2022 for the team's contribution to COVID-19 research.

Weaknesses and risks linked to the context

An aspect that could be improved is the limited number of researchers holding the Habilitation à Diriger les Recherches (HDR) qualification, which is limited to the team leader.

Most of the contribution to society was made during the COVID-19 pandemic. The team needs to position itself for the future.

There is a lack of publications in applied mathematics journals. Even if these journals are not widely read in comparison with generalist journals, it is an important aspect towards this scientific community.

Analysis of the team's trajectory

Business was booming at the time of the pandemic. As a result, the team was totally overwhelmed. The team's reputation and its work are outstanding, and the evolution of its scientific output is excellent.

The trajectory of the team will focus on further developing methodological tools as well as implementing experimental aspects, keeping in mind that these two facets of their research contribute to give insight in the analysis of complex epidemic data and feed support to health agencies in their policy making.

One topic in the analysis of complex transmission data to better characterise transmission risk factors will target the household contact patterns; these methods will be then exploited to study dengue transmission in Cambodian households. Methods will be also developed to model and forecasting seasonal epidemics of seasonal diseases such as influenza, Respiratory Syncytial Virus and endemic COVID-19.

One of the experimental projects that the team proposed to carry out is to better understand the complex interplay between the history of infection of an individual, their immune response and risks of subsequent infection. It is planned to characterise antibody landscape of 3,000 individuals sampled in France in 2020–2021 by using a Luminex multiplex diagnostic assay. Statistical analysis will be developed to redefine the individual histories of infection from the antibody patterns. These approaches will be later on extended to other countries.

RECOMMENDATIONS TO THE TEAM

Interactions with other UMR teams are not obvious. Common projects are planned and have yet to be implemented. A joint research policy should be defined and made more systematic.

Similarly, the team's work is almost entirely dependent on the leader. This is a weak point in the event of departure. A human resources policy needs to be defined. Recruitment of staff might be obtained through the INSERM labellisation.

Team 5: Microbial Paleogenomics (MP)

Name of the supervisor: Nicolas RASCOVAN

THEMES OF THE TEAM

The team works on paleogenomics, with a broad research program ranging from evolutionary human genomics, to ancient pathogen genomics and reconstruction of ancient dental calculus microbiomes.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

NA (new team)

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	1
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	4
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	3
Doctorants	2
Sous-total personnels non permanents en activité	7
Total personnels	11

EVALUATION

Overall assessment of the team

The team has joined the Pasteur Institute less than three years ago. Despite challenges caused by COVID-19, the team was able to successfully recruit. The team is well resourced with an ERC grant and Pasteur start-up funding and occupies an area with considerable potential.

The team has a broad and ambitious research portfolio ranging from projects in ancient human genomics, ancient pathogen genomics and ancient microbiome reconstruction. Those projects all sound promising but have not yet led to fruition, with the publication output of the team remaining scarce.

Strengths and possibilities linked to the context

The team has initiated four major research projects, namely:

- 1) Leprosy in the America in pre-Columbian times, with pilot evidence of a yet unknown bacterial agent.
- 2) Analysis of >100 ancient human genomes from South America
- 3) The phylogenomic analyses of 2,800 ancient and modern *Yersinia pestis* (plague) genomes, including half representing new data,
- 4) The characterisation of the oral microbiome of Aboriginal Australians from dental calculus.

All four projects have considerable potential. The leprosy project is probably the most important if it were to be confirmed that Native Americans were harbouring a distinct species of leprosy prior to the arrival of European colonists,

All four projects open the possibility of longer-term follow-up investigations that could turn into sustainable research programs. This being said, they are all in a highly competitive field, and there are other well-funded larger groups that may be making similar progress along those lines.

The goals of the MP team are 1) to investigate at the genomic level how human pathogens emerged and spread in order to better understand the complexity of modern infectious diseases, and 2) to investigate particular events of the human history, for example the importation of agriculture in the Americas by the Europeans colonizers.

The research of the team solicitates a variety of disciplines and approaches: handling ancient DNA and genomics and addressing phylogenomic, evolutionary biology, history, archaeology, and population genetics issues.

The team has been created in September of 2020. It is funded by an ERC Starting Grant (1.5 M€) and by a starting package from Institut Pasteur (~1 M€). Additional fellowships fundings were obtained to host two postdoc (FRM, Marie Curie) and three PhD (Inception, CNRS and PPU).

In 2019, i.e. before the opening of the lab, the PI published in *Cell* an article describing the 'Emergence and Spread of Basal Lineages of *Yersinia pestis* during the Neolithic Decline'. The topic of such study received great interest (<http://nicorascovan.wordpress.com/media-outreach/>). Of note, since 2020, no article has been published in which the PI is a major author.

Weaknesses and risks linked to the context

The team has initiated several ambitious projects in parallel. The limited workforce (capped to a maximum of eight team members) may delay progress in any of them. This is a highly competitive field and there is a risk that the team may get scooped repeatedly. Moreover, even in the absence of external competition, the team may fail to capitalise on their efforts as run out of steam, or fail to allocate sufficient energy and time to any single project to bring it to fruition.

Some of the planned work is in collaboration with Argentinian collaborators. The severe economic crisis this country is currently going through may cause problems.

Analysis of the team's trajectory

Given the recent establishment of the team, it feels premature to analyse its trajectory.

RECOMMENDATIONS TO THE TEAM

The committee was unable to understand from the self-evaluation document at what stage of progress the different projects were at this stage. Should it be the case that none of them were in the process of being submitted, we would recommend the team tries to prioritise them in order of importance and short-term feasibility, and dedicate the necessary energy and resources on one or two of them at this stage.

Team 6: Genetics and Genomics of Insect Vectors (GGIV)

Name of the supervisor: Kenneth VERNICK

THEMES OF THE TEAM

The team's principal focus is the interactions between mosquito hosts and their pathogens (principally Plasmodium and the O'nyong nyong virus, but also the enteric microbiome) during host infection, with a particular focus on the interplay between pathogenesis and mosquito host immunity. Approaches taken principally leverage on linkage mapping and wild pedigrees of natural populations in West Africa, to identify genetic immune mechanisms (including non-coding regulatory elements) for further analysis in the lab context. The team has also examined ways to complement existing vector control tools, and in this regard runs an insectary for mosquito growth, and works in long-term close collaborations in Africa in Burkina Faso, Mali and Guinea.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

This group was not evaluated in the previous assessment on the Department of Genomics and Genetics

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	8
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	0
Sous-total personnels non permanents en activité	2
Total personnels	10

EVALUATION

Overall assessment of the team

The overall assessment of the team is excellent. Team GGIV has an excellent scientific production (20 articles). The team's visibility is outstanding at the national or international level (e.g. ERC AdG) and excellent in outreach activities (including in Africa). The team has less presence in socioeconomic transfer.

Strengths and possibilities linked to the context

The team composition and its trajectory reflect the fact that the team leader aimed to enter retirement in 2023, thus this presumably factored into the overall relatively low number of non-permanent researchers such as postdocs (3) and PhD students (3) throughout the evaluation time period. The team has an excellent reputation, as evidenced by several factors detailed below.

The team has had history of continuous funding from external sources (1.684k€ over the period). In this regard the team leader held not only an ERC AdG (until 2019), but was partner on an NIH R01 Grant, PI on an ANR collaborative grant, and PI on H2020 Infrastructure project InfraVec2. This latter was a 24 partner collaboration aimed at integrating and rendering more accessible insect vector research infrastructures in Europe. Notably the team leader led this research while also acting (since 2017) as Adjunct Director of the Institut Pasteur

Department for Parasites and Insect Vectors. Additional funding is held by one of the researchers, enabling them to run an independent group within the team.

The team's scientific output consisted of twenty research articles in this period, spanning a wide range of journals that include both discipline specific (e.g. Pathogens and Global Health, Parasites and Vectors, PLoS Neglected Tropical Diseases, Malaria Journal, etc.) as well as more general journals (e.g. eLife, BMC Genomics, Scientific Reports, PLoS ONE, Frontiers in Genetics, etc.). These publications are principally with co-authors from external institutes.

Supplementing this were three doctoral theses. In support of the careers of the junior scientists, the team has a policy of ensuring that all collaborators on projects (technical or research roles) are offered co-authorships on publications, all junior collaborators are mentored by more experienced team members, and that junior collaborators are first author on publications that they were primary scientific collaborator to.

With regards to other contributions, the team has been involved in extensive training and professional accompaniment of junior African researchers as part of their collaborations with West Africa. They also have contributed to public outreach and education as part of the above mentioned H2020 funded vector biology infrastructure, and are partners in the LabEx Integrative Biology of Emerging Infectious Diseases program, and a participant in the Institut Carnot Pasteur Microbes & Santé initiative.

Weaknesses and risks linked to the context

Given the plan for the team leader to enter retirement at the end of this evaluation period, the principal risks that can be identified relate to this. In this regard a plan is in place to ensure the transfer of resources and knowledge after the retirement.

Analysis of the team's trajectory

The team's trajectory over the evaluation period reflects the movement of the team leader towards retirement, and as such, a new plan is not presented to be evaluated.

RECOMMENDATIONS TO THE TEAM

In light of the closure of the group, no recommendations are made.

Team 7: Molecular Mycology (MM)

Name of the supervisor: Françoise DROMER

THEMES OF THE TEAM

The team focuses on invasive fungal infections caused by two agents (*Cryptococcus neoformans* and *Aspergillus fumigatus*) causing cryptococcosis and aspergillosis, respectively. The work ranges from clinical management to the study of host/pathogen interaction and innate immunity. The work is both fundamental and applied.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team should enhance collaborative work intra- and extra-team (mostly with teams 1 and 3).

The previous evaluation of this team during the campaign 2018–2019 was performed in the context of the Department of Mycology, which is not the case in the context of this 2023–2024 campaign. Consequently, there is no possibility to evaluate the level of collaboration with other teams than those present in GEMS.

The team should increase the number of scientists with HDR qualifications, and subsequently the number of PhD students.

The limitation in hosting PhD and post-docs (2 and 5, respectively) was probably due to the limited number of full-time researchers, one DR and four IR.

The team is sufficiently strong to address more intensely mechanistic insights and generation of new diagnostic or therapeutic tools. Recommendations include to explore the anti-Cryptococcus/Aspergillus vaccine field since there is now full competence to embark in this difficult but potentially very rewarding public health area, to re-establish an Aspergillus unit, and to more fully exploit the collection of fungal isolates using genome sequencing.

These concerns have been taken into consideration; two publications in Plos Pathogens report mechanistic data that could explain *C. neoformans* dormancy and other forms of resistance.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	12
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	2
Sous-total personnels non permanents en activité	5
Total personnels	17

EVALUATION

Overall assessment of the team

The assessment of the team is excellent. The team has been remarkably productive in terms of publications, with over 120 over the last evaluation period. Beyond the sheer number of publications, the team managed to keep up with the quality. The team also played a critical role in terms of diagnostics of invasive fungal invasion and identification of novel fungal pathogens.

Strengths and possibilities linked to the context

The team contributed to basic knowledge but also had a clear translational impact, both through their activity in diagnostics, prognostics and contribution to the management of fungal infection.

Research on fungal pathogens is often underfunded and undervalued. Despite this, the team performed remarkably well. Among the seven grants obtained through the ANR, the team coordinated four of them, for a total amount of 500 k€. Through local partnerships and private contracts, five grants were obtained and four coordinated (about 150 k€). A total of seven contracts led by the team were engaged with charities and foundations (amount about 170 k€).

The scientific production is remarkably with over 120 over the last evaluation period. The team has been involved in several European and/or international committees that published guidelines for the management (diagnosis and treatment) of invasive fungal infections and participate to describe the landscape of those infections in the context of COVID-19. These surveillance studies led to publications in high quality generalist journals (mBio, Environmental Microbiology) beside specialised reviews. Team members were also involved in more basic research as two publications in Plos Pathogens reported mechanistic data that could explain *C. neoformans* dormancy and other forms of resistance.

Managing the National Reference Center for Invasive Mycoses combined to close interaction with the Center for Diseases Control (Santé Publique France) allowed the team to be in pole position to investigate emergence of new pathogens or outbreaks of rare fungi. It also contributes to discussions about health policies regarding fungal infections.

Weaknesses and risks linked to the context

No particular weakness nor risk were identified, given the circumstances.

Analysis of the team's trajectory

None because of the team closure

RECOMMENDATIONS TO THE TEAM

The retirement of the leader in 2022 led to dismantle the team. The committee does not have recommendation beyond encouraging the former members of the team to pass on as much expertise, know-how and resources to others. We commend the whole team on their productivity and impact in the field over the last years. They clearly finished on a high level. The team clearly played a critical role in the research on fungal pathogens in recent years, an often underfunded and largely neglected field. There is serious concern that with the team leader retiring, there will be even less research effort into fungal pathogens, which may contribute to a serious public health crisis.

CONDUCT OF THE INTERVIEWS

Date

Start: 18 janvier 2024 à 8 h

End: 18 janvier 2024 à 19 h

Interview conducted: online

INTERVIEW SCHEDULE

8:45 a.m.	Presentation of the HCERES evaluation process
8:45 a.m. – 8:50 a.m.	Introduction of the HCERES committee
8:55 a.m. – 9:20 a.m.	Presentation of the unit's achievements Lluís Quintana-Murci
9:30 a.m. – 10 a.m.	Genetics and Genomics of Insect Vectors (GGIV) Kenneth VERNICK
10 a.m. – 10:30 a.m.	Insect-Virus Interactions (IVI) Louis LAMBRECHTS
10h30 – 10h45	Break
10:45 a.m. – 11:15 a.m.	Ecology and Emergence of Arthropod-borne Pathogens (EEAP) Anavaj SAKUNTABHAI
11:15 a.m. – 11:45 a.m.	Human Evolutionary Genetics (HEG). Lluís QUINTANA-MURCI
11h45 – 12h15	Microbial Paleogenomics (MP) Nicolas RASCOVAN
12h15 – 12h45	Mathematical Modelling of Infectious Diseases (MMID) Simon CAUCHEMEZ
12:45 p.m. – 13h15	Presentation of the unit project Louis LAMBRECHTS
1:15 p.m. – 1:30 p.m.	Lunch Break
1:30 p.m. – 2 p.m.	Debriefing-1 committee
2 p.m. – 2:30 p.m.	Meeting with ITAs
2:35 p.m. – 3:05 p.m.	Meeting with researchers
3:10 p.m. – 3:40 p.m.	Meeting with postdocs/students
3:45 p.m. – 4 p.m.	Break
4 p.m. – 4:30 p.m.	Meeting with institution representatives
4:30 p.m. – 4:45 p.m.	Debriefing-2 committee
4:45 p.m. – 5:15 p.m.	Meeting with the Unit direction
5:15 p.m. – 7 p.m.	Redaction of the final report
7 p.m.	End of the interview

GENERAL OBSERVATIONS OF THE SUPERVISORS

Paris, le 21 juillet 2022

Direction Générale Adjointe Scientifique

De : Christophe d'Enfert

Téléphone : 01 40 61 30 98

E-mail : christophe.denfert@pasteur.fr

Objet : Rapport d'évaluation de l'Unité " GEMS – Génomique évolutive, modélisation et santé " -
DER-PUR25002450

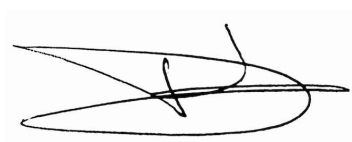
Madame, Monsieur,

Je vous remercie de nous avoir transmis de ce pré-rapport.

Je vous prie de bien vouloir noter que l'Institut Pasteur n'émettra pas de réponse institutionnelle de type « observations de portée générale ».

L'Institut Pasteur remercie le comité HCERES pour le travail d'évaluation qu'il a réalisé et reste à votre disposition pour tout complément d'information.

Bien à vous,



Christophe d'Enfert
Directeur Général Adjoint Scientifique

cc. Lluis Quintana-Murci, Louis Lambrechts, Patrick Trieu-Cuot, Didier Mazel

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2 rue Albert Einstein
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