Research evaluation

EVALUATION REPORT OF THE UNIT

VIM - Virologie et Immunologie Moléculaires

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Institut national de recherche pour l'agriculture, l'alimentation et l'environnement - INRAE

Université de Versailles Saint-Quentin-en-Yvelines - UVSQ

EVALUATION CAMPAIGN 2024-2025

GROUP E

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High Council for evaluation of research and highter education

In the name of the expert committee :

Juan Reguera, chairman of the committee

For the Hcéres :

Stéphane Le Bouler, acting president

In accordance with articles R. 114-15 and R. 114-10 of the Research Code, the evaluation reports drawn up by the 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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CHARACTERISATION OF THE UNIT

- Name: Virologie et Immunologie Moléculaires
- Acronym: VIM
- Label and number: UMR0892
- Number of teams: 7
- Composition of the executive team: Ms Sabine Riffault (directrice d'unité) & Mr Pierre Boudinot (directeur d'unité adjoint)

SCIENTIFIC PANELS OF THE UNIT

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

SVE3 Living molecules, integrative biology (from genes and genomes to systems), cell and development biology for animal science
SVE5 Neurosciences and nervous system disorders
SVE7 Prevention, diagnosis and treatment of human diseases

THEMES OF THE UNIT

VIM scientists study pathogens affecting animals and humans and the immune responses induced by these pathogens, and especially respiratory viruses, fish infections and prions.
Two new themes have emerged consisting of innate responses in lung transplantation and immune determinants of human respiratory diseases.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The Molecular Virology and Immunology unit (VIM) is part of INRAE's Animal Health Division (AHD) and has been affiliated with the UFR Santé Simone Veil of UVSQ since 2020. Founded in 1988, VIM created two teams in 2001 to study prion diseases, which merged in 2010, and established an Influenza virus research team in 2006. Important infrastructure upgrades involved the construction of a biosafety level 3 (L3) lab for viruses in 2010 and the renovation of an L3 prion lab in 2014. In 2020, VIM became a joint research unit (UMR) with UVSQ, bringing in hospital-based researchers to work on lung transplantation and chronic respiratory diseases. In 2021, a new team was formed to study coronaviruses in response to the Covid-19 pandemic. Located at INRAE's Ile-de-France-Jouy-en-Josas-Antony research center, VIM also operates a small site at Foch Hospital and its labs became Restricted Access Zones in 2020, requiring special authorization for personnel.

RESEARCH ENVIRONMENT OF THE UNIT

The unit is part of the Animal Health Division (AHD) of INRAE. VIM created the SAPS regional scientific network with other INRAE units. VIM is a contributing member of the Institut Carnot France Futur Elevage led by AHD-INRAE. VIM scientists use INRAE facilities: IERP (Experimental Unit for Infectiology of Rodent and Fish) and CIMA (Animal Surgery Platform of MIMA2) at INRAE Jouy-en-Josas (affiliated to the SAPS network). For experiments on farm animals (bovine, porcine, poultry), VIM scientists have access to the PFIE platform (Infectiology Platform) at INRAE Nouzilly-Val-de-Loire or to Anses facilities at the laboratory Ploufragan-Plouzané-Niort. The Anses and INRAE facilities for farm animal infectiology are part of the Emerg'in national research infrastructure (coordinated by INRAE AHD).

VIM is part of the UFR Santé Simone Veil and the HUs members of VIM belong to Hospital Foch. The Foch Foundation and UVSQ joined forces in 2018 to create France's first "Chaire de Transplantation" (Chair in Transplantation), with the aim of better understanding, innovating and training. A PU-PH of the unit, was president of the Chair until 2023 . VIM is part of the regional cluster Université Paris-Saclay (UPSay).

VIM teams are all affiliated to the Graduate School (GS) "Life Science and Health" (LSH), and to the GS "Biosphera" except for the BMP team affiliated to the GS "Health and Drug Sciences". In addition, they are part of the Interdisciplinary Objects: "Healthi", "Microbes" and "LivingMachines@Work". The two main doctoral schools are ABIES (affiliated to Biosphera) and SDSV (affiliated to Life Science and Health).

The director of VIM unit has been very active in the construction of a scientific priority domain financed by the region Ile de France (DIM for "Domaine d'Intérêt Majeur") and dedicated to One Health research projects linking human and animal infectiology (DIM One Health 2017-2020 and DIM One Health 2.0 2022-2025). She is part of the scientific advisory board since 2017.

Two VIM teams, namely FLU and MAP2 have been involved in the creation of national GdR scientific networks financed by CNRS. The GdR MéDynA (assembly mechanisms and dynamics of self-organised protein-based complexes) brings together French labs studying the dynamical pathways by which self-organised protein assemblies or protein-based assemblies form and evolve. It was created in 2019 with a senior MAP2 team as member of the pilot committee. The GdR ResaFlu brings together French teams working on the influenza viruses that cause flu in humans and animals. It was created in 2019 with a senior member of the FLU team as member of the pilot committee . Both GdR have been prolonged for another 5 years. ResaFlu joined with FLURESEARCHNET (Germany).

UNIT WORKFORCE: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	6
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	15
Chargés de recherche et assimilés	10
Personnels d'appui à la recherche	31
Sous-total personnels permanents en activité	**63**
Enseignants-chercheurs et chercheurs non permanents et assimilés	3
Personnels d'appui non permanents	7
Post-doctorants	1
Doctorants	14
Sous-total personnels non permanents en activité	**25**
Total personnels	**88**

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons at 31/12/2023. Non-tutorship employers are grouped under the heading "others".

Nom de l'employeur	EC	C	PAR
INRAE	0	25	27
UVSQ	6	0	0
Autres	1	0	4
Total personnels	**7**	**25**	**31**

GLOBAL ASSESSMENT

The global assessment of the VIM Unit is excellent to outstanding.

The Molecular Virology and Immunology unit (VIM), part of INRAE's Animal Health Division and UVSQ's UFR Santé Simone Veil since 2020, focuses on pathogens and immune responses affecting animal and human health. Established in 1988, VIM has evolved structurally and thematically, with notable milestones including the creation of prion and influenza virus research teams, and infrastructure upgrades such as L3 bio-contained labs. Recent developments include becoming a joint research unit (UMR) with UVSQ, expanding into coronavirus research during the Covid-19 pandemic, and addressing prion-related safety concerns following two Creutzfeldt-Jakob Disease cases (incl. one at the VIM). Based at Jouy-en-Josas and partially at Hospital Foch, VIM operates under strict biosafety regulations and studies diverse pathogens and immune responses, supported by shared facilities and robust administrative and technical services.
The VIM unit consists of seven research teams. Four focused on respiratory viruses and immunity: 1) The BMP team studies the multiplication steps of Pneumoviruses, from replication/transcription of the viral genome to virions' assembly, 2) The CORONA team, created during the Covid-19 pandemic, studies the physiopathology of SARS-CoV-2 in the nasal cavity, and the development of nanobodies to block the entrance of the virus. 3) The Flu Team which focuses on understanding Influenza A virus host-virus interactions, immune response and virulence.

4) the Vaccine Immunopathology Immunomodulation team (V2I) focuses on investigating the immunopathological mechanisms associated with respiratory diseases in animals and humans and on the development of intervention strategies based on immunity. Two teams work on Fish health: The VMP and IIP teams (5 and 6) focus on the study of viral and bacterial infections and the mechanisms of immune response. One team (MAP2) studies the molecular mechanisms and pathogenesis of prion diseases, aiming to better understand prion replication and its impact on neural networks. These teams share expertise and facilities, such as biocontained laboratories, protein purification labs, and biophysics equipment, to further their research on pathogen-host interactions, immune responses, and the development of novel diagnostics, therapeutics, and vaccines.

Highlights of the VIM production are the description of the IFN response on RSV infection in neonates (Muc Immunol. V2I), the discovery of drugs inhibiting RSV replication by hardening viral condensates (Nature, BMP & Flu), the generation of biosynthetic proteins targeting SARS CoV 2 spike protein (Plos Path, CORONA), the generation of VHSV based vaccines against fish betanodavirus infections (Front Immunol, VMP team), the role of STAT 2 for viral resistance and INF signaling in fish and the identification of germinal center in fish (J Immunol & Science Immunol. IIP) or the identification of two structurally different prion subpopulations in early stages of prion assembly (Com Biol, MAP2).

The organisation of the unit is excellent, with regular meetings to maintain cohesion among the 98 staff and an excellent financial situation (13 M€). The unit has done a good job in supervising PhD students (34), but could improve its mentoring role by hosting more post-doctoral researchers. The visibility of the VIM is also remarkable, with the production of 460 scientific publications including 265 as main authors in the period. However, the level of implication in the articles with respect of external coauthors, is moderate. Also, the profile of the journals often targeted is not very high and this is an aspect that should be improved. VIM scientists have done 205 presentations at conferences, including 89 abroad and 128 invited talks. This visibility in the academic world is similar to that in the industrial world, with contracts worth more than 2 M€. Unfortunately, and for reasons explained below, public engagement was reduced in the last evaluation period. Overall, the VIMs have achieved most of their objectives and produced great science. They have presented a detailed and exciting roadmap for the next five years, with great input from each team.

Among the respiratory viruses teams the BMP team outstands for the amount of high-impact research achieved and its capacity for establishing productive internal and external collaborations. V2I and IIP have also been outstanding in terms of scientific production and funding.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

There were no recommendations for the scientific production. Scientific outputs, interactions with non-academic world and training were rated excellent to outstanding.

The last evaluation suggested merging into two fish teams. The VIM did not share this view. It is true that both teams (IIP and VMP) had an excellent scientific output and very good attractiveness. The unit explained that both structures work together when necessary. Both teams would need an increase in staff, but both are very successful in their own field. Our committee does not see any urgency to merge the two teams.

Finally, the committee emphasized the need to find a balance between animal/human pathogens (more INRAE) and translational model (more medical) in order to maintain a clear objective. Since then, the V2I team incorporated six medical doctors working on pig model for lung transplantation. The V2I team have maintained attractivity and scientific outputs in both veterinary and human research. The team is now working at the cross-road of these two research area with the objective of improving Ex-vivo Lung Transplantation procedure.

B - EVALUATION AREAS

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

Assessment on the scientific objectives of the unit

The scientific objectives of the unit are outstanding. They have the potential to have a high impact in human and animal health at the prevention, diagnosis and treatment levels of infectious diseases and on lung transplantation and fish farming.

Assessment on the unit's resources

The unit's resources are excellent. The financial situation is outstanding but some teams would need additional staff to be more efficient. In addition, animal facilities need improvement.

Assessment on the functioning of the unit

The functioning of the unit is excellent to outstanding with regular meeting and a great team spirit. The VIM unit could promote more collaborative work between its 7 teams. But, most importantly, VIM managed 2 important crisis that hit the unit (Covid-19 and prion).

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The scientific objectives aimed at understanding key mechanisms of infections by pathogens and host response in animals and humans. They have evolved and are planned to further evolve. Their objectives have been adapted, taking into account both the human and technical challenges they have faced and the current state of the art. They include and plan to include a higher proportion of projects directly related to human health and non-infectious topics such as lung transplantation and chronic respiratory diseases. These objectives are consistent with the integration of several HU members in the team and are split into three axes (Molecular basis of virulence and host-pathogen entanglement, tissue tropism, host and immune response, extrinsic modulation of infection and host response), which seems pertinent. Other adaptations include the creation of a team

dedicated to coronaviruses, reducing significantly the FLU team and a reorientation of experiments on prions without animal facilities.

Weaknesses and risks linked to the context

Projects based on AI approaches rely on individual recent collaborations, with a lack of structured objectives and a secured access to expertise.

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 able to generate stable resources to promote its activities and to regularly renew its equipment to maintain their quality. The main part of the executive budget comes from research grants.

Although there are disparities between teams, the unit has valuable national and international collaborations (within Europe, Asia, with the USA), and industrial partnerships, which highlight their international competitiveness and visibility.

VIM demonstrated outstanding capacities to secure funds from both public and private origins, with a total of 105 contract for a total sum close to 13 M€. There are still 24 contracts running in the next period (for a total of 2,588 k€).

After the moratorium and the impossibility to work on prion research in any animal facility in France a collaboration with the Spanish Center for Research on Animal Health (CISA), institute dependent of the Spanish INIA and the CSIC, has been established. This key collaboration allows the researchers of the MAP2 team to carry out experiments in an animal facility until the facilities adapted for prion research are operative again in France.

Weaknesses and risks linked to the context

Thirteen permanent employees will reach retirement age in the next five years. This will require careful planning to manage turnover and retain key research topics.

Some facilities need improvement. In addition, some other facilities that could have been used by the VIM are also closed, limiting alternative options.

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

Strengths and possibilities linked to the context

The unit is structured with dedicated staff for all necessary support activities (administrative work, logistics...) and to satisfy good practice requirements (good laboratory practice, health and safety...). There are monthly meetings between team leaders and the direction team of VIM, where both scientific and management issues are discussed, and also one or two meetings per year of the scientific board with and scientists and engineers.

General HR management is outstanding, offering balanced recruitment and career growth, with gender parity. Leadership training has been prioritized to improve working conditions, and psycho-social risk prevention has been strengthened, especially after the tragic events related to Creutzfeldt Jakob disease.

VIM's organizational structure protects critical assets. The computer maintenance team ensures cybersecurity and IT management in line with INRAE's protocols. The addition of a biosafety engineer in 2023 strengthens the unit's capacity to meet safety regulations, particularly in high-risk laboratories.

VIM aligns with INRAE's sustainability initiatives, with actions to reduce energy consumption and develop a greenhouse gas emissions balance sheet, reflecting a commitment to environmental preservation. Ongoing projects offer potential for further progress in sustainability.

Weaknesses and risks linked to the context

Despite its strengths, VIM faces challenges in human resources management, including high turnover of both staff and funding, which strains staff to secure resources and manage administrative complexity. While gender parity has improved, the lack of a formal gender equality policy may prevent long-term diversity and inclusion goals. Career progression for technical staff, especially in non-scientific roles, remains limited, potentially affecting motivation and retention.

In terms of risk prevention for scientific assets and information systems, VIM has made progress, such as recruiting a biosafety engineer and implementing restricted access protocols. However, increasing regulatory complexity poses a risk that current staff may become overwhelmed, leading to potential oversights in safety or data protection. This is particularly critical in a high-stakes environment involving hazardous materials and advanced research, where mistakes could have severe consequences.

VIM has made environmental commitments, though there are constraints with safety being prioritized in all sustainability efforts. Energy-saving measures, such as adjusting freezer temperatures to -70 °C, have been implemented. The unit's reliance on travel and energy-intensive laboratory processes may limit its ability to significantly reduce its carbon footprint.

Despite overall relevant scientific objectives, several teams are facing challenges in human and/or technical resources and have to refocus their scientific objectives in a context of international competition.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the unit is excellent based on its grant leverage (national and international) and scientific visibility. Although the PhD training is more than satisfying an effort should be made to attract post-docs.

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 and attractiveness of the VIM is well evidenced by successful international (5x, all coordinators) and European (18x, including 5 as coordinators) grants. In total, these grants amounted to about 4 M€. VIM scientists have a good visibility with 205 presentations at conferences (89 abroad), including 128 invited talks. They also organize international conferences such as the International Network in Protein Engineering Center, Paris-Saclay Microbes day (2019). In particular, the IIP team has been organising an international meeting on marine flavobacteria in 2018 and 2024.

Several VIM members are on the editorial boards of international journals such as Veterinary Research, Journal of Heart and Lung Transplantation, Anaesthesia and Critical Care Medicine, Scientific Reports, PlosOne, Developmental and comparative Immunology, Fish and Shellfish Immunology. Importantly, the VIM hosts the journal Veterinary Research (editor-in-chief and assistant editor). VIM scientists are also active in the review of international grants (Norway, Sweden, Switzerland, UK). Finally, in 2018, two senior researchers were recognised nationally, both receiving the "Lauriers de l'INRAE" awards.

To improve the management and well-being of the staff, the team leaders attended a "management training" and a workshop on the prevention of psychosocial risks. During the last five years, 34 PhD students have been or, are being trained in VIM. This is a good number when compared to the number of researchers with an HDR

(25). On average, PhD students defend their thesis after 3.4 years, which is very good. All PhD students have at least one article as main author during their thesis and almost 16% of the scientific papers from VIM had a PhD student as author (note that this may be biased by some PhD students having more than 13 papers during their PhD). To train PhD students to talk to their peers about their research, PhD students are required to present their data at least once during their training and VIM maintains a small budget to support PhD students to attend at least one international meeting. Although there has been a high turnover, the VIM has recruited more young researchers than the number of departures (15 recruitments for 12 departures INRAE and 4 recruitment for UVSQ). In addition, VIM encourages CR to apply for a DR position and six have succeeded (including two women). A total of 22 international collaborators were welcomed at the VIM during this period. This includes three senior researchers: two from China and one from the University of Quebec (Canada). VIM also welcomed eleven international post-docs and eight PhD students. In order to facilitate their integration, international staff are encouraged to take French lessons, paid for and organised by VIM. Note that this is quite heterogeneous within VIM: V2I had zero international visitors, IIP had eight.

VIM demonstrated outstanding capacities to secure funds from both public and private origins, with a total of 105 contract for a total sum close to 13 M€. There are still 24 contracts running in the next period (for a total of 2,588 k€). VIM managed to obtained grants from a large variety of sources: 5 internationals, 18 European, 34 national (mainly ANR), 6 PIA, 23 with industries, 14 with DIM1Health and 5 with association (such as FRM). The scientist of VIM are very often the coordinators of these grants (71/105), which is a remarkable effort.

VIM has level 2 & 3 biocontainment laboratories, which allow research on SARS-COV-2 and other important viruses (maintenance at 60 k€/year).

Finally, VIM team has acquired new equipment that could improve collaboration. The VMP and V2I have received funding for an IVIS spectrum. The MIMA2 imaging facility has invested in a microscope light sheet in 2021. V2I recently received funding for a CytoFlex cell sorter and a Chromium 10X genomics for scRNA-seq (ANR 2020).

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

There is a large heterogeneity on the conference International/national communication where two teams (MAP2 and V2I) represent more than 70% of the presentations.

Only 17 post-docs seem to have been recruited over the five years in the whole unit, including eleven international, highlighting a poor attractivity for French post-docs. During the visit there were no post-docs in the interview with post-docs / PhD students, but there was a large number of PhD students (10-20). This is far from an optimal post-doc / PhD ratio for a lab of the VIM characteristics. It is important to note that VIM has gone through two major crisis (Covid-19 and Prion) and that the Fish teams are struggling to get funding for post-docs and PhDs. Nevertheless, this should not impact the equilibrium of post doc / PhD rates.

The committee notes that the large grants (over 300 k€) that VIM has obtained are now all finished: H2020-SAPHIR grant (V2I, 1219 k€), Influenza aviaire (FLU, 533 k€), NOVATION (VMP, 560 k€), RSV Janssen (BMP, 375 k€), FRANKLAB (MAP2, 466 k€), Equipe FRM (MAP2, 384 k€).

As mentioned above, VIM uses that are either closed due to prion moratorium or obsolete ((IERP A3, A3). This will greatly discourage scientists to join the VIM for postdoctoral positions or slow down international collaborations.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of the unit is excellent to outstanding because of the exceptionally high number of scientific publications, however mostly in rather specialised journals and with only few examples of outstanding publications where the teams play a major role among the authors.

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's teams have published several key scientific discoveries in all three scientific areas (Respiratory Virus and Health; Fish Infection and Health; Prion Diseases) over the last five years. This list includes, but is not limited to, the identification of a key protein IRAP in the modulation of the neonatal IFN pathway during RSV infection (Muc Immunol); a publication on PB1-F2 - a virulence factor of influenza A - and its role in the proinflammatory response respiratory distress of infected mice (J Biol Chem); a cryo-EM analysis of respiratory syncytial virus nucleocapsids (Nature Comm); a critical discovery of fish germinal center-like structures (Sci Immunol); and a study showing that PrPC expression is key to prion tropism for the spleen (PLoS Pathogens).

VIM has produced 460 publications (review and research articles), including 265 signed VIM scientists as main authors (first, corresponding, last = 58%). VIM published in various journals covering the unit's topics: Immunology, Respiratory system, Microbiology, Biochemistry and Virology. Many of those publications have been published in excellent, well-respected international journals, such as Allergy (17), American Journal of Transplantation (5), Journal of Immunology (5), PLoS Pathogens (6). Many articles were published in multidisciplinary journals, such as Scientific Reports (9) or PLoS One (5). Some papers have been published in high-profile multidisciplinary journals (Nature, Cell, Science).

All VIM teams have contributed to publications, in proportion to their staff numbers. The 34 current or former PhD students have co-authored 75 publications or reviews (16%), resulting in more than two manuscripts per student. Note that the publication of two V2I PhD students "boosts" this statistic: without V2I, there are 41 publications for 26 students. In addition, in several teams, the supporting staff PAR is first author (nine publications).

VIM scientists have published most of their papers in open access journals (381/460 = 82%), stored in HAL, and discuss with the direction about data that need restricted access. A part-time consultant (10% of time) helps the researchers with data management. Scientists have also been involved in Data Management Plans (DMPs), which are usually required for EU grants. The unit has organised a conference on scientific integrity in 2023 and all staff received a "Charter of Deontology, Scientific Integrity and Ethics" on arrival. The unit ensures that all experiments are carried out in accordance with French and European legislation and that all staff involved in animal experimentation receive appropriate training, certified by a diploma.

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

There are only a few publications in high-profile journals with VIM as lead author (e.g. 1x Cell as middle author, 1x Nature as 2nd author, 2x Science Advances incl. 1 as corresponding author, 2x Nature Comm. as first author & 2nd author). In addition, a large number of articles were published in "grey" journals (e.g. Frontiers journals (35) and MDPI (21)). VIM has published 36 articles involving at least two teams of the unit out of the 460 (7.8%). This is on the low side and interactions between VIM teams should be promoted.

The total number of publications is distorted by the merger of the PU-PH staff from the FOCH hospital and its transplantation theme, with a more clinical approach. Indeed, V2I produced 196/460 publications (the team published 7-8 papers per year before the merger, about 45/year after the merger). Similarly, 66/176 presentations were made by these six PU-PH.

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 of VIM is excellent to outstanding. The unit has obtained many contracts with companies but public engagement was rather uneven amongst the teams.

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

All of the unit's teams are linked to industrial partners active in both animal and human health. They are linked to several areas, often using the expertise of the VIM team for vaccines or antivirals treatments. The different teams establish partnerships with large companies (such as RSV Janssen or Zoetis, Pfizer) or smaller ones (PILEJE, Curovir, Xeolas). These contracts total 2,226 k€, with MAP2 receiving the largest amount (781 k€). These contracts finance research but also doctoral fellowships (3x Cifre).

The VIM teams have filed 23 patents and DI-RVs, mainly on new antiviral drugs or new vaccine methods. (coronavirus, RSV). This is an enormous effort. The V2I team has also collaborated with Bio-Rad to commercialize a new antibody against porcine CD11c. Another proof of the VIM team's expertise is their level of involvement with guidelines such as FELASA for animal experimentation, ANSM for protocol when working with prions, or CEUCO for GMO.

Although an open day is out of the question due to the ZRR and that the unit has limited the public engagement due to backlash, the VIM has shared their passion with the public whenever possible. Some scientists have given lectures in secondary schools or published articles in magazines aimed at the general public (such as La Recherche or The Conversation). The results of the research teams are regularly published in INRAE press dossiers (seven examples given by the VIM).

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

The number of DI-RV and patent across the unit is rather heterogenous. Some team have eleven (BMP), other none (V2I, IIP)

The unit's involvement in the interaction between science and society is rather uneven across the teams, with some teams not engaging with the public at all. In addition, communication activities are mainly based on press releases. The VIM management has explained that public engagement was deliberately reduced after the prion crisis due to threats and backlash from associations. The unit is now planning more face-to-face interaction with the public (such as the "Salon de l'Agriculture").

ANALYSIS OF THE UNIT'S TRAJECTORY

VIM was created in 1988 to study the molecular biology of viral pathogens and the immune response to infection. The unit has implemented over the years a structure of seven teams focusing on virology and immunology of respiratory infectious diseases (BPM, Flu, Corona and V2I teams), Fish viral infection and immunology (VMP and IIP) and prion research (MAP2). The unit has achieved an increasing relevance on human health topics related with the translational aspect of animal and human health, particularly under the One Health concept where infectious diseases have to be addressed from both animal and human perspectives for the proper understanding of infection dynamics, detection, prevention and treatment. In addition, the know-how of the animal research is instrumental for the development of therapies in humans. An excellent example of this is the lung transplantation research carried out by the V2I team. This context has induced VIM to approach institutions oriented to human health as the Foch Hospital, where several HU members of the V2I team are currently hosted, and Inserm.

This trajectory of the unit has been interrupted by two events during the period, first the 2019 Covid-19 pandemic and secondly the decease of two research engineers by prion disease, one associated to VIM, which has triggered a period of investigation, frozen the prion research as well as the institutional approach to Inserm and put the VIM and the governing bodies into a difficult societal pressure. For the next period the unit can progressively resume the approach to Inserm and the activities on prion research with the guidance and support of the governing bodies in terms of budget and safety regulations combining the highest level of and also the efficiency of the experimental workflows.

For the next period the research of the VIM unit is centered around three topics: 1) Molecular basis of virulence and host-pathogen entanglement; 2) Tissue tropism, host and immune response; and 3) Extrinsic modulation of infection and host response. The three axis includes the activities of all the teams thus fostering collaboration and pursue of common goals. Common goals however should be better defined, in agreement and with the participation of all the teams, into more concrete objectives in order to be eventually materialised. A regular exchange of the teams towards this confluence will be necessary for the definition and achievement of the goals.

The future organization of the VIM unit is both strategic and adaptive, ensuring alignment with its research ambitions and the goals of its teams and themes. By adopting cutting-edge methodologies such as systems biology, optogenetics, organoid/assembloid models, and predictive approaches, the unit is well-positioned to tackle the complexity of host-pathogen interactions and pathogen evolution. For example, the implementation of genomic and conformomic tools will enhance the detection of tissue tropism and biochemical factors driving virulence.

Investments in infrastructure, such as the upgrade of imaging platforms (e.g., light sheet microscopy), neuro-imaging devices, and microfluidic systems for 3D tissue modeling, will provide teams with state-of-the-art resources to conduct innovative experiments.

New collaborations will also play a crucial role in realizing the unit's ambitions. Strengthened ties with Inserm will enable translational research opportunities, while partnerships with international institutions like the Crick Institute, Cornell University, and Wageningen University will bring fresh perspectives and facilitate access to diverse funding opportunities. Within the Paris-Saclay cluster, the unit's integration with regional platforms such as the MIMA2 imaging facility will bolster interdisciplinary efforts.

By combining innovative methodologies, advanced infrastructure, and robust national and international partnerships, the VIM unit is poised to lead advancements in "One Health" research. This comprehensive approach ensures the successful execution of its research projects while fostering a dynamic and collaborative environment for future scientific breakthroughs.

RECOMMENDATIONS TO THE UNIT

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

First of all, it is important to praise the VIM unit for its handling of two major crises in the last five years (Covid and Prion crises).

In the next five years, the VIM should ensure that communication and cooperation between the teams is promoted. It will also be important to find a good balance between animal (INRAE) and human research projects (FOCH and potentially Inserm). Key scientists and ITAs will retire within the next five years. It will therefore be crucial for VIM to recruit new permanent staff in order to maintain the technical knowledge and scientific network.

A general feeling among ITAs and non-team leader researchers (shared across many units) is that ITAs struggle with the time they spend organising shared platforms or services (quality, prevention, metrology, BSL2...) and the scientific experiments they are responsible for. Some ITA have a clear definition (% per week, clear mandate), others do not. This could be discussed at an Assemble Generale. It was also noted that vertical communication could be improved. Depending on the team leader, ITA and researchers do not always get all the information from the monthly board meeting. A written document on the intranet could solve this problem.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit is encouraged to maintain their leading position in ANR grants and EU grants. After the success of the EU SAPHIRE grant as well as other H2020 and International grants, successful teams should consider applying to ERC grants (this point was hinted in the Unit trajectory p30).

The number of post-docs have decreased since 2020 (eleven in 2020, five in 2023). It is crucial that the unit and each team make an effort to improve the attractiveness for post-docs. Marie Curie and EMBO, although very competitive, are a good way to attract French post-docs who want to come back to France as CR/DR.

It will be essential to follow up frequently with the different supervising institutions to release funds for the renovation of the BSL A3 non-prion as a priority. A PRION biomodule would also greatly facilitate the continuation of the unit's work on prion diseases and strengthen its international expertise.

Recommendations regarding Evaluation Area 3: Scientific Production

The unit is encouraged to maintain the high number of publications, perhaps with research that links and human health when possible. Many of the key discoveries made by VIM scientists are worthy of publication in high-profile journals and teams should try to publish in those journals rather than journals such as MDPI and Frontiers (which are now in a 'grey' area).

Encouraging collaboration between VIM's teams is crucial to the scientific success of the unit. We encourage the unit to support the Flu and CORONA teams by fostering scientific culture elements such as self-questioning and constructive criticism. This approach aims to enable scientific synergy by prioritizing the pursuit of scientific progress and minimizing the impact of personal disagreements. The BMP team appears to be a good example to follow.

Some teams note that it is more difficult to publish than human immunology in generalist journals. The unit and teams should try to promote their relevant, emphasizing the One Health concept and climate change (zoonoses, new viruses), and should not stop trying to persuade journal editors to publish. Becoming a member of an editorial board is one way to work on this.

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

The unit has outstading links with industrial partners and is encouraged to continue this way of exploiting its discoveries. On the other hand, the level of public engagement is rather low. The committee has noted and understands the reason for this reduction in public engagement (threats following the prion crisis). However, we encourage the scientists, when ready, to take part in more public events such as "le salon de l'agriculture", which is already planned by the Direction. The teams could discuss among themselves in order to share the burden.

The unit needs to set certain standards on the participation in national and international congresses of researchers and students. We propose the goal of one oral presentation per year per permanent researcher and at least one oral presentation per each PhD student and post doc.

TEAM-BY-TEAM ASSESSMENT

Team 1: Molecular Biology of Pneumoviruses (BMP)

Name of the supervisors: Ms Marie Galloux & Mr Jean-François Eléouët

THEMES OF THE TEAM

The BMP team focus on the understanding of pneumoviruse infection addressing the essential aspects of viral replication and interactions with the host. By combining methods using in vitro reconstituted proteins and protein complexes, studies in infected cells the team manages to have a broad multiscale view of the infection and is able to apply different techniques for the discovery of drugs and vaccines.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations of the previous evaluation where about increasing the level of editorial work in more relevant reviews, to attend more international meetings, look for more collaborations with industries and increase outreach activities. It was suggested to increase the HDR among PIs to rise PhD recruitment and boost the Post-Doc productivity. All these recommendations are important for facing the ambitious research program proposed, as well as the establishment of collaborations with top laboratories.

During the period the team obtained two more HDRs resulting into an increase of PhD recruitment (five PhD students). In addition, two permanents INRAE agents have joined the team (CRCN and AI) and one post-doc, as well as a CNRS visiting scientist.

New collaborations have been stablished with structural biologists at IBS Grenoble, Imea and Weizmann I. cellular and innate immunity labs at CIRI-Lyon, CNRS Gif-sur-Yvette; structure prediction at Montpellier and Pasteur I. high resolution optical microscopy at IRIM- Montpellier and chemists at Gif-sur-Yvette and Sion-Switzerland.

The recommendations have therefore been addressed satisfactorily.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**8**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**4**
Total personnels	**12**

EVALUATION

Overall assessment of the team

The performance of the team on the evaluation period has been excellent to outstanding based on the number and quality of publications, including relevant authorships in outstanding journals, and the capacity of the team to obtain funding from national and European funding agencies.

Strengths and possibilities linked to the context

The team focuses on viral diseases of high medical relevance as respiratory syncytial virus (RSV) and human metapneumovirus (MPV) and is perfectly integrated in the aims of the unit and in synergy with the scopes of the different surrounding teams.

During the period the team has been able to obtain nine ANR grants, two with the team leaders as coordinators, funding from EU H2020 as partner and other local, national and international grants allowing a continuous funding of the team reaching 1168 k€ in the period. The team has achieved an excellent output of publications by maintaining a good balance between quantity (52 articles) and Quality (e.g. one Nature and one Nat Commun).

The team leader has managed to lead a major publication in Nature Journal with other senior researchers on the effect of cyclopamine and A3E as molecules hardening the inclusion bodies condensates which leads to the inhibition of RSV replication. The team has also participated in two publications on Nature Communications about the structural characterization of RSV nucleoproteins and their relationship with the P protein and RNA. In both the works are achieved through collaborators with structural biologists with the contribution of team members.

In addition, the team has a large number of publications in more specialised journals where the team members reach more relevance as last corresponding or first authorships. Most of the five PhD student of the laboratory have first author publications, some of them with relevant first authorships in Nat Communications, JBC or Journal of virology. In the last period the team has increased the permanent staff (8) and the capacity to recruit PhD students by increasing the personnel HDR (+2) and master 2 students (6). This is important to build up a context where young students and researchers can be properly advised for the development of their careers.

The team has been active in the development of protocols and inventions out of their research, with methods and patents registered (9+2).

The researchers and PhDs of the team have given 16 oral presentations in international congresses as the NSV congress in Braga, or the RSV in Belfast, national contexts as the French national virology meeting (four consecutive years), and invited talks in the AFMB Marseille or the CIRI in Lyon. The evaluation activity in terms of grants, committees (16 HDR and PhD), journal editor activities are covered mainly by team leaders (member of the editorial board of veterinary research journal since 2019).

The above-mentioned oral presentation, collaborative grants and publications provides high visibility to the team at the national and international level.

The BMP team counts now, following the recommendations of the previous report, with a strategic collaboration network on critical aspects of their research for the generation of new antivirals and vaccines.

Weaknesses and risks linked to the context

The international competition on the field is very strong however the team is dealing with this reasonably well. The structural biology discoveries since the development of the cryo electron microscopy in the domain of negative stranded viruses replication has been hectic and the team has a moderate access to these technologies only through collaborations. Actually, INRAE has not the technology accessible in-house. In addition, and in line with the scopes of the team, the development of cryo CLEM and in situ characterisation of macromolecular structures is already providing ground-breaking information on the research topics of the team as the architecture of replication factories, the viral particle formation or the generation of viral driven phase separation (non membranous organelles) in the cell.

The departure of the team leader will leave an empty space in the team. The replacement is assured by the deputy team leader. It is important to clarify how this transition will happen and how the scientific and administrative roles assumed now by the team leader will be distributed within the team. It is also important to preserve the collaborative network of the team after his departure.

The development of AI approaches for the protein structure prediction are having a strong impact on the structural biology field. Is important that the team includes these approaches in the workflows related with project applications and scientific research.

The highest impact of the team is dependent of collaborations, in consequence is very important to maintain and expand, if necessary, the network for keeping the high impact. In addition, the team is in the position now to incorporate certain critical skills in the team related with newly developed AI tools and the newest Cryo-EM techniques in order to progressively be less critically dependent on collaborations and enhance their leadership for high impact research.

The outreach activities of the team are not very developed. The society engagement of the public research includes a closer contact and communication with the public by participating in outreach events or generating material for the broad-public scientific communication. Also, the teaching activities of the team need to be expanded in order to have a closer contact with students and be more attractive for recruiting Master and PhD students.

Analysis of the team's trajectory

The recent development of vaccines for RSV prevention is a concern for the team since the perspectives of funding on RSV research could be jeopardised. However, the development of antivirals or even better vaccines in the future are still challenges that the team can perfectly address. In any case the team is in a good position to deploy his know how to start new research projects on related Mononegavirales of importance for human and animal health. An example is the research extension to Human Metapneumovirus.

In conclusion, the team is in an exceptional position to face the new technological and scientific challenges on the field of the Mononegavirales research.

RECOMMENDATIONS TO THE TEAM

The transition between the new direction of the team needs to be well coordinated and clear for all the team. It is also important to conserve critical collaborations for keeping key expertise and collaborations that are provided by the team leader and confer to the team the potential for the development of therapeutic solutions for Pneumovirus infection.

Since new therapeutic solutions has been approved for RSV is important for the team redefine the societal challenges to address for the research. Options can be the development of new better vaccines or the development of antivirals, which are still missing and always needed. New pathogens from the Mononegavirales order could be envisaged, particularly those where the expertise and the technical skills of the team can make a difference. This needs to be thought to maintain the chances of funding in the near future.

The team is in the best position for addressing the in vitro reconstitution of functional nucleoproteins (L+P+N) also in complex with host factors, this would have a very high impact together with structural and functional studies. The team needs to self-positioning towards new technologies related to nano Cryo CLEM putting in value its capacity to develop fluorescent tools and work in cell culture or even in the context of mice infection. Cell and animal infection will be the new substrates for structural characterization of macro molecular complexes at nanometric resolution. This combined and the in vitro reconstitution and structural/biochemical characterization will provide an unprecedented multi-scale understanding of viral infection.

Team 2: Coronaviruses (CORONA)

Name of the supervisor: Mr Nicolas Meunier

THEMES OF THE TEAM

The CORONA team focuses on coronaviruses, particularly SARS-CoV-2, building on expertise from porcine coronaviruses and influenza studies. They develop antiviral strategies mainly targeting the SARS-CoV-2 spike protein-ACE2 interaction, aiming to block viral entry. Their research also extends to nasal cavity immunity, where they uncovered mechanisms such as anosmia, showing how SARS-CoV-2 damages the olfactory epithelium and triggers immune cell infiltration.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The CORONA team was created in 2021 within the VIM research unit, evolving from the former Flu team. The original team had been advised to increase its participation in international meetings and symposiums and to strategically expand collaborations to better define its objectives. These actions were expected to enhance the team's capacity to recruit PhD students. During the period, the team was able to recruit seven PhD students. A total of 15 communications were reported, among them three abroad. Additionally, three posters were presented in collaboration with other teams from VIM. The collaborative network, for its part, is still underdeveloped in the context of advancing the new research theme on coronaviruses.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

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

EVALUATION

Overall assessment of the team

The CORONA team has shown strong capacity in addressing urgent SARS-CoV-2 issues. Since its establishment in 2021, it has rapidly built its research profile, offering insights into viral tropism in the olfactory epithelium and antiviral development. The team has been effective in securing competitive funding. Its small size and high turnover may limit its ability to manage multiple large-scale projects simultaneously and to publish extensively, even though ten articles were published during the period, which is noteworthy. The team's performance during the period was very good.

Strengths and possibilities linked to the context

The CORONA team's focus on SARS-CoV-2 and coronaviruses is highly relevant, given the ongoing public health challenges posed by Covid-19 and the potential for future coronavirus pandemics. It benefits from advanced infrastructure, including access to BSL3 laboratories, enabling effective research on highly infectious respiratory pathogens like SARS-CoV-2. The team has made significant contributions to the development of nanobodies and biosynthetic proteins targeting the SARS-CoV-2 spike protein, as well as to the characterization of SARS-CoV-2 infection in the nasal cavity. This research provides crucial insights into viral entry mechanisms and local immune responses, which are essential for the development of effective treatments and preventive measures.

During this period, the team secured 13 grants, including four ANR projects as coordinators and three as work package leaders, collectively amounting to €1.4 million in research funding.

Despite being relatively new, the team has established a commendable publication record, with ten articles in high-profile international peer-reviewed journals. Six of these articles were authored by team members as both first and last authors. Publications include *PLoS Pathogens*, *Cellular and Molecular Life Sciences* (multidisciplinary journal), and *Frontiers in Microbiology*. Additionally, PhD students who have defended their theses are associated with these publications. The development by the team of novel molecules targeting viral entry mechanisms and the design of therapeutic proteins demonstrates significant potential for both academic impact and clinical applications. The team's work on nasal cavity immunity and the mechanisms of olfactory damage caused by viral infections addresses a relatively unexplored area with substantial clinical implications. Moreover, two patents related to SARS-CoV-2 were filled. The team has hosted seven PhD candidates, two postdoctoral researchers from Chile and the US, three M1 students, and five M2 students. The researchers of the team have been involved in 17 individual PhD monitoring committees and eight thesis defense juries. Team members also contribute approximately 30 hours of teaching annually in master's programs, primarily in virology. Furthermore, the team has engaged in science communication, publishing several popular science articles, contributing to newsletters, and participating in media coverage.

Weaknesses and risks linked to the context

While the team has been effective, its relatively small size may limit its ability to undertake multiple large-scale projects simultaneously. This poses a risk, especially if senior researchers or essential technical staff are unavailable. The retirement of one of the principal researchers could pose a significant challenge to the team's continuity in the years ahead. Moreover, the limited number of senior researchers could impact leadership and mentorship for junior researchers and postdoctoral staff. The team, established only recently, has a limited network of national and international collaborators. This restricted network poses challenges for accessing diverse expertise and resources. It may also hinder the team's ability to contribute to and benefit from larger collaborative research efforts. Although the team has been successful in securing grants, its heavy reliance on competitive funding could pose a vulnerability for long-term projects if future grant applications are unsuccessful due to the high competition in coronavirus research. The team's research output may face limitations if funding or interest in SARS-CoV-2-specific research declines in the future. Furthermore, the team's funding sources are not very diversified and primarily depend on ANR funding. The development of studies on porcine epidemic diarrhea virus could be a step in this direction.

Analysis of the team's trajectory

Since its creation, the CORONA team has made significant strides in addressing urgent global health needs related to the Covid-19 pandemic. Its trajectory has been one of rapid growth, characterized by successful grant applications, and several publications. Key achievements include advancements in antiviral screening and the development of molecules targeting viral entry mechanisms, along with patented findings on spike protein inhibitors. A key focus will be the optimization of antiviral bioavailability, particularly for aReps nanobinders, which have shown promising neutralization of SARS-CoV-2 in vitro. The team will also focus on better understanding the immunity of the nasal cavity following SARS-CoV-2 infection. To maintain momentum in the post-pandemic era, it is necessary to diversify the research focus beyond SARS-CoV-2 to ensure long-term sustainability. Moving forward, the team will need to transition from an immediate pandemic response to a more sustainable long-term research strategy focused on broader coronavirus research and potential zoonotic threats. Diversifying its portfolio will be crucial for maintaining its relevance in a post-pandemic context. In this goal the team is investigating the mechanisms of PEDV (porcine epidemic diarrhea virus) entry for understanding viral pathogenesis and host interactions. The scientific priorities of the team are supported by efforts to stabilize technical expertise through key recruitments and planning for upcoming retirements within the team. The team's challenges will therefore be to increase its staff to successfully carry out ongoing and upcoming projects, continue diversifying its study models, develop its network of collaborators, and enhance its international visibility in a competitive environment.

RECOMMENDATIONS TO THE TEAM

Expand the Team: To handle the increasing complexity of projects, the team should consider recruiting more researchers and technical staff, including senior researchers, to enhance its capacity.

Diversify Funding Sources: While the team has been successful in securing competitive funding, it would benefit from exploring more stable, long-term funding sources, including partnerships with industry and participation in larger consortia (such as EU Horizon or NIH grants).

Broaden Research Focus: The team should look beyond SARS-CoV-2, expanding its research to include other emerging coronaviruses or related zoonotic viruses. This would help ensure the team's relevance in the years to come.

Strengthen Collaborations: The team already has a few international partnerships, it should seek to build additional collaborations to further increase its research impact and funding opportunities.

Enhance Valorization of Research: Given the potential for clinical and commercial applications of its work, the team should focus on translating its findings into therapeutic products, including antiviral drugs or diagnostic tools, and pursue efforts in patenting its innovations.

Team 3: Influenzae Virus (FLU)

Name of the supervisor: Mr Ronan Le Goffic

THEMES OF THE TEAM

The Flu team focuses on the influenza A (IAV) infection focusing on i) the PB1 protein relevance on host interactions and its role to allow viral strains to spread across species. ii) the generation of new more potent vaccines for IAV, iii) Functional characterization of NS1 protein and iv) the impact of prion proteins on IAV infection which is linked to the regulation of neutrophil cells recruitment.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was recommended to increase participation in international meetings and symposium, and expand strategically the collaborations to better define the team objectives. All those actions should enhance the capacity of the team to recruit PhD students.

However, during the period there have been a split of the team into Corona and Flu teams. We therefore consider the previous recommendations as valid for both teams now.

During the period the team has presented two posters in national congresses. Twelve oral presentations in France, two in Canada and one in UK. The oral presentations on international congress are still very limited.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

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

EVALUATION

Overall assessment of the team

The Flu team addresses one of the most imminent viral threats for human health. In particular focuses on understanding the spread of avian flu into humans which is one of the most important threats for future pandemics. The team has published a relevant number of publications in specialized journals with 19 as main authors and obtained the funding of fourteen projects in the period. The team will have to face the challenges posed by the excision of the team and the lack of teaching, mentoring and outreach activities. Considering all these factors the team performance in the period was very good to excellent.

Strengths and possibilities linked to the context

During the period the team has 47 publications with 19 main authorships including the single PhD student of the team in five of them, two as first author. This is a good output attending to the size of the team most articles are published in rather specialized journals as frontiers in immunology or viruses, with some notable exceptions as the Nature paper in collaboration with the BMP team and others on antivirals targeting phase separation of viruses or a Nature Materials where the team does not have a main role.

The team has provided a new influenza vaccine consisting on incorporating IAV epitopes from hemaglutinin and the matrix protein 2 in nanorings made by RSV nucleoprotein. The vaccines conferred protection to mice but not chicken against the H5N8 highly pathogenic strain. The team also reported that the protein PB1 F2 is able to trigger. The team subsequently associated the inflammatory response triggered by the protein to the formation of amiloid like fibers. Now the team to study how this protein is important for breaking the cross species barrier.

The team is participating in national grant reviews (8), recruitment jury (3) thesis committees (8), PhD thesis defenses (7) and HDR (5) with the main implication of the team leader and two other researchers to a lesser extent. The team has managed to finance their research achieving through fourteen international and national grant from ANR (as coordinator in an ANR REACTIV grant), DIM One Health Livestock Vaccine innovation Fund Canada and the Bill and Melinda Gates Foundation (as co-coordinator), the FRIA2019 among others. This has provided more than 1265 k€ in the period. The team has expertise and access to BSL3 and BSL2 laboratories and mice and poultry models, this is an important asset.

The team has deposited a patent of a vaccine comprising the M2E nanoparticles and HA1 protein. It has also a research contract with Pileje Laboratories.

Weaknesses and risks linked to the context

The team has experienced an excision which has reduced the number of permanent researchers and as a consequence the publications output, the grant money obtained, and probably a reduction on the research lines proposed. In this context the team seems to be dropping the axis related to the development of new vaccines.

The team has been carrying out a very good research on influenza vaccines and the study of viral PB1 F2 and maintained a good rate of success on grant applications, however some of the grants were obtained by researchers that now are in the CORONA team thus reducing the capacity of the team to fund the research.

For outreach the team published an article in the Dossier grand public INRAE about IAV spread in farms and the participation in Biosis Days 2020 in Annecy where a seminar was presented after invitation of Ideas For Animal Feed (ID4Feed). There is not a regular activity for outreach in the team in line with the unit in general.

The IAV is a very competitive field. Some interesting results can come out from the proposed research, however there is the risk of neglecting or decontextualizing these results from other critical viral factors could limit the impact of the research carried out. Is important to relate the findings on PB1 F2 and NS1 on basic and essential molecular mechanisms of infection as replication, budding or essential host-pathogen interactions. This will be a way to increase the impact of the research and the international leadership of the team in the field of Influenza virus infection and spread.

Analysis of the team's trajectory

The team focuses on the biology and the interactomes of two proteins of influenza virus (IAV): PB1 F2 and NS1. Both proposed to form lipid phase separation that can be structurally characterized by soft x ray and FIB-SEM and potentially targeted with antivirals.

The team proposes the Yeast 2 hybrid screening technique for the study of the interactome of both proteins. Through a strategic collaboration with the National Veterinary School of Maisons-Alfort as well as colleagues from ANSES in Ploufragan, they will have access to viral strains which has achieved the break through the interspecies barrier. The characterization of these strains in mice through fluorescent tracking of infection will allow to track the tropism particularly in brain damage and infection of pregnant mice. The latest will allow to study the trans-generational consequences of viral infection. There is a crosstalk between the two approaches by comparing NS1 and BP1 F2 proteins of these strains and incorporate them in the interactomic workflow or in the study of phase separation for these particular strains.

Due to the excision of the team after the Covid19 pandemic the publication and grants were proportionally reduced and now the challenge is, keeping IAV as central research theme, to grow again in order to achieve a stable context of personnel and resources. The reduction on research goals is unavoidable, as the elimination of vaccine development from the project. Now the team will focus on two viral factors important for host interactions. The project is very exploratory and this comes with uncertainty for assessing the future impact of the research. Is thus important to have collaborations allowing to mitigate the risk and improve the impact of the research.

The success of the team in the next period will depend on the capacity of the team to attract talent. Improving the teaching and oral communications in national and international contexts will be instrumental for this goal. The increase on impact of the research will also help on that sense.

Despite the challenges, the team has extensive experience and multidisciplinary approach relying on exceptional biocontainment facilities, including BSL3 and BSL2 laboratories. Based on its robust research capabilities and a good leadership the team has a huge potential for facing the challenges ahead.

RECOMMENDATIONS TO THE TEAM

Establish new strategic collaborations: in addition to the strategic collaborations allowing for access to viral strains, and accounting for the capacity of the team to work in BSL2 and BSL3 laboratories, it would be interesting, in order to rise the impact, to find collaborators addressing the same issues at different levels as the structural or the biochemical. In this way new viral host interactions should be better characterized in order to provide clues on the mechanism of action underlying virulence and cross species infections.

Teaching and mentoring: The number of PhD students should improve. In order to achieve this objective, teaching activities should be regularly performed in the university to be in contact with Master students. Hosting master students will also increase the chances of successful recruitment of good PhDs.

Activate the full potential of permanent researchers: Increase on the participation of researches in evaluation bodies, besides the group leader, would be convenient. This also apply for grant application efforts and PhD direction. The incorporation of personnel by recruiting new researchers and the recruitment of one PAR in the team should be a goal. Perhaps the creation of a mutualised platform related to the expertise of the team could be instrumental for the recruitment of one PAR.

Increase visibility by trying to reach one oral presentation per year in national or international meetings or seminars per permanent researcher of the team.

Increase of funding. In order to optimise effort vs income regarding funding applications, the team should focus on obtaining perhaps less but more substantial grants (250 k€ or above) through ANR and European or other international consortia. Consider that small grants are fine for young researchers but are too short lasting and still time consuming for established researchers.

Many scientific objectives where presented, is important to be realistic and prioritize research objectives for effectively carrying out research in a context of reduced manpower and funding (until these two deficits are overcome).

Team 4: Fish Infection and Immunity (IIP)

Name of the supervisors: Mr Pierre Boudinot & Mr Eric Duchaud

THEMES OF THE TEAM

The main themes of the IIP team include investigation of fish pathogenic flavobacteria and the mechanisms of the immune response in fish against viruses and bacteria.. This research is being developed across six areas: i) Analytical, comparative, and functional genomics of flavobacteria; ii) Epidemiology, diagnostics, and molecular phylogeny of pathogenic flavobacteria; iii) studying the immune response of fish to viruses, with a particular focus on the type I interferon pathways; iv) deciphering the mechanisms of B cell responses; v) investigating the immune response to pathogenic Flavobacteriaceae; and vi) investigating the genetics that drive resistance to infection in trout.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous Hcéres has six recommendations: 1) strengthen the leadership in EU/INT projects. The team has successfully obtained EU and INT grants (eight, incl. four still running in 2025-26) and has been involved in INT collaborations for research, workshop, teaching (Canada, Chile, Japan...); 2) licence or patent, scientific committees. The IIP team has collaborated with several industrial partners (e.g. VIRBAC, LaboFarm), and has participated to FELASA committee; 3) number of masters. The team supervised ten trainees, a significant improvement on the previous evaluation; 4) the parity**.** Since the last evaluation, the team has worked on the parity problem. Among the permanent staff, there are still three DR men and two CR women (one CR woman left in 2020 and one CR woman joined in 2023), 3W/2M for the post-docs, and one woman PAR (joining in 2020). It is important to note that due to the INRAE recruitment type, the team is not able to choose the gender of the new recruits; 5) possible merger with VMP. The unit disagrees. In accord with the unit direction team, our committee did not see any urgency to merge the two teams which have clear distinct research themes; 6) coordinating common grant applications and recruitment of technical help. IIP has received several European collaborative grants (coordinating the project FLAVOCONTROL). Finally, since last evaluation, two technicians have been recruited (for two leaving) and three CDD (IE and AI) and five post-docs have been recruited during the five years.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

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

EVALUATION

Overall assessment of the team

The IIP team has an outstanding track record in terms of scientific production and attractiveness. The team has also an excellent level of collaboration with companies such as VIRBACH although none has led yet to patents. The team has increased the number of internships (Masters, BTS), but the number of PhD students could be increased. The overall assessment of the team is therefore outstanding.

Strengths and possibilities linked to the context

The team has made important discoveries in all areas over the last five years. In collaboration with a US team, they identified the B cell germinal centre in trout and its role during infection (work published in *Science Immunol* 2023; *Science Advances* 2023; *Journal of Immunology* 2021-2022). They also collaborated on a manuscript that characterise the STING-dependent inflammation (*Science Advances* 2020). They have performed a gene expression profiling analysis of the pathogen Flavobacterium psychrophilum in 32 different biological condition (ISME Commun, 2021). This work highlights key pathways that could be targeted for future research. Finally, a massive effort was made to characterise the genetic resistance of trout to Flavobacteriaceae and VHSV (AQUAFAANG and EUROFAANG projects, BMC Genomics).

IIP has an outstanding attractiveness. The IIP team benefits from a large number of grants including six national (three ANR coordinator, one INRAE Métaprogram coordinator), three Carnot FFE as coordinator, seven EU (one as coordinator) and one international (as coordinator) over the five years, totalling 615 k€. This has led to an increase in collaborations (such as DTU in Denmark or GWNU in South Korea) and a large scientific outreach (five international visiting post_docs, fourteen conferences talk, incl. six international such as the « *Evolutionary scales of the immune system* » Max Planck, in Dresden (2022). The IIP has also an outstanding scientific expertise. The IIP has published a large number of manuscripts (112 publications, including 72 in the 4 research topics of the team) and has participated in teaching workshops (such as the Fish Immunology Course at Wageningen University) and committees (FELESA recommendation). All team members have published a large number of articles - With team leader having published the most. The scientists have published In high-profile Journal such as *Science Advances* and *Science Immunology*, and in very good specialised journals such as *NPJ Vaccines*, *Journal of Immunology* or *Virulence*. IIP has also been instrumental in constituting a collection of KO fish cells lines for genes linked to the type I Interferon responses and in leading to scientific breakthroughs on the B cell response and germinal centers in fish. The team is also expert on the Flavobacteriaceae family (known to be difficult to culture) with the aim to develop new vaccines. Finally, the IIP has an excellent position with industrial partners and for obtaining patents: The team has been collaborating with several industry partners (Labofarm, Biochenevert, VIRBAC) placing them in a good position for Cifre PhD funding (already two acquired in 2017 and 2020) and potential patent applications for vaccines (one ANR with industrial partner, one FUI-PSPC and three Carnot FFE).

Weaknesses and risks linked to the context

The team has been very effective in obtaining grants (Int, EU, National, Local) but the amount of energy needed to complete these projects requires a large staff. Four ITAs (one IR, one IE, two technicians) for five scientists is still a good ratio for a research team, but may not be enough to run more than ten projects simultaneously. With only one postdoc at the time of the evaluation (2023-2026), it is important for the team to recruit new non-permanent staff to carry out the project and help supervise PhD students. For a team of five scientists, the team still has a low number of PhD students for five years (five have passed, and only one current but co-supervised by another team: INRAE GABI). The committee noted the difficulties in recruiting PhD students via the ED route. Finally, the team did not engage in debate or knowledge sharing with the public. While it is understood that the VIM unit limited public engagement due to the negative impact of the prion crisis, the IIP could have been more active in vulgarisation articles, school lectures.

Analysis of the team's trajectory

The IIP team has been an excellent research group over the past decade, producing high quality scientific articles and important advances in knowledge of fish immunology. Over the next five years, the team will continue to work on all of the current topics and can be expected to have a major impact on the fish science community. The team will continue to establish a cell collection of ISG-KO cells and annotate sequencing data (FAANG and ENCODE projects). Both will be extremely useful to the community and great tools to add value to

European/National projects. The team also plans to extend its work on the Flavobacteriaceae family, research that is urgently needed to understand the immune response mechanism during fish infections.

This is a monumental task with its own challenges, partly due to limited staffing, but the IIP is well placed to succeed. To facilitate the success of this project, it is important for the team to consolidate and create new collaborations with the private sector for research funding, patent creation and student/post-doc funding. In addition, this research could be supported by the French government's plan to strengthen aquaculture.

RECOMMENDATIONS TO THE TEAM

There was a peak in funding in 2022 with eleven concurrent projects (only four permanent scientists at that time). The team needs to carefully balance the number of projects with the number of staff. Continue to recruit CDD/post-docs to support the manpower of the team. Continue to work towards parity within CR-DR. While it is understandable that the gender gap is hard to fix due to the concours type of recruitment, it is an important message to make an effort to balance the gender in the different grades. All three DRs are men, encourage CR women to become DRs if they are interested. The IIP team should also recruit more PhD students. If the team struggles to get funds from the *Ecole Doctorale*, it should continue its efforts to find PhD students through other means (Cifre, ANR, international scholarships). Finally, the team should try to valorise its research results. Taking advantage of its developing partnership with industrial and commercial applications of a vaccine (VIRBACH), the team should focus on translating its results into patents.

Team 5: Fish Molecular Virology (VMP)

Name of the supervisor: Mr Stéphane Biacchesi

THEMES OF THE TEAM

Team VPM develops prophylactic measures against viral pathogens in aquaculture while studying virus-fish molecular interactions. Their work includes creating live attenuated vaccines via reverse genetics and structure-guided vaccinology, ensuring high immunity and preventing reversion to virulence. They identify virulence markers to distinguish pathogenic from non-pathogenic viruses and study virus-host interactions, focusing on proteins inhibiting RIG-I-mediated interferon induction. High-throughput screening using zebrafish larvae aids antiviral discovery. Since Covid-19, the team has also studied zoonotic and epizootic coronaviruses, contributing to aquaculture and broader virology research.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations to the team were about maintaining a strategic balance between fundamental and applied research, with a focus on vaccines and diagnostics to adapt to limited funding. A long-term collaboration with a private partner on novirhabdovirus vaccine vectors was encouraged. The team was commended for continuing publishing in leading virology journals and advised to further boost their scientific capacity by increasing the number of PhD students. Considering the small size of the team, limiting projects to two main axes was recommended.

Over the evaluation period, the team trained two PhD students (one starting in 2023), three postdocs, and six students (four at the Master 2 level). In parallel, the team secured four funding grants from INRAE and the Carnot France Institute, as well as equipment funding for the L2-IVIS platform, in addition to the ANIHWA ERA-Net funding, which concluded in 2019. Research focused on two areas, including coronaviruses, demonstrating robust scientific output in both domains.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

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

EVALUATION

Overall assessment of the team

The team has an excellent record of scientific production, collaboration, and attractiveness, with excellent complementarity between fundamental and applied approaches. This synergy has led to the development and implementation of several infection models in addition to a patent. Thus, the overall assessment is excellent.

Strengths and possibilities linked to the context

The team has strong expertise and visibility, particularly in studying virus impacts on innate immunity and developing molecular tools to distinguish virulent viruses. They created an effective vaccine platform targeting Novirhabdovirus strains and published 28 papers during the period, including eleven on fish viruses and a patent. Their productive coronavirus collaboration resulted in 17 publications. Dedicated to securing funding, their future success in obtaining grants is expected to sustain and enhance their activities. The expertise of the team's two researchers in viral genetics is a significant asset to its projects. The high researcher-to-technical staff ratio (1/1) further strengthens the team's capabilities. The integration of both applied and fundamental research ensures diversified outcomes, including scientific publications (Front Microbiol, Front Immunol, J Virol, Fish Shellfish Immunol, for which, members of the VPM team are key authors (forst, last authors, or both), patents (Invention disclosures DI-RV-21-0059 and DI-RV22-0142; Patent WO2024/003007), and outreach to a broad audience (through INRAE website and media interviews). The team has a strong track record of delivering valuable products to the economic and social community (vaccines, infection model of zebrafish larvae by fish rhabdoviruses for screening of antiviral and immunostimulant compounds, antibodies directed against a salmonid alphavirus, Expression vectors derived from spring carp viremia virus).

National and international (Cornell University, IA USC (Spain), DTU VET (Denmark), IZSVe (Italy), CEFAS (UK)) collaborations, play a key role in driving the team's success and enhancing its scientific output.

Weaknesses and risks linked to the context

The diversification of the project's research axes, previously highlighted as a potential risk during the last evaluation, has not proven to be a significant weakness, as substantial progress has been achieved in each area. This success likely required considerable effort, especially given that the team leader also manages a technological platform. A notable challenge, as acknowledged in the self-assessment, is the difficulty in securing sufficient funding for all these axes despite active participation in ANR calls. The team has a full potential to secure fundings that will support its research and strengthen its capacity to train and host more PhD students and early-career researchers. It is worth noting that the team has just received an ANR grant, just after the expertise period (starting in 2025). So, the team is on the right track.

Analysis of the team's trajectory

The work developed by the team builds on the expertise of its members in fish virology and virus genetics. In addition to their strong skills in generating recombinant RNA-based vaccines, the team has developed high-throughput screening methods for identifying new antiviral mechanisms. The NOVIVACC approach, in particular, has proven highly successful. The leadership change during the evaluation period did not impact the team's productivity, demonstrating successful supervision and management by the current PI. The prospective will address fish viral infections at both applied and fundamental levels through five research axes: (i) expanding the NOVIVACC platform: developing additional antigens for important fish viral pathogens, supported by EU AH&W funding from 2024 to 2026. (ii) viral proteins and virulence: investigating the role of viral proteins like nucleoprotein N in the virulence of VHSV and IHNV in rainbow trout. (iii) global warming impact: studying the effect of elevated temperatures on VHSV and IHNV, with funding for a PhD thesis. (iv) tools and models: developing zebrafish larvae models and high-content imaging for studying antiviral and immunomodulatory compounds. (v) aquatic alphaviruses : exploring mutations in the E1-E2 envelope protein complex to understand virulence and improve diagnostics and therapeutics.

The project is ambitious and of high interest both for advancing knowledge and combating fish viral infections. However, substantial funding is needed for four of the five axes.

RECOMMENDATIONS TO THE TEAM

Remain steadfast despite limited support for aquaculture research and sustain efforts to secure additional funding (e.g. possible new plan from French government). Keep working closely with industrial partners. Strengthen efforts in training young scientists (PhD and Early-Career Researchers). To prevent overloading the team, avoid further diversifying the developed research topics.

Team 6: Protein Macro-Assemblies and Prion diseases (MAP2)

Name of the supervisors: Mr Davy Martin & Mr Pierre Sibille

THEMES OF THE TEAM

The MAP2 team is dedicated to Prion diseases, studying their replication, spreading and toxicity.
They present three main themes: replication with a dynamic approach of PrPsc assemblies, host and PrPc characteristics, the characterisation of emerging prions strains.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Regarding the recommendation to improve the development and the exploitation of the intellectual property associated with the team's research: The team has strongly followed this advice in collaboration with the Animal Genetic and Integrative Biology Unit (GABI, UMR 1313), coupled to their worldwide recognized expertise in the prion field for obtaining industrial contracts. However, the closing of the dedicated to prion experimentation at IERP now drastically reduces the possibility to carry on this type of work and thus threatens the team's income.

Attending the recommendation that all permanent principal investigators (PI) must have their HDR: the team has defended in the period one more HDR (2022). It was recommended to attract more postdoctoral fellows. On the period the team has had five post docs.

It was also recommended that the great expertise accumulated by the MAP2 team during the evaluation period should be increasingly used to extend our knowledge in protein misfolding disorders to open new research avenues in human neurodegenerative diseases. In this context the team has not achieved yet collaborations with medical experts in neurodegenerative disease but they are conscious of the need.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

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

EVALUATION

Overall assessment of the team

The overall assessment is excellent to outstanding because of the high productivity in terms of number of publications and the funding. The team has been able to obtain funding through competitive calls and contracts with the private sector. This assessment needs to be framed into the perturbations that the team has gone through during the period and how it has managed to continue its research adapting to the new situation.

Strengths and possibilities linked to the context

The MAP2 team combines biological, biophysical, structural biology and mathematical modelling approaches for the understanding of prion dynamics and propagation. Through mathematical models they describe the dynamics of network of exchange between different PrPssub-assemblies. The team is contributing to change the paradigms for the understanding of prion diseases and has provided evidence on different aspects of the causes and spread of the diseases as the oxidative stress in the origin of prion diseases rather than PrP protein concentration in the organism or the relationship with perturbations in the internal vesicle trafficking of the cell, the determinants of prion amyloid spread or the interactions with A-beta 1-40 amyloids. They have developed very interesting tools for the diagnosis and the study of the disease such as strain-specific AlphaReps or in vitro amplification systems.

The combination of these important conceptual discoveries and development of biosanitary tools is a powerful combination of basic and applied science that the team carries out with success.

The publication track of team in the period is very good with 47 articles published, 18 as main authorships in journals such as Cell and Tissue Research, Plos Pathogens, Scientific reports or Viruses.

The team has a remarkable visibility through education, evaluation and communication activities: The prize Lauriers de l'INRAE was received by two team leaders for the socio-economic impact of their research on prions. Six researchers of the team have participated altogether in summer schools (2) courses in different universities and institutions as Pasteur institute or the ENS Paris, safety training lectures at masters (2), overall, an excellent participation enhancing visibility. The laboratory has trained four PhD students, five post-docs, one US PhD student stayed six months in the laboratory. Nine M1 and two M2 students, seven Erasmus students, two BTS and two engineers. The evaluation activity of the team is remarkable. Team leaders have been actively reviewing eight national and ten international grants as FRM, ANR or SBSF or NIH, respectively. The activity on peer reviewing is also remarkable (149 for the whole team) with editorial activity in Scientific Reports, Plos One or Current research in microbial sciences. The team has also covered PhD Juries (18) and participated in recruitment juries (7). Two team researchers are and have been members of many scientific councils in INRAE animal health department and other organisms as CEUCO, Hcéres, French committee in virological safety, ANSM or Anses.

The team is attractive because of their success in grant and contracts funding achieved: The team has obtained 26 grants and contracts with the ANR, European Horizon 2020, DIM one Health programs and contracts with six entities including Franklab and the SATT Ouest. The total amount of funding achieved in 2,358 kE in the period.

Weaknesses and risks linked to the context

The team has been through very delicate moments from the human and professional point of view with the loss of an ex-collaborator because of a prion disease. This has had the following implications: 1) The closing of the animal facilities dedicated to prion experimentation at IERP which now drastically reduces the possibility to carry on this type of work, 2) Activity slowdown due to audits, enquiries and moratorium (2019-2022) with still ongoing, 3) a reduction of the permanent staff with the departure of three persons working on cell biology and 4) A tremendous personal shock for the team members.

The lack of collaborative networks with medical experts in neurodegenerative disease still persists and this is reducing the funding opportunities, visibility and publication impact of the team (which is however evaluated as very good).

Even if the publication rate is good the journals are rather specialized journals. This is limiting the access of the team to fundamental research grants.

We have found only, in the publication list, three of the four PhD students in the articles and not always as first author. A first author publication for a PhD student is paramount to be able to carry out a scientific career.

Analysis of the team's trajectory

The team is a referent team for prion research in animals and is carrying out excellent research on different aspects of the disease. Research, funding, contracts with industry, training... The team is addressing all these key aspects successfully. They manage to tackle from the mechanistic aspects at the molecular and cellular levels to the spread in animals, from the early diagnosis of prion diseases to the mathematical modelling of the prion disease spread. This versatility is rare and reflects an open mind spirit that has a strong impact on the team's trajectory.

The uncertainties about the use of L2-L3 laboratories must be unblocked at some point. The team will have the opportunity then to resume their research activity back to highest potential and be able to reconstitute the team architecture (in terms of expertise, personnel and experimental workflows). For the next period this will probably be a major objective.

The team has thus an enormous potential and, with the full support of the supervising institutions and regulatory agencies, will have access to Inserm labelisation at some point, get in the circuit of the national medical research and expand their influence towards providing diagnostics and therapeutic solutions to patients.

In conclusion, the path is being very hard for the team but the past, present and future work can truly contribute to save lives, and this really matters.

RECOMMENDATIONS TO THE TEAM

Publication in journals with more impact: Even if the results provided are very interesting and worthy is important to identify and pursue those breakthroughs more relevant for the field and increase the impact of the publications (at least of few hits on the period). This will also an effect on increasing the funding opportunities in basic research and the visibility of the team internationally.

Establish collaborations with human medical laboratories: This is still unmet recommendation from the last evaluation. It has potential to meet a one health approach, will give more impact to the research work and the opportunity to bring early diagnostic tools to society.

Establish a comprehensive framework of the prion research in L2 and L3 laboratories: Together with INRAE and other organisms concerned it is important to set the right safety framework to resume the research on prions and bring to the top the extraordinary labor of the team. The mathematical models are very important but cannot substitute.

Redynamise the team (this is a recommendation beyond the team): After the struggles of the last years the team needs to recover the full awareness and passion about the importance of their research and feel the support of the unit, the society and the supervising institutions. Is important to look to the future with optimism. A safe environment for working with PrPs and go back to resuming the full activities of the team is possible.

Team 7: Vaccine, Immunopathology & Immunomodulation (V2I)

Name of the supervisors: Ms Delphyne Descamps & Ms Isabelle Schwartz

THEMES OF THE TEAM

The V2I team is investigating 1) the immune pathways and mechanisms in the pulmonary diseases in human and 2) how to manipulate this immune response with vaccinal strategy, use of microbiota or targeting of specific proteins (such as IRAP or TAX1BP1). 3) Since 2023, the V2I has welcomed 6 HU researchers and thus develop their theme.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Three points were raised in the previous evaluation: 1) Improving the quality of scientific production. The team has remarkably improved the number (71 papers as main authors) and the quality of scientific production either linked to the hospital team (The Lancet Respiratory Medicine, The Journal of Heart and Lung Transplantation) but also to the INRAE team (Mucosal Immunology, NPJ Vaccines). 2. Parity. Since the last evaluation, the team has improved its parity. There are three women DRs and the team leader and her deputy are women. The arrival of the hospital team has minimised this, as this subgroup is made up of 5/6 men. Two AI women have retired and one IE woman has been recruited. 3. The valorisation of the vaccine project needs to be evaluated. The H2020-SAPHIR project aimed at the vaccine in livestock has ended in 2019. This project was extremely rich in results: 1) new follow-up projects (NEOVACC, PAW&H); 2) manuscripts and 3) organisation of conferences (European Veterinary Immunology Workshop, International Congress on Lung Transplantation). 4) SAPHIR also enabled collaboration with the private sector (e.g. Vaccibody, Xeolas...). 5) Two PhD scholarships were obtained through this EU grant. 6) Finally, the V2I team also uses SAPHIR to improve inter-team collaboration with BMP, FLU, I2P.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	6
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	**14**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	**5**
Total personnels	**19**

EVALUATION

Overall assessment of the team

The V2I team is a team of experts in respiratory diseases, both human and animal. They have benefited from the arrival of six PU-PH in the team in 2020-2023, which has significantly increased their scientific production and strengthened their expertise in transplantation. The team also coordinated 21 research programmes (EU/ANR) and successfully established contracts with non-academic partners. There is still room for improvement in attractivity, such as number of PhD students and international visitors, and choice of journal for publications. The overall assessment of the team is therefore excellent to outstanding.

Strengths and possibilities linked to the context

The team has made important discoveries in all three areas over the last five years. For example, they identified a novel regulator of the type I IFN response during respiratory syncytial virus infection. IRAP has a suppressive function in alveolar macrophages of neonatal mice and could be targeted to improve the immune response to viral infection. This work was published in *Mucosal Immunity* and was selected as an Editor's Choice 2021. The team also reported on several innovative therapies that could aid transplantation: A case report using C1-esterase inhibitors (published in European Respiratory Journal); and another on the use of imlifidase, an IgG-degrading enzyme derived from Streptococcus pyogenes, which could desensitise lung transplant candidates.

The V2I team has an excellent track record in terms of scientific production and attractiveness in the field of humans. The merger with the FOCH administration has been very positive, resulting in 196 publications, including in highly visible journals (such as European Respiratory Journal or Allergy) and more than 90 seminar invitations (international and national). The team coordinated the large EU H2020 SAPHIR project (which ended in 2019) and, keeping the momentum, established successful follow-on research programmes (such as NEOVACC to plan vaccination strategies for neonatal animals) as well as industrial partnerships. V2I obtained nine competitive grants of ANR type (total sum of 1879 k)) and six industrial/regional grant (456k). In addition, scientists have editorial responsibilities: in Anaesthesia and Critical Care Medecine, Journal of Heart and Lung Transplantation. They have also organised several national and international events such as European Veterinary Vaccinology Workshop in 2018 or the International Congress on Lung Transplantation.

The succession of the team leadership in the coming years has been carefully planned, with co-leadership between one INRAE DR (team leader) and one PU-PH (deputy leader), further strengthening the synergy between the two subgroups and complying with parity requirements. The team is well organised with annual/monthly and bi-weekly meetings, allowing good interaction between the two research sites.

The team has established a large number of collaborations in all its three research pillars: perinatal lung (e.g. Pilege), transplantation (e.g. XVIVO-Perfusion) and human respiratory diseases (e.g. Oxyvie). These collaborations have so far contributed to the recruitment of non-permanent staff, equipment and seminars, but will undoubtedly lead to patents in the future. Bio-rad commercialised an antibody developed by V2I (2023).

With their funds, V2I has acquired key equipment such as the Luminex, the IVIS-Spectrum or the Chromium 10X genomics). This will help to carry out unique projects and collaborate with other teams within the VIM.

Weaknesses and risks linked to the context

Although the number of senior scientists has increased significantly in 2020/2023 (three DR + six PUPH), the V2I team has only supervised eight PhD students (including four that have passed in 2018/2019). There is only three PhD at the moment and no PhD students have been enrolled since 2022. Instead, the team relied on a large number of M2 students (11), CDD and post-docs.

V2I is the only team in VIM to have not welcomed any international scientists, whether they are students, post-doc or experienced researchers.

Outreach activities are lacking but were explained by the DU as a voluntary reduction of public engagement due to backslash and threats.

As noted in the self-evaluation, many publications have been in MDPI and Frontiers. Although it is true that Frontiers is heterogeneous in terms of reviewing practices, the team could try to publish in more reputated journals first if the results are novel enough.

Analysis of the team's trajectory

The V2I team has been carrying out excellent research. Their research project, divided into three pillars, is ambitious but successful in terms of publications, grants and industrial partnerships. The recent acquisition of equipment and new techniques (sc-RNAseq, organotypic lung cultures) should also propel them as a sought-after research group to collaborate with. V2I has a clear and ambitious trajectory, consolidating its knowledge of immunomodulation in the two areas in which it is already an expert (perinatal lung immunity, lung transplantation). The third axis, the multi-omic approach, will provide a wealth of information on biomarkers in lung diseases. This could feed several future research projects.

An important objective of the V2I will be to maintain a constant balance between the interests of INRAE and FOCH in order to promote research on animal and human respiratory diseases. In particular, it will be advantageous to promote projects that combine both sides, rather than having each side compartmentalised.

The team now has what it takes to become a major player in lung disease/transplantation research. The 2030 plan and the management of the team (co-leadership, CR/ITA recruitment, meetings) show a clear vision of the research goals of the team for at least the next 5 years.

RECOMMENDATIONS TO THE TEAM

Maintaining the momentum: the results of these 5 years have been outstanding. The team should build on these very successful five years and continue to obtain grants from national and European agencies and strengthen links with industrial partners (patents will eventually come).

Training the next generation of researchers: V2I has supervised eight PhD students (currently only three). The team now has nine HDRs and should supervise more PhD students over the next five years. The team would also benefit from international staff (PhD students, post-docs or senior researchers). Finally, the team needs a new ITA and a CR to replace the staff that have left (two ITA and one CR) or will leave the team in the future.

Balanced research topics: as human disease topics become more attractive (grants and student projects), it will be a delicate task to navigate between the team's 2 topics. The team should be careful not to lose the veterinary side of its research (INRAE).

Finally, as the unit is now considering reinstating these outreach activities, V2I should be fully involved. The public would probably be very interested in the team's research (vaccines and transplantation).

CONDUCT OF THE INTERVIEWS

Dates

Start: 04 décembre 2024 à 09h00

End: 05 décembre 2024 à 18h00

Interview conducted: on-site

INTERVIEW SCHEDULE

Agenda 4 décembre

9:00-9:10	Hcéres, règles et procédures par B. Bartosch Public (tous les membres de l'unité)
9:10-10:00	Présentation administrative et scientifique de l'unité
10:00-10:20	Temps de débriefing et pause (huis clos)
10:20-11:00	Équipe "V2I "
11:00-11:40	Équipe "FLU"
11:40-12:00	Temps de débriefing et pause (huis clos)
12:00-13:30	Déjeuner du comité de visite (huis clos)
13:30-14:10	Équipe "BMP"
14:10-14:50	Équipe "CORONA"
14:50-15:20	Temps de débriefing et pause (huis clos)
15:20-16:00	Équipe "VMP"
16:00-16:40	Équipe "IIP"
16:40-17:20	Équipe "MAP2"
17:20-18:00	Temps de débriefing (huis clos)

Agenda 5 décembre

09:00-09:45	Entretien avec les ITAs En l'absence des responsables hiérarchiques
09:45-10:30	Entretien avec les chercheurs
10:30-11:15	Entretien avec les post-docs, les doctorants, les étudiants en master, etc
11:15-11:45	Temps de débriefing (huis clos)
11:45-12:30	Entretien avec les représentants des tutelles (huis clos)
13:30-14:15	Entretien avec la direction de l'unité (huis clos)
14:15-18:00	Rédaction du rapport final (huis clos)

GENERAL OBSERVATIONS OF THE SUPERVISORS

UVSQ
université PARIS-SACLAY

Le Président de l'Université de Versailles Saint-Quentin-en-Yvelines

A

Monsieur Stéphane Le Bouler,
Président
Haut Conseil de l'évaluation de la recherche et de l'enseignement supérieur
2 rue Albert Einstein - 75013 PARIS

A Versailles,
Le jeudi 23/01/2025

Ref. DER-PUR260024782 - VIM - Virologie et immunologie moléculaires

Objet : Evaluation des unités de recherche – Volet Observation de portée générale

Monsieur le Président,

Nous avons pris connaissance avec le plus grand intérêt du rapport de l'HCERES concernant la demande de renouvellement de l'Unité de Recherche (UMR 0892), dénommée « Virologie et Immunologie Moléculaires (VIM)», portée par Mme Sabine RIFFAULT.

Nous remercions l'HCERES et le comité pour l'efficacité et la qualité de leur travail d'analyse et pour leurs recommandations constructives que le directeur d'unité et son équipe ne manqueront pas de mettre en œuvre avec le soutien de l'Université en collaboration avec l'ensemble des tutelles de l'unité pour la période quinquennale 2026-2030.

Nous vous prions de croire, Monsieur le Président, à l'expression de nos cordiales salutations.

Professeur Loic Josseran
Président de l'UVSQ

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Jouy-en-Josas, Februray, 5th 2025

To the HCERES evaluation committee

We would like to extend our sincere thanks to the entire HCERES board for their time and dedication during the evaluation process. We collectively appreciate the professionalism and kindness demonstrated throughout the evaluation. This thorough review will undoubtedly help us strengthen our scientific efforts and enhance the overall cohesion and collective life within the VIM unit.
We were particularly pleased with the positive review of our request to form a UMR with the INSERM label.

We are committed to implementing the recommendations provided and continuing to pursue scientific excellence, meaningful collaborations, and impactful contributions to both academic and societal fields.

Once again, thank you for your time, effort, and thoughtful evaluation.

Yours sincerely,

Human Rezaei
Head of the unit
Molecular Virology and Immunology

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