Research evaluation

EVALUATION REPORT OF THE UNIT

RETRO-ENDO - Physiologie et pathologie moléculaires des rétrovirus endogènes et infectieux

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université Paris Saclay

Centre national de la recherche scientifique – CNRS

Institut Gustave Roussy - Cancer campus grand Paris

EVALUATION CAMPAIGN 2024-2025

GROUP E

Report published on May, 05 2025

High Council for evaluation of research and hgher education

In the name of the expert committee :

Gaël Cristofari, 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

Chairperson:	Mr Gaël Cristofari, Inserm, Nice
Experts:	Mr Patrick Lomonte, Université Claude Bernard Lyon 1 (representative of CoNRS) Ms Cécile Malnou, Université Toulouse 3 (representative of CNU)

HCÉRES REPRESENTATIVE

Ms Birke Bartosch

REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Ms Marie-France Delauw, CNRS
Mr Éric Deutsch, UPS
Ms Emma Pailler, IGR
Ms Anne Paoletti, IGR
Mr Frédéric Valès, CNRS

CHARACTERISATION OF THE UNIT

- Name: Physiologie et pathologie moléculaires des rétrovirus endogènes et infectieux
- Acronym: RETRO-ENDO
- Label and number: UMR9196 CNRS
- Composition of the executive team: Ms Anne Dupressoir

SCIENTIFIC PANELS OF THE UNIT

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

THEMES OF THE UNIT

The research unit (UMR 9196) focuses on immuno-virology, particularly retroviruses and endogenous retroviruses (ERVs). The themes span basic retrovirology, immunology, physiology, evolution, oncogenesis, vaccines and innovative therapeutics. Key areas include studying retroviral envelope proteins, identifying coopted retroviral genes involved in placentation, and developing therapeutic applications related to human ERVs in tumours. Within the unit, a group is also specialized in electron microscopy.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The research unit was created in 2015 and renewed in 2020. It was a continuation of the former research unit UMR8122. It is located at the Gustave Roussy Institute in Villejuif, one of the leading cancer centres in Europe. The unit is housed in the Pavillon de Recherche 2, which contains about half of the Research units at Gustave Roussy. In September 2024, CNRS informed the unit members that the unit will not be recreated given the insufficient number of CNRS permanent researchers (1 CR). Therefore, the unit will close at the end of 2025.

RESEARCH ENVIRONMENT OF THE UNIT

The research unit is composed of a single team and is integrated within the exploratory and translational research division of Gustave Roussy Institute. The unit is a founding member of the LabEx LERMIT (Laboratory of Excellence in Drug Research and Therapeutic Innovation) and a partner team of IRMIT (Institut de Recherche sur le Médicament et l'Innovation Thérapeutique) at the University Paris-Saclay since 2020. The unit benefits from access to various technical platforms developed by the Research Department at Gustave Roussy, which are grouped within the UMS AMMICa (CNRS UMS 3655 / Inserm US 23). These platforms include a Biological Resource Centre, Animal Facility, Genomics Platform, Imaging and Cytometry Platform, Experimental Pathology Platform, Bioinformatics Center, and Small Animal Imaging Platform.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	9
Sous-total personnels permanents en activité	**12**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	3
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**9**
Total personnels	**21**

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
CNRS	0	2	3
Autres	0	1	6
Total personnels	**0**	**3**	**9**

GLOBAL ASSESSMENT

The RETRO-ENDO unit is a mono-team unit (UMR 9196) located at the Institut Gustave Roussy in Villejuif. During its 25 years of existence, the unit has made seminal discoveries and outstanding contributions on the role of endogenous retroviruses on health and disease. They have successfully translated their findings into veterinary applications and promising therapies in human oncology and infectiology.

During the last period, the overall unit assessment is excellent, albeit the unit's foreseen closure at the end of 2025.

The originality of the unit's research relies on a complementary approach between basic and translational research, focused questions with a strong expertise on retroviral envelopes, and broad methodological approaches. By employing multiple tools including in vitro studies, high-throughput library screening, and animal models, the team has developed innovative diagnostic and therapeutic strategies.

Over the assessment period, the unit has made significant scientific advances. It expanded understanding of endogenous retrovirus expression in placental evolution and tumor development while simultaneously developing novel viral-based vaccine platforms. A particularly noteworthy discovery was a unique retroviral envelope gene in hyenas associated with their distinctive placental structure. The unit also identified HEMO, a human endogenous retroviral envelope protein with potential as a cancer biomarker and therapeutic target. Moreover, the unit contributed to develop a recombinant measles virus vaccine showing promise against HIV and other diseases. Recent work on the characterization of envelope receptors and their use in therapy has been published in 2024.

The unit's research productivity is very good to excellent with 30 research articles (Cancer Immunol Res, NPJ Vaccines, and Mol Oncol) and one review (Mol Cell) published, alongside three patents filed. Two additional notable articles were published in 2024 (J Virol, Life Sci Alliance) for a total of nine articles featuring unit members as first, last, or corresponding authors.

The unit shows outstanding research funding and industrial collaboration. The unit secured approximately 1.5 million euros through national contracts and association funding. A formerly established spin-off company, Viroxis, is working in close synergy with the unit. Through this collaboration, it obtained five ANR PRCE funding grants during the review period and generated royalties from past industrial valorisations, such as the FeLV vaccine.

The involvement of the unit in training through research is strong. Six doctoral theses have been completed, with four ongoing doctoral PhD theses. Unit's researchers have also supervised 15 student internships for five HDRs. The exceptional expertise of a unit member in electron microscopy has led to national and international collaborations (Japan).

Despite these achievements, the gradual retirement and transition of senior principal investigators have compromised the long-term perspective and stability of the unit, and have not been compensated by the recruitment of young permanent researchers. In this context, CNRS has decided to close the unit at the end of 2025, obliging the remaining personnel to transfer their activity to other units.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous report made the following recommendations to the unit:

1. **to increase its participation in international activities.** This issue was partially addressed by the unit through the participation to international meetings by several members of the unit including PhD students.
2. **to increase the number of PhD students trained.** The unit has trained 10 PhD students during the period, with supervision from four different members of the unit.
3. **to maintain a healthy balance between funding sources (public vs. industrial).** The financial unit has successfully secured grants from PRCE national calls by ANR for 2/3 of its resources and relies on collaborative contracts with industry and patent royalties for 1/3 of its funding.
4. **to ensure the emergence or recruitment of a new group leader.** The unit has attracted a new researcher (January 2023), and has internally promoted one of its researchers as unit Director (January 2024).
5. **to recruit an expert immunologist and additional technical support for the animal facility.** The unit has attracted an immunologist from the Cochin Institute at the beginning of 2023. The supervising bodies of the unit have not allocated a new research assistant position to the unit.

B - EVALUATION AREAS

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

Assessment on the scientific objectives of the unit

The assessment of unit scientific objectives is excellent, based on the unit's focused research on human endogenous retroviruses, which are being translated into novel therapeutic approaches.

Assessment on the unit's resources

The assessment of unit resources is excellent given its diverse and substantial funding sources, and strategic partnerships with startup, and effective use of research platforms available in its environment.

Assessment on the functioning of the unit

The assessment of unit functioning is excellent, showing compliance to research regulatory requirements, as well as effective management practice toward commitment to staff well-being and professional development.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The unit has coherent scientific objectives, based on the strengths and expertise that researchers have developed over many years in virology, immunology and oncology. The discovery by the unit of the syncytin

envelope genes co-opted by eukaryotic genomes for placental formation has been an asset for the development of the unit. A vaccine directed against envelopes of the FeLV has been developed in collaboration with Mérial/Boehringer and led in 2008 to the creation of the start-up company Viroxis, a spin-off from the Research unit. This brings royalties to the Research unit, which benefits its overall activity.

The unit aims to maintain a high level of ambition in terms of innovative therapeutic strategies to develop original tools against a wide range of diseases, in line with the research strategy of Gustave Roussy, but also with the policies of the CNRS and the University of Paris-Saclay.

The originality of the unit's research is based on (i) the complementarity of basic and applied approaches, (ii) the focused nature of the research areas, and (iii) the combination of different methodological tools (*in vitro* studies, high-throughput library screening, animal models, etc.), for the development of innovative early diagnostic approaches and new therapeutic strategies.

One member of the unit is at the board of the Structure du Bien-Etre Animal, and the Comité d'Ethique en Experimentation Animale (CEEA) n°26 of the University of Paris-Saclay.

Weaknesses and risks linked to the context

Scientific objectives are at risk due to the fact that researchers need to relocate due to upcoming closure of the unit.

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 well funded, and during the period under review a major effort was made to obtain national contracts and funding from associations. During the 2018-2023 period, average recurrent funding was 64 ± 9k€/year including recurrent funding allocated by the supervisory authorities (CNRS and University Paris-Saclay), as well as royalties from patent licensing (average 60 k€/year), and grants or industrial partnerships. This has made it possible to finance group projects and encourage the emergence of independent programs. Overall, the team members have obtained funding through calls and partnerships amounting to a total of more than 1.400k€ over the period.

The basic and translational research carried out by the unit's researchers takes full advantage of the resources platforms, biobanks, etc. - and the high-quality research environment of the Gustave Roussy medical campus. The unit has a strong and long-term history of commitment toward clinical translation. Moreover, it has established a long-term collaboration with a spin-off of the unit (Viroxis), which brings technological expertise and significant funding to the unit. This virtuous circle has benefited to the basic and translational science in the unit.

Weaknesses and risks linked to the context

Three of the leaders who enabled to reach these scientific objectives are already Emeritus or getting retired. The tasks forces to continue the scientific project will be dispersed in several units, which could hinder future interactions with Viroxis that has been extremely fruitful in the past.

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

Quarterly meetings are organized with IGR management and the unit's team leaders, as well as a representative of the various technicians, students and post-docs, to discuss specific research plans as well as unit problems or needs.

Every two months the "Research Directory" holds a meeting including the unit directors and head of the platforms to communicate on common matters, including investment in novel device and development.

The unit relies on two major organizations provided by the IGR, the Safety and Security Service, and a Health & Safety (H&S) manager, to ensure work safety, to prevent accidents, to protect staff health, and to guarantee compliance with current regulations.

The unit complies with the rules and regulations defined by the CNRS, the Paris-Saclay University and IGR in terms of human resources and training, career development, health and safety and psychosocial risks.

The unit has one assistant prevention working in close collaboration with IGR H&S manager to comply with the applicable laws, regulations, policies and procedures of the regulatory authorities.

Gender balance is respected with 12/11 w/m ratio in the team; 4/6 among team scientists; and 5/5 among students.

Research, development and evaluation of new therapies are supported by an effective and ambitious co-development program with Viroxis Biotech.

Weaknesses and risks linked to the context

Closure of the unit implies relocation of unit members, which is associated with anxiety and could raise psychosocial risk. It will require proper accompaniment of the concerned personnel by their respective employers.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The assessment of the unit's attractiveness is very good, showing strong scientific reputation through high-quality publications, successful competitive research funding, theses supervision and expertise in electron microscopy.

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

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

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

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

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

The unit benefits from international appeal, first through the quality of its research work published in highly reputable journals. There are 31 publications involving team members between 2018 and 2023. Team members also have responsibilities at local and national level (Hcéres). The team is attractive for student training, with six theses defended during the term, and four theses in progress, as well as numerous student internships (15), for five HDR in the team. The team has recently succeeded in attracting a CNRS researcher (arriving in January 2023), in promoting a technical staff member (from technician to assistant engineer), and is also supporting the doctoral training of one of its technical staff who started a thesis in December 2020. The team also manages to fund its research through competitive national calls (5 ANR PRCE between 2018 and 2023, four of which as coordinator, for a total amount of 2,552 k€, among them 1,243 k€ for the team) and contracts with foundations (3, for a total amount of 147 k€). Finally, the unit also benefits from the technological platforms of the Gustave Roussy Institute, where it is housed. One member of the team has specific expertise in electron microscopy technologies, giving this skill a high visibility and leading to national and international collaborations (Japan).

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

Team members are not involved in journal editorial boards. Participation in congresses has been moderate for a unit of this size, with only five oral communications and five poster presentations (+2 in 2024) at national or international congresses, mostly at the Journées Francophones de Virologie, throughout the duration of the mandate, which may have hindered the team's visibility. Participation to conference organization was limited to a single regional conference. The unit has limited involvement in international activities (e.g., international funding or research networks) and institutional responsibilities have been restricted to the local level. Unfortunately, the unit has not been successful in attracting and/or recruiting young permanent researchers to maintain a critical unit size.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The assessment of the unit scientific output is very good to excellent, with significant contributions in retrovirology and vaccine development, supported by high-quality publications. However, the valorization strategy may have negatively impacted the academic record of the unit, particularly for early-career researchers.

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

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

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

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

The scientific production of the unit reflects the broad expertise of its members in retrovirology, immunology, and electron microscopy. Over the past five years, the unit has made significant contributions to our understanding of the expression and role of endogenous retroviruses in placental evolution or in tumours, and developed novel viral-based vaccine platforms. They discovered a novel retroviral envelope gene in hyenas linked to their unique placental structure and identified a human endogenous retroviral envelope protein, HEMO, with potential as a cancer biomarker and therapeutic target. Additionally, they developed a recombinant measles virus vaccine demonstrating promise for combating HIV and other diseases. Recent work on the characterization of envelope receptors and their use in therapy has been published in 2024.

The unit has a very good publication record, with 30 research articles and 1 review published. Additionally, they have filed three patents. The articles are published in general and speciality international peer-reviewed journals, including seven with first, last, or corresponding authorship from the unit (Cancer Immunol Res, NPJ Vaccines, Mol Oncol, J Virol x2, Bone Reports, and a review in Mol Cell). Two additional notable articles were published in 2024 (J Virol, Life Sci Alliance) with unit members as first or last author.

Senior authorship is well distributed between unit researchers, with at least one last author article for each permanent researcher of the unit.

The unit has appointed a dedicated scientific integrity officer. Animal experimentation and research involving human subjects are conducted within the strict framework of the law, with necessary approvals obtained from the local ethics committee and the ministry. Furthermore, published articles are deposited in the HAL open archive.

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

Publications of research articles with senior authorship from the unit are predominantly in very good but specialized journals in their field, rather than in high-profile journals with a broad readership.

Only a small fraction of the unit's PhD students and postdocs have published articles as first authors. This appears to be a direct consequence of the valorisation strategy of the unit, which prioritizes patenting and consequently imposes embargo periods.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The assessment of the unit's contribution of research activities to society is excellent to outstanding, based on its strong industrial collaborations and translational impact. However, public outreach and engagement efforts could be improved.

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

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

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

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

The unit has forged remarkable links with society, particularly the industrial world. A spin-off from the unit, Viroxis, was created in 2008 and works in perfect synergy with the unit's members. They share the same facilities and staff to drive forward research projects and their translational applications, mainly focused on the development of innovative therapies. Thanks to this collaboration, the team has obtained several ANR PRCE funding (5 during the last term), has filed three patents from 2018 to 2023, and benefits from resources derived from its past industrial valorisations (royalties from FeLV vaccine). A member of the team is also a scientific advisor to Viroxis.

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

Given the significant socio-economic impact of its research, the unit has made limited promotion of its work to the general public, for example by participating in public events (e.g., DECLIC, Science festival) or sharing its research through the media and social networks. In addition, the team's work could be presented more effectively to university and secondary school students at research presentation events.

ANALYSIS OF THE UNIT'S TRAJECTORY

The unit has made seminal discoveries and contributions on the role of endogenous retroviruses on health and disease, and has successfully translated their findings into medical and veterinary applications. However, the retirement or transition to emeritus of main investigators of the unit has threatened its future scientific developments. Although the unit has recruited several permanent researchers or lecturers over the years, it has not fostered a sufficiently favourable environment to establish a new generation of principal investigators and research lines. In this context, CNRS has decided to close the unit at the end of 2025.

Given the strategic importance of the ongoing projects and their potential impact on cancer therapies and immunology, several recommendations can be made to prevent a loss of knowledge and expertise, and to ensure the continuation of the most promising projects.

RECOMMENDATIONS TO THE UNIT

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

Particular attention should be paid to ensure the continued scientific supervision of PhD student supervised by a researcher who will be retiring in February 2025.

Particular attention should be paid to assist administrative and technical staff for their relocation in neighbouring units/units of relevant scientific themes.

Maintaining close proximity between the relocated scientists and the Viroxis members will be essential for the continuity of successful synergy between basic and translational projects.

Recommendations regarding the Evaluation Area 2: Attractiveness

Particular attention should be paid to maintain the unique expertise for cellular electron microscopy on-site, as it benefits the whole scientific community at the IGR and contributes to fructuous external collaborations.

Recommendations regarding Evaluation Area 3: Scientific Production

Not applicable.

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

Not applicable.

CONDUCT OF THE INTERVIEWS

Date

Start: 29 November 2024 at 08:00

End: 29 November 2024 at 18:00

Interview conducted: online

INTERVIEW SCHEDULE

9:20-9:30	Hcéres Rules and procedures by *B. Bartosch, Public Session*
9:30-10:30	Administrative and Scientific presentation of the Unit *Overall presentation of the unit followed by discussion, Public Session*
10:30-11:00	Réunion avec les ITAs (in French)
11:00-11:30	Meeting with researchers
11:30-12:00	Meeting with students
12:00-12:15	Debriefing committee *(closed-door meeting)*
12:15-13:15	Lunch Break
13:15-13:35	Meeting with institution representatives *(closed-door meeting)*
13:35-14:00	Debriefing committee *(closed-door meeting)*
14:00-15:30	Meeting with Director of the Unit *(closed-door meeting)*
15:30-18:00	Redaction of the final report *(closed-door meeting)*

GENERAL OBSERVATIONS OF THE SUPERVISORS

The institution responsible for submitting the application, which is also responsible for coordinating the response on behalf of all the research unit's supervisors, did not submit any general observations.

The Hcéres' evaluation reports are available online:
www.hceres.fr

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