Research evaluation

EVALUATION REPORT OF THE UNIT

GIRC - Intégrité du génome, ARN et cancer
SRC - Signalling, Radiobiology and Cancer

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Institut Curie,
Centre national de la recherche scientifique - CNRS,
Institut national de la santé et de la recherche médicale - Inserm,
Université Paris - Saclay

EVALUATION CAMPAIGN 2024-2025
GROUP E

Rapport publié le 15/04/2025

High Council for evaluation of research and highter education

In the name of the expert committee :

Mr Claus Storgaard Sorensen, Chairman of the committee

For the Hcéres :

Coralie Chevalier, 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 Claus Storgaard Sorensen, University of Copenhagen, Danemark
Co-Chairperson	Michele Trabucchi, Institut national de la santé et de la recherche médicale - Inserm (representative of CSS Inserm)
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Ms Carine Giovannangelli, Inserm
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Ms Tatiana Malherbe, Institut Curie
Ms Helene Maury, Inserm Regional Delegation
Mr Philippe Oger, Cnrs
Mr Bruno Quesnel, Inserm

CHARACTERISATION OF THE UNIT

- Name: Genome Integrity, RNA and Cancer
- Acronym: GIRC
- Label and number: UMR 3348
- Composition of the executive team: Mr. Stephan Vagner, unit director and team leader, Ms. Sarah Lambert, deputy unit director and team leader

SCIENTIFIC PANELS OF THE UNIT

SVE3 Molécules du vivant, biologie intégrative (des gènes et génomes aux systèmes), biologie cellulaire et du développement pour la science animale

THEMES OF THE UNIT

Unit Structure. The UMR3348, established in 2020 and based at the Institut Curie in Orsay, is a multidisciplinary research unit focused on genome integrity and RNA biology in cancer. It operates under the leadership of Director Stephan Vagner and Deputy Director Sarah Lambert, currently (2023) with five research teams exploring complementary themes. The teams are supported by shared platforms localised on the Paris and Orsay Institut Curie sites, services, and administrative staff, totalling 63 members as of late 2023. The unit has undergone significant evolution recently including the addition of new teams led by Albertas Navickas and Reini Luco following international recruitments. In 2026, two teams from the CNRS UMR3347/Inserm U1021 unit will integrate into UMR3348, further broadening its research scope. The unit has its basis in multiple supervisory institutions, including CNRS, Inserm, Institut Curie, and Université Paris Saclay. It is affiliated with several doctoral schools in Paris-Saclay.
Main Research Themes. The research at UMR3348 focuses on understanding genome integrity and RNA dynamics in both normal and pathological contexts, with an emphasis on cancer. The work also spans DNA damage responses, RNA metabolism, and cytoskeletal regulation, using advanced techniques and diverse biological models. The five teams specialize in the following areas:
RNA Biology, Signalling, and Cancer (Team Vagner) This team investigates RNA-binding proteins (RBPs) and their roles in post-transcriptional gene regulation, particularly in cancer biology and therapy resistance. Focus areas include alternative polyadenylation, translation regulation, and the impact of RBPs on genome stability in various cancers.
DNA Recombination, Replication, and Genome Stability (Team Lambert). The team explores the molecular circuits that maintain genome stability under replication stress. By studying repair, recombination, chromatin, and RNA-based processes, they aim to prevent replication fork instability and its pathological consequences.
Controlling Microtubule Dynamics with the Tubulin Code (Team Janke). This team examines the role of tubulin post-translational modifications and isotypes in regulating microtubule behaviour. Their work links these molecular mechanisms to broader cellular and organismal functions, with implications for neuronal homeostasis and disease.
Chromatin and RNA Splicing (Team Luco). Research focuses on non-canonical mechanisms of alternative splicing regulation during epithelial-to-mesenchymal transition (EMT), which contributes to metastasis. They study chromatin-mediated splicing mechanisms to identify therapeutic strategies for preventing tumour dissemination.
RNA, Tumour Microenvironment, and Cancer (Team Navickas). This team studies the molecular underpinnings of metastatic niche formation, particularly in triple-negative breast cancer metastasis to the lungs. They focus on RNA regulatory networks mediating communication between tumour cells and host tissues.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

Historic and Geographical Location of the UMR3348 Unit
The UMR3348 unit termed Genome Integrity, RNA, and Cancer (GIRC), is located at the Institut Curie in Orsay, France, within the building 110 on the Orsay campus. The unit is placed in a major French research hub, leveraging proximity to other renowned research centres and institutions within Paris-Saclay, a leading French cluster in life sciences.
Historical Background
The origins of UMR3348 trace back to the establishment of the "Genotoxic Stress and Cancer" unit in 2015, under the leadership of Mounira Amor-Gueret as director, with Stephan Vagner serving as deputy director. On January 1, 2020, the unit transitioned into its current form, reflecting an expanded focus on RNA biology alongside genome integrity and cancer research. This evolution involved recruitment of new teams and the adoption of advanced scientific approaches, including translational research. Teams have transitioned in and out of the unit due to retirements, relocations, and new recruitments, including the integration of the junior team led by Albertas Navickas and the senior team led by Reini Luco in 2021. Furthermore, an Inserm unit (U1278) was

created under Stephan Vagner's leadership to extend research on RNA biology and cancer. Looking ahead, the unit will integrate two additional teams from the neighboring CNRS UMR3347/Inserm U1021 unit in 2026, further broadening its scope and collaborative potential.
Geographical Context
Located within the Institut Curie's Orsay campus, UMR3348 is in a multidisciplinary scientific environment that can foster collaboration across various disciplines. The Paris-Saclay region, notably including Institut Curie facilities, provides access to state-of-the-art infrastructure, technological platforms, and a dynamic scientific community. This geographical setting allows training and interactions with affiliated doctoral schools, promoting the development of the next generation of scientists.

RESEARCH ENVIRONMENT OF THE UNIT

The UMR3348 unit is located at the Institut Curie's Orsay campus, the Institut Curie combines a leading-edge hospital group with a research center dedicated to understanding the mechanisms of living organisms and addressing the challenges posed by cancer. This integrated environment supports interdisciplinary collaboration between researchers and clinicians, fostering translational research and innovation.
UMR3348 is part of the Research Center's thirteen joint research units, which are affiliated with CNRS, Inserm, and universities such as Sorbonne Université, Université Paris-Saclay. Institut Curie is an associated-member of PSL University. These partnerships enable interdisciplinary research spanning cell biology, epigenetics, genetics, immunology, and more. The unit benefits from access to Institut Curie's nineteen state-of-the-art technology platforms (CurieCoreTech) distributed between the Paris and-tably Orsay Institut Curie sites, as well as extensive clinical databases and sample collections. UMR3348 teams contribute to the Institut Curie's third Siric (Site de Recherche Intégrée sur le Cancer), focusing on cancer relapse and recurrence across tumour types. They participate in the Institut des Cancers des Femmes, established in 2023, highlights the unit's focus on gender-specific cancer research.
Sarah Lambert co-coordinates the "Nuclear Functions and Maintenance" axis. The Janke team contributes to the "Engineering Life" initiative, connecting biology, physics, and chemistry within PSL's interdisciplinary research efforts. With the Janke team specifically, the Unit is a member in the Labex Cell'n Scale and the Institut Convergences QLife further integrates UMR3348 into PSL's life sciences research landscape.
UMR3348 engages with several Paris-Saclay interdisciplinary objects (OI):

- HEALTHI OI, a multidisciplinary consortium addressing health, disease prevention, and care, includes Luco and Vagner teams. Vagner also co-coordinates one of its cancer-focused poles.
- Living Machines@Work OI, a task force exploring biological machinery and its applications, involves Lambert, Luco, Janke, and Vagner teams. Sarah Lambert also co-organized the first "Living machine at work meeting" days in 2023. She serves on its scientific council, and Janke has organised workshops for the consortium.
- At Paris-Saclay, Lambert is part of the Graduate School "Life Sciences and Health" scientific council, while Luco is on the Scientific Board of the Oncology Doctoral School.

UMR3348 benefits from participation in several initiatives established under the Programme Investissements d'Avenir (PIA). These include involvement in projects such as: A) Labex Cell(n)Scale from PSL University: "from Molecules to Tissues: where Physics & Chemistry meet Biology", that aims at leveraging physical and chemical tools and concepts to address key questions on cell and tissue functions and dynamics. B) Idex Paris-Saclay: Promoting excellence in research and education by facilitating interdisciplinary collaboration. UMR3348 is integrated into national infrastructures like France Génomique, enabling cutting-edge genomic research. The unit also collaborates within European research networks, strengthening its international research impact.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	5
Chargés de recherche et assimilés	4
Personnels d'appui à la recherche	23
Sous-total personnels permanents en activité	**34**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	2
Post-doctorants	5
Doctorants	18
Sous-total personnels non permanents en activité	**27**
Total personnels	**61**

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
INST CURIE	0	0	14
CNRS	0	5	8
Inserm	0	4	1
U PARIS SACLAY	2	0	0
Total personnels	**2**	**9**	**23**

GLOBAL ASSESSMENT

The GIRC is a dynamic research unit addressing critical topics in genome integrity, RNA metabolism, celullar stresses, and their implications for cancer research. Over the evaluated period (2018–2023), the unit has demonstrated substantial progress, marked by its interdisciplinary approaches, impactful publications, and robust contributions to societal advancements. The unit's work also bridges from fundamental research towards clinically relevant disease questions, which is a significant strength. However, there may be a challenge in fully integrating its diverse research themes into a unified strategic framework, especially in light of continued thematic diversification. This dispersion of research interests might dilute the unit's ability to establish a cohesive scientific direction, which could impact future strategic growth and resource allocation.
GIRC benefits from substantial financial backing, with €19.85 million secured from competitive national and international sources, including prestigious grants from ERC, ANR, and private foundations like FRM and ARC. The infrastructure available is state-of-the-art, including access to advanced technologies through the CurieCoreTech platform and its integration with the Core for Life alliance, enhancing its research capabilities. The dependency on external funding exposes the unit to financial risks, particularly in times of reduced grant success. The physical premises of the unit are also nearing a critical phase of renovation, and are part of a renovation programme planned for the coming years. Current conditions—such as low building temperatures—could compromise both staff well-being and research productivity. The unit benefits from an organised governance structure with clear leadership roles and a commitment to maintaining a collaborative and inclusive environment. Furthermore, gender equality and diversity are actively promoted, ensuring an inclusive work culture.

GIRC has built an excellent reputation both nationally and internationally at an excellent to outstanding level. The unit's leaders are recognised figures in their respective fields, regularly invited to high-profile conferences, and contributing to major scientific initiatives. Their participation in organising conferences and editorial boards further enhances the unit's visibility on the global stage.
The inclusivity and commitment to international collaboration are key components of GIRC's attractiveness. The unit's hosting policy has successfully attracted researchers from over fourteen countries, and its international recruitment efforts have been particularly effective. GIRC's diversity initiatives, such as gender parity and the promotion of programs like Women in Science and EU-Life GEDI, may further bolster its appeal to top talent. Recruitment success is evident from the hiring of prominent researchers from around the world, including CNRS permanent researchers and assistant professors.
The scientific output of GIRC is excellent to outstanding. With over 140 peer-reviewed publications, the unit's research has consistently made innovative contributions in the fields of RNA biology, chromatin dynamics, microtubule function, and genome stability. These fields are central to understanding fundamental biological processes and their implications in diseases like cancer.
GIRC's scientific success is demonstrated through high-profile publications in journals such as Nature Medicine, Science, Molecular Cell, and Genome Research. Notably, the work on RNA biology and cancer, which led to over 40 articles, has had a major impact in the field, with twenty of these publications being primary data contributions in top journals. The team with a focus on microtubules, has also produced significant findings, contributing 40 publications, including a prestigious paper in Science. The team investigating genome integrity, achieved 27 publications in excellent journals, many of which were collaborative efforts with international researchers.
GIRC has made meaningful contributions to society through both its industry collaborations and public engagement initiatives: creation of Ribonexus, a cancer therapy start-up, has secured €6 million in funding, showcasing the potential for GIRC's research to make a direct impact on cancer treatment. Similarly, collaboration with Biogen through a Cifre PhD contract illustrates the strong ties between GIRC and the pharmaceutical industry. The unit's outreach activities further demonstrate GIRC's commitment to disseminating scientific knowledge. They engage in public science outreach through exhibitions and seminars, and foster science education in schools, helping to cultivate the next generation of scientists. These efforts contribute to increasing public understanding of science and highlight GIRC's role in bridging the gap between academic research and societal needs.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The UMR3348 unit has taken steps to address the recommendations from the 2018 Hcéres evaluation. Below is an evaluation of its actions in response to these recommendations:
1. Encouraging Interactions Between Teams and Disciplines. The unit has made significant efforts to foster interdisciplinary collaboration within its teams. Evidence provided suggests initiatives aimed at enhancing internal interactions, which align with the goal of increasing interdisciplinary research. The Janke team is especially positioned with its focus on largely cytoplasmic and neurological themes that differ somewhat from the RNA, genome integrity and cancer focus. However, collaborations are established between Janke and other teams such as the Lambert group, which may lead to new interdisciplinary findings. Moreover, the emphasis on technological development is evident through the integration of advanced tools and methods within the unit's research activities. However, partnerships with industries to support translational research programs appear to have seen limited progress. The unit acknowledges this gap, citing its primarily research-oriented focus as a reason for the limited engagement with industry partners.
2. Increasing High-Impact Publications and Visibility. The unit has made marked progress in producing scientific publications with excellent visibility, contributing to its international profile. This improvement likely enhances its attractiveness to prospective ERC grant applicants, as well as talented students and post-docs. Participation in international meetings by team leaders and members demonstrates an active effort to engage with the broader scientific community and increase the unit's visibility.
In conclusion, the unit's increased publication output and international presence signify meaningful strides towards meeting its goals. Continued focus on addressing areas with limited progress, such as industry collaborations, can further enhance its impact.

B - EVALUATION AREAS

Guidelines for all areas of evaluation (1, 2, 3 and 4): Considering the references defined in the unit's evaluation guidelines, the committee ensures that a distinction is made on the outstanding elements for strengths or weaknesses. Each point is documented by observable facts including the elements from the portfolio. The committee assesses if the unit's results are consistent with its activity profile.

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

Assessment on the scientific objectives of the unit

The scientific objectives of GIRC focus on understanding genome integrity, RNA metabolism, and their roles in cancer. The Unit mainly investigates molecular mechanisms behind DNA damage response, cellular stress mechanisms, gene expression regulation, and their deregulation in diseases like cancer. The objectives are very topical, and the Unit bridges fundamental research with clinical applications, aligning with the priorities of the Institut Curie, CNRS and Inserm. The teams efficiently integrate expertise in DNA replication, repair, RNA biology, and cell biological processes with diverse model systems (yeast, mice, human cells) and advanced technologies (such as Crispr, single-cell transcriptomics),

Assessment on the unit's resources

GIRC operates with substantial resources adequate to address the scientific objectives, including a budget of €19,850k (2018–2023). Funding is sourced from competitive national and international grants (e.g., ANR, ERC) and private foundations (FRM, ARC). While funding management is team-specific, core funding is partially redistributed. The Unit benefits from cutting-edge infrastructure, upgraded regularly, and collaborative grant applications enhance equipment acquisition. It leverages the Institut Curie's CurieCoreTech, offering 19 advanced technology platforms and expertise, further enriched by the Core for Life alliance, ensuring access to state-of-the-art facilities and fostering innovation.

Assessment on the functioning of the unit

The unit operates with a well-structured governance model led by the Director and Deputy Director, supported by team leaders and the Laboratory Council, ensuring collaborative decision-making. Regular meetings, annual assemblies, and retreats foster communication and cohesion. The Unit adheres strictly to Institut Curie's guidelines on health, safety, ethics, and data management, with dedicated roles such as the Prevention Agent and Scientific Integrity Officer. Gender equality and diversity are prioritised, aligning with Institut Curie's Gedip plan. The Unit integrates scientific integrity and responsible data practices into its operations, creating a collaborative and inclusive research environment.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The scientific objectives of GIRC are highly relevant and well-aligned with current advancements in DNA damage, cellular stress, RNA metabolism, and cancer research, situating the unit at the intersection of several cutting-edge fields in the vibrant greater Paris area. This alignment with the scientific priorities of CNRS, Inserm, and Institut Curie ensures strong institutional support and strategic synergy. The unit's diverse yet complementary teams facilitate interdisciplinary collaborations, leveraging shared resources and fostering a cohesive scientific culture. The ability to secure funding from a variety of prestigious national and international sources (ERC, ANR etc) highlights the unit's academic standing and its integration within influential research networks. Moreover, the unit's active participation in initiatives addressing societal challenges, such as cancer research and gender equality, underscores its ability to connect research outputs to broader societal needs. Weekly meetings and scientific retreats further enhance team cohesion and encourage the cross-pollination of ideas, supporting the unit's robust operational strategy.

Weaknesses and risks linked to the context

The unit faces some challenges in fully integrating its diverse research interests into a unified strategic framework. While collaboration between teams is encouraged, limited core funding and the largely independent management of individually secured (highly competitive) project funds may limit opportunities for broader, unit-wide initiatives. The unit's dependency on external funding, though diverse and successful, introduces potential vulnerabilities in sustaining long-term research agendas in a competitive funding landscape. Furthermore, while the unit excels in addressing societal challenges at the basal (fundamental) research level, there is limited explicit articulation of its strategy for engaging non-academic stakeholders, which could enhance its societal impact. Internally, while governance structures such as the Laboratory Council provide consultative support, the frequency of meetings may limit their capacity to adapt swiftly to evolving scientific priorities or emerging risks. Addressing these challenges can help maintaining the unit's relevance and strategic alignment with stakeholders such as supervisory authorities.

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

GIRC is well-positioned to capitalize on its research environment, given its strategic alignment with the Institut Curie, CNRS, and Inserm priorities. Its focus on DNA damage, RNA metabolism, organism models, and cancer is both relevant and synergistic with institutional goals. The unit benefits from substantial external funding, having secured approximately €19.85M during 2018–2023, from diverse national and international agencies, private entities, and foundations, which includes prestigious ERC and ANR grants. This indicates a robust capacity to mobilize resources effectively. Collaboration within the unit is bolstered by shared equipment, common meetings, and an integrated use of the CurieCoreTech platforms, which provide access to state-of-the-art technologies and expertise. Moreover, the CurieCoreTech's membership in Core for Life extends the unit's access to advanced resources and networking opportunities across Europe. The unit's gender balance, diversity initiatives, and participation in mentoring programs such as the Women in Science and EU-Life GEDI also enhance its capacity to attract and support talented researchers.

Weaknesses and risks linked to the context

Certain structural aspects could present risks for UMR3348 and governing bodies should be prepared to provide resources to the unit in this regard. The premises are approaching time of building renovation and resources as well as well-planned efforts are needed to solve this issue without compromising research output. It was noted by the committee that physical premises were in suboptimal conditions with very low temperatures. Moreover, lack of a core funding pool and the individually managed budgets of teams might limit opportunities for large-scale, interdisciplinary projects. The reliance on competitive funding could also introduce financial vulnerability in periods of reduced grant success. The allocation of premises based on fixed staff limits set by the Institut Curie's scheme may constrain the unit's capacity to expand or attract additional researchers to highly successful teams. Additionally, while collaboration within the unit is facilitated, further integration and joint strategy among Orsay site units could optimize resource usage, research and innovation. Finally, handling and analysing the extensive and diverse data generated by research activities demand sustained resources and advanced bioinformatics capabilities to mitigate risks of data mismanagement.

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 demonstrates a robust commitment to human resources management, emphasising gender parity and diversity. With a gender ratio of 1.8 (women/men), a balanced leadership structure including a male and female director, and active participation in programs like the Paris-Saclay Women in Science initiative and the EU-Life GEDI mentoring program, the unit upholds inclusivity. The adherence to the Gender Equality, Diversity, and Inclusion Plan (Gedip 2022–2025) by Institut Curie further strengthens this approach. Working conditions are meticulously managed, with continuous investments in safety measures such as collective protective equipment and e-learning training modules for occupational risks. The prevention of psychosocial risks is bolstered by the active role of the Agent de Prévention (AP), who ensures compliance with safety regulations and promotes an inventory of potential hazards.
In terms of safeguarding scientific assets and information systems, the unit benefits from the dedicated Data Office established by Institut Curie. This department ensures the secure storage and processing of extensive research data, including anonymised patient information, in coordination with relevant platforms and legal entities. Additionally, the "HR Excellence in Research" label awarded to Institut Curie underscores the institution's supportive and progressive environment.
Environmental preservation efforts are notable, with the unit integrating Institut Curie's broader measures for sustainable practices. Coordination with the CurieCoreTech facilities enables resource-sharing and minimizes redundancy, while the energy-efficient operation of advanced platforms aligns with sustainability goals. Shared use of equipment across multiple teams maximizes utility and reduces the carbon footprint. The focus on reducing travel-related emissions and efficient waste management further illustrates the unit's commitment to environmental responsibility.

Weaknesses and risks linked to the context

Despite these achievements by the Unit supported by the Institut Curie, certain weaknesses and risks persist. Environmental measures, though integrated into broader Institut Curie policies, lack detailed unit-specific targets or comprehensive monitoring frameworks. These gaps could dilute the impact of environmental sustainability efforts while also impacting the well-being of staff. For instance, the building interior appeared very cold (experienced by the committee, highlighted by staff), suggesting that buildings are up for a renovation that should limit Carbon footprint.
Furthermore, while the unit complies with ethical research practices and data protection, the rapidly evolving nature of data security risks may necessitate more dynamic, unit-specific strategies. The reliance on centralised oversight from Institut Curie's Data Office might not fully address unique challenges or vulnerabilities faced by Unit 3348.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The GIRC excels nationally and internationally due to its strong scientific reputation and contributions to the European research area. Its globally recognised team leaders enhance the unit's visibility through roles in high-profile conferences, academic training, and awards. The unit's inclusive hosting policy attracts diverse talent, recruiting researchers from over 14 countries. Competitive success in funding, including ERC, ANR and MSCA grants, underscores operational excellence. Advanced infrastructure like the Orsay Curie CoreTech ensures cutting-edge research capabilities. However, challenges include sustaining funding, talent recruitment, and addressing infrastructure demands to maintain its competitive edge.

Strengths and possibilities linked to the context

The GIRC unit possesses an outstanding scientific reputation, bolstered by significant contributions to the European and global research area. Team leaders are globally recognised experts in their respective fields, evidenced by their numerous invitations to international conferences, roles in organising scientific events, editorial board memberships, participation in steering committees, and accolades such as awards and honors. Their influence extends to academic training, as the unit coordinates two out of the ten to twelve yearly Curie international courses and regularly provides lectures at prominent national and international venues. These activities enhance the unit's visibility and collaborative potential across Europe and beyond.
The unit's hosting policy is another area of strength, demonstrating inclusivity and a strong commitment to international collaboration. The five team leaders represent four different nationalities, and the unit has hosted a diverse range of talent from over fourteen countries during the 2018–2023 period. Notable examples include the recruitment of two group leaders through a highly competitive international call, attracting 46 applicants from eighteen countries, with a significant proportion of outstanding candidates. Furthermore, the successful hiring of permanent CNRS researchers (e.g., Maria Magiera and Sudarshan Gadadhar) and assistant professors (Patricia Uguen and Frederic Coquelle) illustrates a robust ability to attract and retain top-tier talent.
Success in competitive funding calls underscores the unit's scientific and operational excellence. Teams have secured diverse funding sources, including prestigious grants from national agencies (e.g., multiple ANR projects) and international bodies (e.g., MSCA doctoral training networks). Specific achievements include the Janke team's ERC Synergy Grant (as coordinator) and the Lambert team's coordination of three ANR projects and one INCA PLBIO project. This success not only validates the quality of research but also ensures long-term sustainability and capacity for innovation.
The unit benefits from state-of-the-art equipment and infrastructure, ensuring that researchers have access to cutting-edge tools necessary for their work. Facilities such as the Orsay Curie CoreTech Multimodal Imaging Center provide advanced technologies, including multiplex IHC/FISH and QIBC. Regular equipment maintenance, renewal policies, and multi-year contracts ensure operational efficiency and minimize downtime. These resources enhance the unit's ability to conduct innovative research and attract high-caliber scientists.

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

GIRC faces challenges that could impede its long-term attractiveness and competitiveness. While the unit's scientific reputation is strong, maintaining this standing requires continuous output of high-profile publications and successful collaborations. With the lack of substantial core funding, a potential risk lies in the growing competitiveness of international research funding, where even slight dips in success rates could affect resource availability and strategic priorities.
The hosting policy, while commendable, may face difficulties due to increasing competition among institutions for global talent. The reliance on international recruits and the growing number of outstanding applications per position could lead to higher turnover or the inability to secure the very best candidates. Additionally, the integration of diverse personnel into cohesive teams poses ongoing challenges that require sustained effort and resources.
Funding, although a strength, presents vulnerabilities due to its fragmented nature and reliance on competitive grants. While individual teams have demonstrated success, the unit as a whole must mitigate risks associated with fluctuating funding cycles, especially as private foundation support can be unpredictable. Thus, recruitment policies are required that ensure GIRC competitiveness.
Lastly, while the unit has robust technological capabilities, it is essential to ensure that equipment remains cutting-edge in the rapidly evolving field of genome integrity and RNA biology. The current reliance on the

Institut Curie's centralised infrastructure, while beneficial, might become a bottleneck if demand exceeds capacity or if novel technologies require significant additional investment. Moreover, for teams with very high demand the geographical distance could be an issue that might be mitigated by local solutions. Failure to address these needs could undermine the unit's competitive edge and its ability to maintain high productivity.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of GIRC is of notable quality and quantity given the modest size of the unit, with over 140 peer-reviewed publications from 2018 to 2023. Teams have consistently contributed to innovative research, particularly in RNA biology, chromatin, microtubuli research, and genome stability. They have produced papers in prestigious journals like Nature Medicine, Science, and Molecular Cell, with many publications led by junior researchers. The unit fosters open science through preprints and maintains rigorous ethical standards. GIRC's reliance on publications with large audience places pressure on teams to maintain consistent output, especially for newer teams or teams with declining funding. Uneven resource distribution and the competitiveness of securing funding may hinder long-term sustainability, while reliance on external grants poses a risk to foundational research.

Strengths and possibilities linked to the context

The scientific production of GIRC demonstrates a strong commitment to high-quality research aligned with international standards, producing over 140 peer-reviewed publications from 2018 to 2023. The unit maintains rigorous quality criteria to ensure its results are irrefutable, with consistent application of theoretical and methodological rigor. Teams have prioritised innovative and high-risk research areas, reflected in groundbreaking findings in RNA biology, chromatin, and genome stability.
The Vagner team, for instance, has made significant contributions to RNA biology and cancer, publishing 40 articles, including twenty as primary data contributions (PDC) in top journals such as Nature Medicine, Genome Research, and Nature Communications. Similarly, the Janke team has excelled in microtubuli research, producing 40 publications (including Science), including collaborative efforts across multiple countries. A notable strength is their inclusivity of junior researchers, with eighteen publications led by PhD students or postdocs. The Lambert team, known for its genome integrity research, achieved 27 publications (including Molecular Cell & Nature Communications) with multiple internationally co-authored studies and junior-led projects, further emphasising collaborative and educational priorities. The Luco team, previously based at the Institut de Génétique Humaine in Montpellier, has transitioned to Institut Curie while maintaining high productivity. Their research on chromatin and splicing yielded seven impactful articles (including Nature Communications), with PhD students leading or co-authoring each. Similarly, the newly started Navickas team (obviously smaller in output) has previously shown excellence with groundbreaking post-doctoral research published in Nature Cell Biology and Cell Genomics.
The unit's editorial policies promote recognition of their results through contributions to reviews in top-tier outlets such as Science as well as the leading journals from Cell Press and Nature Publishing Group, underscoring leadership in the field. Further, the unit actively supports open science by making research accessible through preprint servers (e.g., BioRxiv) and repositories, enhancing transparency and reproducibility.
GIRC demonstrates a proportional scientific output relative to its staffing structure. Its policies ensure inclusivity, equitable authorship distribution, and opportunities for junior scientists to develop their own projects. Research support staff are consistently recognised as co-authors, reflecting the collaborative ethos. The unit's culture of promoting open science and prioritising ethical research ensures adherence to the highest standards, bolstered by internal peer-review mechanisms, data traceability practices, and workshops on scientific integrity.

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

While the scientific output of GIRC is impressive, certain challenges and risks could affect the sustainability of this high productivity. The unit consists of rather few teams and displays heavy reliance on high-caliber publications. Though commendable, this places pressure on all teams to maintain consistent output of this highly demanding research where projects often span multiple years joint between internationally collaborative teams. This dependence could strain resources for individual teams at risk, particularly starting teams in emerging research areas or during funding shortfalls. Newly started teams have limited production due to its recent establishment, which could pose a challenge in achieving a comparable trajectory to more established teams. Mentoring strategies can to some extent provide experienced guidance mitigating the risk.

An uneven distribution of resources between teams (related to funds, staff scientists, teaching burden etc) generally leads to some discrepancies in output. Thus, the large and well-established Vagner, Janke, and Lambert teams have been highly prolific. The variability in publication volumes indicates that newer or smaller groups need more time and support to balance their contributions.
Moreover, the increasing competitiveness in acquiring funding, especially for high-risk or innovative research, may pose a challenge. While the unit has successfully secured national and international grants, fluctuations in funding cycles and grant availability could disrupt long-term research projects. The unit's heavy reliance on external funding for infrastructure and personnel might also risk underinvestment in exploratory or foundational research, critical for future breakthroughs.
The ethical and open science policies, while robust, require constant vigilance to maintain compliance. As scientific practices evolve, the unit must ensure that internal systems for data traceability, reproducibility, and ethical standards keep pace. Any lapses could undermine the credibility of the research. Additionally, the increasing emphasis on preprints and open access poses logistical and financial challenges for ensuring universal accessibility to publications.
Finally, maintaining international collaborations and multidisciplinary research efforts, which are strengths of the unit, depends heavily on stable geopolitical and institutional contexts. The dependency on international talent necessitates proactive integration policies to address cultural and operational challenges.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

GIRC demonstrates marked non-academic interactions, fostering partnerships that drive societal progress. The Vagner team's creation of Ribonexus, a cancer therapy start-up with €6 million in funding, exemplifies impactful industry collaboration. The Janke team's Cifre PhD contract with Biogen also highlights successful industry ties. The Luco team engages in public science outreach through exhibitions and seminars, while the Navickas team promotes science education in schools. While GIRC engages with the non-academic world, the necessary focus on research supervision makes non-academic partnerships time-consuming, requiring a balance between scientific output and societal engagement. GIRC's reliance on external funding exposes it to risks such as fluctuating resources and changing geopolitical factors, which may hinder the sustainability of its outreach and industry collaborations.

Strengths and possibilities linked to the context

The scientific activities of GIRC demonstrate strengths in its non-academic interactions, particularly in fostering valuable partnerships that contribute to societal advancements. Notably, the Vagner team's research in RNA biology and cancer has led to the creation of Ribonexus, a start-up focused on developing innovative cancer therapies, securing €6 million in funding. Additionally, the Janke team has secured a Cifre PhD contract with Biogen, exemplifying successful collaboration with major industry players. The Luco team actively participates in science dissemination, engaging with both children and adults through seminars and exhibitions, notably collaborating with the Faculty of Science at Université Paris-Saclay. This team's outreach activities also include mentoring programs like "Make Science". The Janke team is concerned by the "apprentis chercheurs" program, fostering the next generation of scientists. Similarly, the Navickas team engages with local schools, offering students direct exposure to research, thereby enhancing the public's understanding of science. The diversity of these collaborations and outreach efforts enriches the unit's societal impact and supports the integration of scientific innovation into real-world applications.
In addition, GIRC's development of scientific products contributes meaningfully to the socio-economic landscape. For example, the Janke team's commercialisation of antibodies has created a valuable resource for research communities worldwide, contributing to advancements in multiple scientific domains. Moreover, the unit's involvement in collaborative science-art projects and public outreach activities, such as the annual science-art event organised by the Janke team and the various initiatives led by the Luco and Lambert teams, demonstrates a strong commitment to bridging the gap between research and society. Through writing articles for popular science publications like *Le Monde*, as well as engaging in media outreach via TV and radio interviews, the unit has been instrumental in translating complex scientific findings for public consumption. These activities highlight the unit's efforts in contributing to public understanding of scientific developments, thus influencing broader societal discourse on cutting-edge research.

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

GIRC is active in non-academic interactions even though the primary focus is on research and research supervision. While several teams have established strong connections with industry and public outreach sectors, the overall volume and scope of these interactions could be enhanced or expanded to reach more diverse sectors of society. This is a delicate balance as teams must keep focus on the scientific production while potentially incorporating time-consuming non-academic aspects. Thus, a cost-benefit line of thinking must be integrated to ensure that non-academic activities are rewarding and meaningful.
Outreach efforts tend to be more sporadic and focused on specific teams, with a few notable initiatives, but a more coordinated and unified strategy across all teams could increase the unit's visibility and societal engagement.
Finally, GIRC's outreach and industry partnerships may be affected by external factors, such as fluctuations in funding availability, public and market developments, or changing geopolitical conditions. The reliance on external funding sources, especially for projects with high-risk or innovative elements, poses a challenge to their long-term sustainability. It is not trivial to secure robust and diverse funding to support these initiatives and ensure that they translate into tangible societal benefits.

ANALYSIS OF THE UNIT'S TRAJECTORY

Over the past five years, the scientific trajectory of the UMR 3348 unit has demonstrated substantial progress, evolving to address emerging challenges in basic biology, as well as cancer and disease biology. This progression has been marked by strategic shifts in research focus, team compositions, and the integration of novel methodologies, particularly in RNA biology, genome instability, and cell regulation.

Successes and Strengths
The unit has consistently achieved impressive advancements in the molecular understanding of cell biology and cancer-related biology, primarily through its multidisciplinary approach. The integration of RNA biology with genome biology is a distinguishing feature, offering new insights into oncogenic signalling, DNA replication stress, and gene regulation in cancer progression. Breakthroughs, such as the uncovering of RNA-protein interactions at replication forks and the identification of novel chromatin-RNA dynamics, are important contributions to the field.
New team recruitments in the areas of RNA biology (Luco), cancer metastasis (Navickas), early neural development and EMT (Monsoro-Burq), and neuro-oncology (Pouponnot) is strengthening the unit's capacity to explore complex biological questions at multiple scales. The emphasis on innovative model systems, including genetically engineered mouse models (GEMMs), Xenopus Laevis, organoids, and 3D tissue models, allows for deep functional-mechanistic investigations that have both basic and translational implications. Additionally, the close integration with clinical and industrial partners, for example in the fields of pediatric cancers and breast cancer, ensures that fundamental discoveries translate into potential therapeutic strategies.
The unit's international visibility has grown, facilitated by collaboration with esteemed partners, and their continued success in securing competitive grants (ANR, ERC) further underscores the scientific and translational potential of the unit.

Areas for Improvement
While the unit has made significant strides in research, there are areas for further enhancement. There is a risk in GIRC becoming too diverse especially if the unit expands in number of teams with diverse topics. This may reach an extent where teams are weakly connected without a joint collegial vision and a vibrant institutional environment. Coordination between the diverse teams could be improved to maximize synergies across projects, particularly in the integration of findings from different biological scales. A more unified strategy for collaborative outreach and engagement with industry (and supervisory bodies) could also help amplify the unit's societal impact and visibility beyond the academic sphere, while also serving to boost unit coherence.
The reliance on external funding, particularly for high-risk, innovative projects, remains a general challenge. While the unit has successfully secured various funding sources, continued attention must be paid to diversify and sustain this funding, ensuring long-term viability for the projects, especially as initial grants conclude. Moreover, optimised recruitment and mentoring strategies are needed to ensure that essentially all teams (including newcomers) have conditions for success.
Furthermore, while the unit excels in the development of new model systems, there remains room to refine these models, particularly in their complexity and relevance to human disease. Continued efforts to improve organoid models and integrate immune components, for example, will enhance their utility in both mechanistic studies and therapeutic testing. Moreover, continuous diversification in terms of model's systems might not be optimal use of resources and could at least to some extent reduce synergies in joint use of models.

Forward-Looking Vision and Recommendations
The unit's five-year scientific project presents a forward-thinking strategy with ambitious goals to tackle unresolved issues in basic and disease-related biology. To support this vision, the unit can consider:

1. Ensure Sustainability of Funding: Focus on securing long-term funding through diverse channels, including public and private sector partnerships. Ensure optimal recruitment and mentoring programmes. Enhanced communication and outreach to potential industrial partners should be prioritised to mitigate funding risks.

2. Foster Greater Collaboration Across Teams: Encourage further integration of expertise between teams to address shared themes such as RNA biology, cytoplasmic processes, genome instability, and cellular response to DNA damage. Collaborative workshops, especially around emerging technologies could stimulate cross-team innovation.

3. Strengthen Non-Academic Partnerships and Outreach: Continue to build relationships with industry and clinical partners to enhance translational research. The unit's public engagement activities could be more coordinated and inclusive of more teams.

4. Support Emerging Research Themes: Encourage the exploration of high-risk, innovative research areas by providing´space and resources for early-career researchers and new team leaders. The recruitment of new, excellent junior principal investigators (JPIs) will be crucial for maintaining the unit's dynamic research environment.

In conclusion, the GIRC unit has an interdisciplinary approach, robust team dynamics, and strong links to both academia and industry which make it well-equipped to address important biological questions as well as the most pressing challenges in understanding and treating cancer.

RECOMMENDATIONS TO THE UNIT

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

The GIRC is a relatively small but well-functioning unit located just outside of Paris and being part of the large Institut Curie. As such, GIRC is embedded in a major research center in France benefitting from major infrastructure, experienced research administration etc.

A few areas of concern with need for future improvement were apparent to the committee. Most importantly, facility improvements must take place to address the suboptimal conditions of the premises, including renovations to enhance workspace comfort and functionality. Governing bodies must prioritize resolving issues such as low temperatures to maintain productivity and support staff well-being. This should also include mitigating risks from structural constraints during renovations with user-involved planning: Proactively plan for potential disruptions during renovations, ensuring research continuity through temporary facilities or other mitigating measures. Structurally, it appears that Institut Curie must consider how to best deal with building operations at the site, in order to maximize research and limit unnecessary issues related to the premises.

The GIRC teams have been able to develop a coherent unit even though there are relatively large distances between themes and approaches amongst the rather few teams. With a continuous expansion into new models systems and research areas, the committee is somewhat concerned that unit research identity will be too dispersed, which will limit synergies and resources while also potentially harming unit coherence. To mitigate such development, the committee recommends that the unit actively encourages strategic collaborations, notably with the new recruited teams: Initiatives could include shared strategic planning, joint grant applications, and co-organised research programs to bolster innovation and impact.

Recommendations regarding the Evaluation Area 2: Attractiveness

The GIRC is currently an attractive unit with a marked international profile at PI and researcher levels. The unit should maintain and, if possible, expand the its strong global reputation through publications in top journals, participation/organisation of international conferences, and leadership roles in collaborative networks.
It is important with international, flexible recruitment policies to address global competition and high turnover risks (of international PIs). The unit should consider to develop its own SAB to strengthen input from and foster relationships with global elite academic networks. This will help attract top PI candidates and ensure implementation of optimal strategies through the unit. Moreover, the SAB should especially guide the unit as it grows to avoid the risks in extensive thematic diversification.
To ensure stable funding and support unit coherence, the committee encourages collaborative, large-scale grants to secure resources for multi-team projects and reduce dependency on competitive cycles.

Recommendations regarding Evaluation Area 3: Scientific Production

The GIRC has very high and quality-focused scientific production. To ensure that junior teams succeed and contribute, the mentoring program should include guidance to junior teams in navigating publication strategies and research development to sustain high-quality output.

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

The GIRC unit is active with regards to societal contributions at a scale that fits its relatively small size, with the remarkable creation of Ribonexus as a highlight. The unit could consider to develop a coordinated strategy to enhance and unify the outreach activities across all teams, this will also raise GIRC's societal visibility.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: RNA Biology, Signalling and Cancer

Name of the supervisor: Mr. Stéphan Vagner

THEMES OF THE TEAM

The team has focused on RNA metabolism and its regulation in several types of cancer cells, including melanoma, non-small cell lung cancer, breast cancer, and acute T lymphoblastic leukemia. In the recent past, the team studied several aspects of mRNA regulation, such as transcription, processing, and translation and its implication in cancer cell pathology and resistance to target therapies. Methodologically, they combined biochemical, genomics/transcriptomics and cell biology approaches to both cancer cell lines, in vivo and human biopsies.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hcéres committee, including keep up with excellent research activities and obtaining international grants (European Doctoral Network) were respected and achieved.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	6
Sous-total personnels permanents en activité	**10**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	6
Sous-total personnels non permanents en activité	**9**
Total personnels	**19**

EVALUATION

Overall assessment of the team

The scientific production is remarkable with original contributions in several cancer types (Nat Med 2018, Nat. Com 2019, Genome Res 2022, EMBO J 2023, etc).
The attractiveness is outstanding with highly competitive national (LNCC; INCA), European (MSCA Doctoral net, Swiss Rising Tide Foundation), and international grants (US Melanoma Research Alliance), recruitment of PhD and postdoc fellows, review articles in prestigious Journals (Cell and Nature Reviews Cancer), and speakers in many international meetings (EMBO).
Valorisation is excellent with the foundation of a start-up in 2021(Ribonexus).

Strengths and possibilities linked to the context

Since 2018, the team has been very successful in attracting young scientists, with seventeen PhD candidates of which thirteen defended their thesis (4 are still in the team to finish their thesis), and six Postdoctoral fellows (one is still in the lab). Most PhD students, expect two, significantly contributed to the scientific production of the team by co first-authoring at least one original article. Importantly, both former PhD students and postdocs found a position to continue research either in academia as postdocs or in private sectors.
The team obtained highly competitive funding as coordinator, as attested by three consecutive labellisations by the Ligue Nationale Contre le Cancer since 2012, several INCa, European grants (MSCA Doctoral network and the Swiss Rising Tide Foundation), and the International US Melanoma Research Alliance, and Several fellowships for PhD and postds. In total the team raised about 6 million euros since 2018.

The team's work is internationally well recognised in their domain, as attested by their numerous publications in highly reputed Journals and the recurrent oral presentations to national and international meetings (> 20 over the past five years including EMBO workshop and Keystone symposia).
Team members received several awards, including one of research excellence from the Inserm and from the ARC Fondation in 2022 and 2023 (2), respectively. They also functioned as experts for different research and evaluation committees, including Journals (Nature, NAR, Nature comm, etc), and charity and public foundations (LNCC, ANR, INCA, Wellcome Trust, Italian telethon, etc..).

The scientific production is outstanding, with 43 original articles, including 23 as first and (co-) last authors (Nat Med 2018, Nat. Com 2019, Blood 2020, Genome Res 2022, EMBO J 2023, etc), and fourteen review and book chapter articles, including seven as first and (co-) last authors in both general or specialised journals, such as Cell 2018 and 2020, and TiBS 2021. Many publications are issued from collaborative works, showing a good interaction with national and internation laboratories. The research activity is multi-disciplinary and characterizes using innovative technologies/techniques that the team implemented and modify for improvement/adaptation.
An illustrative example of the high-quality research conducted by the team is the finding that eIF4F activity surprisingly controls the expression of interferon-induced PD-L1 to promote tumour immune-mediated effects, which can be pharmacologically modulated (Nature Med 2018 and Cancers 2022). Based on these data, the PI created a start-up company, named Ribonexus, to develop inhibitors of eIF4A for anti-tumoural target therapies, demonstrating that high-level basic research could be coupled with economical valorisation.
Finally, the team is continually active in outreach activities, their findings and knowledge to mass media BFM and Smart TV) and participated in open debates on topics of cancer.

Weaknesses and risks linked to the context

Although there may be general difficulties to hire outstanding postdocs, it seems that this staff category may be less productive in terms of publications compared to PhD students. This may result in losing team attractiveness in long terms.
Although the research of the team has potential economical valorisation, the team does not appear to interact with pharmaceutical and biotech companies, which could enable the securing of private funding.

Analysis of the team's trajectory

The team presented a very well-structured project focused on post-transcriptional mechanisms and RNA-binding protein activities to investigate the development of anti-cancer treatment for melanoma and lung cancer based. It is based on published and unpublished data of the team. The project is developed into three axes and is funded for the next three years by national grants, including the LNNC the INCA. Also, the critical mass of the team is in adequation with the proposal. Methodologically the project will be carried out by both candidate and unbiased approaches using cutting edge techniques, such as the CLIP-seq to study the RNA-binding activities and evaluating the therapeutic potential of the findings by collaborating with clinical teams. Different collaborators have been identified to accomplish the proposed project.
The axis "translational regulation in cancer persister cells" is focused on the study of two candidate mRNAs, named 53BP1 and CREBBP, whose m6A modification appears to be upregulated in their 5'UTR to enhance their translation in BRAF and MEK inhibitors treated resistant cells. In this axis the team will study the direct biochemical mechanism leading to the translation upregulation upon 5'UTR methylation and the consequences in terms of epigenetic and gene expression deregulation programmes in cells, preclinical models (PDXes) and human biopsies.
In the second axis "The RNA binding activity of the BRAF kinase", the team is studying the unconventional role of MAP kinase proteins, including BRAF and MEK, as RNA-binding proteins. The team will use both biochemical (i.e. CLIP-seq) and cell biology approaches (i.e. PLA) to study this novel function and the heterodimer formation of BRAF-CRAF increased in resistant melanoma cells treated with anti—BRAF or anti-MEK therapies. This axis will

be mainly conducted on cell lines. The data on BRAF-RNA interaction can be potentially used as marker or therapeutic targets.
The third axis is entitled "Identification and role in cancer of microprotein-coding intronic polyadenylation isoforms". Shortly, the diversity of microproteins originated from intronic polyadenylation isoforms may be deregulated in cancer cells. The aim of this axis is to identify at the genome wide scale these microproteins and define their role(s) in lung cancer cells by genome editing deletion/overexpression/mutation (by Crispr) in cancer cells and detection in patient biopsies. The presence and role of microproteins-coding intronic polyadenylation isoforms will be also investigated melanoma cells.
Together, the trajectory is ambitious but feasible based on the highly standard proven track record of the team, the availability of the funds, and the personnel present in the team. The originality relies on the idea to couple novel fundamental biochemical and molecular post-transcriptional mechanisms to cancer-oriented biology.

RECOMMENDATIONS TO THE TEAM

The committee recommends the team to continue with its outstanding research activities and trajectories, specifically on post-transcriptional regulation of melanoma pathogenesis and drug resistance. We encourage the team to further promote productive post-doctoral research activities.

Team 2: DNA Recombination, Replication and Genome Stability

Name of the supervisor: Ms. Sarah Lambert

THEMES OF THE TEAM

The team is focused on investigation of the molecular basis that prevent genomic instability using the yeast S. pombe and human cells as model systems. In particular the Team is focusing on the molecular mechanisms that preserve DNA replication forks stability when DNA synthesis is challenged by natural obstacles or DNA damaging agents.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The Team has followed the recommendations of the previous report by continuing to produce excellent science, obtaining funding and be internationally recognised. The team size has also been kept rather stable, the will to transfer their findings in mammalian cells has been taken into consideration and efforts have been made to apply to international grants.

WORKFORCE OF THE TEAM: 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	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**3**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	1
Post-doctorants	1
Doctorants	3
Sous-total personnels non permanents en activité	**5**
Total personnels	**8**

EVALUATION

Overall assessment of the team

Internationally recognised team that has generated important and novel insights in the field of replication stress and genome stability. This is witnessed by an excellent publication track record in highly reputed scientific journals. The team is attractive and visible, it has been very successful in securing competitive funding. The team is also actively involved in teaching and public outreach activities. Overall, the performance of the team is excellent.

Strengths and possibilities linked to the context

The team is carrying out excellent science, it has an excellent publication track record consisting of work mainly done by PhD students and postdocs. The team is involved in several national and international collaborations and has international visibility. The team has also been able to secure funding by obtaining competitive grants. The research topics developed by the team are topical and at the forefront of the specific research field. In terms of scientific production, eleven publications are signed by PhD students or postdocs as a first authors. Twelve publications include international collaborations (UK, Sweden, USA, Poland). 70 % of the scientific production is published as "open access" or deposited on preprint servers (HAL, BioRxiv). Key findings involve the discovery of RNA-based mechanisms in protecting DNA replication forks from degradation (Cell Reports & Molecular Cell, 2023). The team has also been very successful in securing competitive funding (5 ANR of which 3 as coordinator, 1 INCA PLBIO as coordinator, ARC, Team Label National Ligue against Cancer, La ligue; Team label Medical research Foundation, FRM). Concerning the work force, the team has gained one supporting personnel (ITA) and has supervised six postdocs. The team is also actively involved in teaching and public outreach activities. Overall, the performance of the team is excellent.

Weaknesses and risks linked to the context

Notwithstanding the excellent science carried out and its international visibility, the team suffers from a restrained number of permanent scientists to secure the perpetuation of the technical knowledge acquired during the past years and ensure the supervision of undergraduate students. Further, the attractiveness for postdoc has declined, although this appears to be a common trend also in several other laboratories. Concerning funding, although excellent at the national level, international attractiveness appears to be lacking or not a team focus.

Analysis of the team's trajectory

The team's trajectory for the next five-years continues the research themes developed in the past five years, which consists in analysing the molecular mechanisms operating at DNA replication forks stalled by natural obstacles or DNA damage. The proposed research will be developed under four axes: 1) involvement of the chromatin remodelling factor CAF-1 in the repair of stalled forks; 2) role of the nuclear architecture in the repair of stalled replication forks; 3) study of RNA-based mechanisms in the restart of stalled replication forks; 4) analysis of the DNA damage response in the nuclear space and under pathological conditions.
Axis 1 is rather straightforward and aims at better defining the role of CAF-1 in mediating DNA replication fork repair and restart. This is extending observations obtained in yeast to human cells and investigating its relationship with the BLM DNA helicase, which has already been involved in stabilisation of stalled replication forks.

Axis 2 is very ambitious and outlined in 4 different aims. In Aim 1 is intended to understand how different sub-nuclear compartments handle stressed replication forks. The identity of these compartments and how stressed forks can be addressed to these nuclear sites was not specified. In the same line, Aim 2 intends to identify proteins associated with stressed forks localised in specific nuclear sub-compartments by proteomics. Aim 3 concerns the role of the SUMO post-translational modification in directing stressed forks in sub-nuclear compartments. Finally, Aim 4 intends to explore whether genome maintenance pathways operating at sites of replication stress change during cell differentiation. For this, the team intends to implement human cells models. The cell differentiation system to be used was not specified.

Axis 3, outlined in 2 aims, concerns the role of RNA in DNA replication fork integrity, a follow up of previous findings of the team. Aim 1 intends to determine whether the KU protein, involved in non homologous end joining, can bind RNA and if this binding may be important to facilitate replication fork stability. In Aim 2 it is proposed to identify proteins interacting with RNA at replication forks, stalled or not. This work will be realised in collaboration with team 1.

Axis 4 focusses on replication stress and diseases. The idea is to use a quantitative flow cytometry method (QIBC) previously developed by the team, to analyse DNA damage response components and activity in the nuclear space, particularly in medulloblastoma (as a collaborative project).

RECOMMENDATIONS TO THE TEAM

The Committee encourages the team to continue the research lines undertaken. The committee is confident that the Team will succeed in securing fundings for the next five years and encourage the PI to persist in the efforts of applying to international grants. As for the team trajectory, although the questions raised are highly relevant, Aim 2 appears to be too ambitious. In several parts, basic details of the methods to be employed have not been described, making difficult to assess the feasibility of the projects. Further, setting up methods to capture RNA-binding proteins can be challenging. Identification of atlas of proteins by mass spectrometry needs

to be followed by molecular characterisation of at least one of them (perhaps after evaluating a handful of lead candidates), which involves a large amount of work. The team also intend to implement new human experimental models that need time and efforts to be established. Hence, the committee recommends to revise and focus the Aims of this axis by taking into account the amount of work required and adapting them to the workforce of the Team. Efforts must be made to recruit at least another permanent researcher and continue the effort to recruit at least one additional postdoc.

Team 3: Controlling Microtubule Dynamics and Function with the tubulin code

Name of the supervisor: Mr. Carsten Janke

THEMES OF THE TEAM

The Team focuses on one main theme: mechanistic understanding of how the "tubulin code" controls long-term cellular functions and homeostasis. They determine how the posttranslational modifications of tubulin, combined with the expression of isotypes genes contribute to the functions of the microtubule cytoskeleton. The team developed an integrated approach combining imaging, biochemical and biophysical studies with cell and whole-organism approaches. They follow four axes to identify the parameters directing the assembly of single molecules to tubulin complexes, their function in isolated neurons as well as in organisms (mice), and finally how the modifications of the tubulin code impact neurodegenerative diseases.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has conducted the relevant actions to take into account the recommendations of the previous expertise.
The team has developed very innovative protocols (Nat Protoc 2019, Nature Cell Biol 2022) that have been critical to firmly demonstrate the existence and the role of the "Tubulin code" that was challenged for many years. They demonstrated that tubulin modifications can selectively control the interaction profile of microtubules with different associated proteins (EMBO J 2023) and by such contribute to the fate of the cell.

The team has raised funds from private foundations and obtained a Cifre PhD contract with Biogen (Boston, USA). Importantly, the team is commercialising antibodies which they develop. This activity has generated a large collection of novel antibodies that are now available worldwide, and that have helped to developed the activity of many new research projects as testified by the increasing number of sales.

The team obtained prestigious international grants: an MSCA doctoral training network funded by the European Commission, a Welcome Trust – DBT "team science" grant with two Indian collaborators, as well as an ERC advanced grant and an ERC synergy grant.

The team is scientific organizer of an annual science-art collaborative project (since 2019) between labs of Q-life and a class of ~30 students of the École Professionnelle Supérieure d'Arts Graphiques Paris.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**7**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	4
Sous-total personnels non permanents en activité	**6**
Total personnels	**13**

EVALUATION

Overall assessment of the team

Although sustained by the discovery of many novel PTM of tubulin in the 80's the concept of the Tubulin code formulated in 1976 was increasingly challenged. The outstanding scientific production contributed to reverse this trend and provided strong outcomes in fundamental as well as in translational research: from Science 2005 to EMBO J 2023 with 40 (20 DC) published between 2018-2023. International recognition is remarkable. The team made efforts with elevated success to help young talents starting a strong career. Composition of the team and the funding are outstanding to secure the project.

Strengths and possibilities linked to the context

Since 2018 the team made efforts with success to help young talents starting a strong career. The team trained eight postdocs, eight PhD students, masters and clinicians. Two postdocs got a stable position as CNRS CRCN in 2020-2021 (one declined, team leader at Instem research centre in Bangalore). All PhD students got postdoc positions in prestigious research centers (Stanford University, NIH, Max-Planck Institute) and published in prestigious journals (EMBO J, Nat Cell Biol, Science). A key strategy is to favor training by collaboration with other teams (DBT Wellcome Teams grant, 2 EMBO short term fellowships).

International recognition of the team is outstanding thanks to the team leader and one of the PI, Maria MAGIERA. In 2022, the team leader as PI obtained, the ERC Advanced grant and the ERC Synergy grant (declined the ERC Advanced grant). In 2019 M Magiera received the "Prix Forcheurs-Jean-Marie-Lehn" and in 2021 C JANKE received the "Grand Prix Charles-Leopold Mayer" French Acad of Sciences. They obtained highly competitive grants for organising international workshops: EMBO/EMBL symposia Microtubules 2018-2024, Company of Biologists Workshop 2024, French-German Fall School "Microtubules in Neurons" 2021, 2023; they are guest editors for Semin Cell Dev Biol and Curr Opin CellBiol and they review MS for Science, *Nature*, etc. The team leader coordinated the Hcéres review of Institut J Monod and the Centre of Interdisciplinary Research, College de France; he is member of NC of the Fondation ARC and member of the EMBO Installation Grant Committee. They supervised eight PhD students, participated to thirteen PhD and one HDR juries, and in 23 Theses Advisory Committees.

Composition of the team and the funding are adequate to secure the project, with two CNRS CRCN recruited, two CNRS research engineers (IR, IE) and 26 highly competitive national (7) and international (19) fundings, five coordinated by the team leader and two by M Magiera.

The team participated to actions to wider the community: interviews in media (France Culture); videos; co-organisation of Art-Science workshop (USA 2022,2023); project with École Professionnelle Supérieure d'Arts Graphiques.

The outstanding scientific production contributed to reverse questioning about the existence of a "tubulin code" proposed in 1976 with identification of PTM of tubulin that play crucial roles in tubulin network (Science 2005; Mol Cell 2007; Cell 2009; Dev Cell 2009; Cell 2010; Mol BiolCell 2014) but also in the outcome of pathologies such as neurodegeneration (EMBO J 2018; EMBO J 2018, EMBO J 2021) and cancer (EMBO J 2014), male fertility (J Cell Sci 2019; Science 2021), ciliary functions (J Cell Biol 2013; J Cell Sci 2017; JCell Biol 2017). The development of novel technologies (Souphron et al., Nat Protoc 2019, Nature Cell Biol 2022) allowed to directly demonstrate that tubulin modifications can selectively control the interaction profile of microtubules with different associated proteins (EMBO J 2023).

Weaknesses and risks linked to the context

An identified weakness is that the players in the non-academic world with whom the team interact for outreach (i.e. artists) encounter financial difficulties in collaborating with academia. No clear strategy is proposed to circumvent this problem.

The interactions with the other teams of the Unit are not obvious. How the project integrates, and create synergism with the Unit objectives needs is not clearly exposed.

There is no clear plan and perspectives for the valorisation of the fundamental results.

Analysis of the team's trajectory

The regulation of the microtubule (MT) cytoskeleton is key to maintain homeostasis. Failure to maintain homeostasis can lead to disease. To perform their numerous biological functions, MTs interact with a large panel of proteins, including molecular motors and a wide variety of mostly underexplored MT-associated proteins (MAPs). At present how various MT interactors
adapt to the ever-changing physiological requirements encountered by cells throughout the lifetime of an organism remains to be deciphered.

The team has made major outstanding pioneer and seminal work sustaining the existence and the function of the tubulin code concept. The tubulin code proposes that MTs can be functionally specialised by specific posttranslational modifications (PTMs) on tubulin and by expression of different tubulin isotypes.

Abnormal accumulation of the PTM, expression of different tubulin isotypes, or tubulin mutations causes neurodegeneration in mice and humans, vision disorders, male infertility, ciliopathies and cancer.
The objective of the team is to determine how the tubulin code alters the behaviour of MTs and their associated proteins at the molecular level, and how this translates into cellular functions and homeostasis in the organisms.

To fulfil this ambitious objective the team built a clear integrated approach combining imaging, biochemical and biophysical studies with cell and whole-organism approaches.

They have deconvoluted the global objective into four axes with well identified complementary objectives and the relevant methodologies and technologies. In addition, the team has built an interactive collaborative and very active network to provide all the technologies that are required for the project and that are not available in the team. This represents a clever strategical element that secures the chance of success of the project.
The first axe will determine how the tubulin code affects biophysical properties of MTs and their interactions with associated proteins. The ambition is to provide the first comprehensive and ultra-high-resolution molecular characterisation of how the tubulin code determines the formation and properties of MT-MAP assemblies.
The second axe, will provide the first system-wide description of how tubulin PTMs control MT functions in neurons, how specific modifying enzymes selectively control single players in this process, and how this collectively affects the function of the MT cytoskeleton in cells.
The third axe, by using unique in vivo imaging will allow to approach the long-standing question of how the tubulin code can adapt MT functions at the scale of an organism over
a lifetime.
The fourth axe will use unique animal models to determine how the tubulin code contribute to neurodegeneration notably in the context chemotherapeutic drugs treatments widely used targeting MTs and induing peripheral neuropathy.

All the conditions in terms of human resources and financing are in place to make this ambitious project a success.

RECOMMENDATIONS TO THE TEAM

The scientific production and almost all the activities of the team rely on few members of the team. It could be useful to stimulate other team members to take more responsibilities, notably for grant applications.

The team encounters few applications from students and postdocs. Possibly, the number of teacher-researchers is too low. They should consider how to make publicity to students, for example, the team could communicate with teachers with teaching responsibilities to mention that the team is looking for students. It may also be worthwhile to approach other schools, such as engineering schools or high schools that offer BTS training.

Another weakness is that the players in the non-academic world with whom the team interact
for outreach (i.e. artists) encounter financial difficulties in collaborating with academia. Participation to an European actions (such as COST) could be an opportunity to finance this type of activities and also to find students and post-docs. The team should look for COST actions related to its research theme (https://www.cost.eu/).

Moreover, the alignment with unit objectives and interactions with the other teams of the Unit should be better explained (perhaps in a joint effort with the unit leadership). it should be clear how joint integrated projects are under development and how they may create synergism.

The team is encouraged to improve or better communicate on its partnership with companies (e.g. Biogen) and its valorising actions, (commercialising of antibodies).

Hence, the team should expose more clearly its vision of the valorisation of the fundamental results and the way they want to interact with the industrial world. The team should better outline what they expect to gain from the antibody commercialisations.

Team 4: Chromatin and RNA splicing

Name of the supervisor: Ms. Reini Fernandez De Luco

THEMES OF THE TEAM

The research team is investigating the interplay between chromatin organisation and alternative splicing, specifically during the epithelial-to-mesenchymal transition (EMT). More specifically, they focus on chromatin- and epigenetics-mediated splicing mechanisms. By understanding how chromatin structure influences splicing patterns, they aim to identify novel regulatory mechanisms that drive tumour metastasis.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Since the team arrived only two years ago (2022) there is no previous evaluation by the Hcéres of this team at the GIRC. Recommendations for the scientific strategy from the previous Hcéres visit at Montpellier do not seem relevant anymore. Recommendations for scientific production have been followed, manuscripts in preparation have been published.

WORKFORCE OF THE TEAM: 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	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**2**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	1
Doctorants	2
Sous-total personnels non permanents en activité	**4**
Total personnels	**6**

EVALUATION

Overall assessment of the team

Since the arrival in 2022 of the team at GIRC there is not yet publication, that is not surprising. However, from the IGH the team has published in top journals. The team is visible and well funded with grants from several sources (ANR, INCA) and has been labelled for 5 years from LCC. The team has also secured funding from Merck's private foundation.

Strengths and possibilities linked to the context

The team is involved in several national and international collaborations and has international visibility. The team has also been able to secure funding by obtaining competitive grants. The move to GIRC seems so far positive with 1 permanent position (1 engineer) in the team. This move will probably be an opportunity to improve their

attractivity and to develop research that is more clinically relevant. The team is rather new at GIRC, however, from the IGH the team has published in highly reputed journals as corresponding author (Cell Reports and Nature Communications) and as partner (Nature Cell Biol). The overall number of publications is 6 (3 as corresponding author) and a preprint. Among the four PhD students mentioned for the evaluated period, three appear as co-first author of a manuscript (BMC Biology 2021, BioRxiv 2022 and Cell reports 2022). Special attention appears to have been given to postdocs, with two publishing first-author papers and one co-corresponding. This is an excellent training supervision for young researchers. The team is very well funded with grants from several sources (ANR, INCA) and has been labelled for five years from LCC. The team has also secured funding from Merck's private foundation.

Weaknesses and risks linked to the context

The main risk seems to be the lack of a strong bioinformatic support. It is mentioned the need of a permanent bioinformatician, however to be efficient this must be associated to a strong bioinformatics community. The interconnexion with the bioinformatics Hub from Curie seems to represent a valuable alternative. Interactions, or accessibility must be reinforced.

Analysis of the team's trajectory

The team has made very interesting discoveries about the link between histone modifications and mRNA alternative splicing, and now want to capitalize on that. This is a very ambitious trajectory, employing a wide range of techniques and addressing a multitude of questions with a relatively small team. Single-cell level projects are challenging but highly interesting and relevant. The proximity labelling approach, while promising, is potentially risky due to the high number of false positives, which would require significant time and effort to screen. Transitioning to more clinically relevant models, such as breast cancer organoids, makes sense in the GIRC environment but represents a substantial challenge.

RECOMMENDATIONS TO THE TEAM

It is important to continue and strengthen the interactions/collaborations with the other teams at GIRC.

Team 5: ARN, microenvironnement tumoural et métastase

Name of the supervisor: Mr. Albertas NAVICKAS

THEMES OF THE TEAM

The team focuses on identifying molecular mechanisms that underlie the establishment of the metastatic niche, an environment in the distant organ that becomes permissive for tumour dissemination. The team is primarily interested by the role played by cell-external RNA in this process.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

None.

WORKFORCE OF THE TEAM: 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	0
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**1**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**4**
Total personnels	**5**

EVALUATION

Overall assessment of the team

As a newly formed team (established in July 2022), it is still too early to fully evaluate its overall performance. To date, all publications and the four BioRxiv preprints stem from the PI's postdoctoral work. Nevertheless, the team appears well-organised, with regular meetings between team members and the PI, as well as weekly lab sessions. Sustaining these interactions will be essential, especially for a team in its early stages of development.

Strengths and possibilities linked to the context

The Principal Investigator (PI) demonstrated strong productivity during his postdoctoral work, and the GIRC provides an excellent scientific environment for advancing his projects. The PI has successfully secured several competitive grants, including the ATIP-Avenir, the PSL Young Researcher Starting Grant, and the Prix Ruban Rose, ensuring financial stability for the coming years. Additionally, the recent appointment of the PI as a tenured INSERM researcher in January 2024, is a significant asset, further strengthening the research team.

Weaknesses and risks linked to the context

Currently, bioinformatics analysis depends solely on a temporarily contracted engineer. Securing sufficient funding to either regularly hire a bioinformatician or establish a permanent position will be crucial, though the latter may not be feasible in the short term. The team pursues demanding high-risk projects, which is challenging in terms of feasibility with potential impacts on next level funding as well as timely publications for team members.

Analysis of the team's trajectory

The team's research trajectory addresses original questions and is highly ambitious, especially considering that much of the work will be undertaken by PhD students. This could raise concerns about their ability to publish first-author papers before the end of their PhDs. Part A appears to be the most well-defined section, while Part B, though very appealing, seems more speculative. It is challenging to determine whether this part is well supported by preliminary data.

RECOMMENDATIONS TO THE TEAM

Ensuring the team's successful integration into the GIRC and facilitating the PI's transition into the French research system is essential. Moving the BioRxiv papers to publication quickly would allow the PI to fully concentrate on advancing the team's projects. The transition from postdoc in the USA to group leader in France can be challenging, so special attention should be given to supporting the PI during this phase. For instance, mentorship from a more senior researcher (outside the unit) could help guide the transition effectively. Additionally, particular care should be given to the PhD students, as the French research system differs significantly from the US model.

Team 6: Signalling and Neural Crest Development

Name of the supervisor: Ms. Anne-Hélène Monsoro Burq

THEMES OF THE TEAM

The theme of the team is focused on the gene regulatory network (GRN) of the neural crest where the team were pioneers. The team develop new tools to study the neural crest biology focused on many aspects (cellular, molecular, bioinformatics, in vivo approach). The objectives are to understand different aspects of neural crest's GRN dysfunction, in physio-pathological development or in cancer development (metastatic melanoma model). More specifically, the team explores how neural crest cells emerge, differentiate and are affected in disease, notably in cancer (melanoma) and in Waardenburg syndrome.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations of the Hcéres were to improve the interactions with other units in the Orsay site or other units, to develop new avenues of research and potential clinical output and reinforce the permanent core. The team has taken into account the recommendations. Indeed, they collaborated with international and national teams and they have been very implicated in the establishment of a research and training network in their field. They also hired a professor.

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

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

EVALUATION

Overall assessment of the team

The team is internationally recognised in the field of neural crest and cancer biology, where they conduct pioneering work. The scientific production is overall excellent. Concerning the work force, this includes training of six PhD and two postdoctoral fellows during the evaluation period. The team is visible, there is active involvement in teaching and invitations to several international and national conferences.

Strengths and possibilities linked to the context

During the 2018-2023 period, the team published seven review articles and seventeen articles, mainly done by PhD students or post-docs. The scientific production is excellent (Science Advances, PNAS, in leading position). The number of publications is in agreement with the size of the team. Of the seventeen articles, this included 15 as first author and 14 as last/ corresponding authors. Six of the seventeen articles involved international collaborators.

The team has a national and international visibility, notably through their implication of the Innovative Training Network NEU Crest project (ITN NeuCrest, coordinated by AH Monosoro Burq). The team's work is recognised in view of the numerous conference invitations (Gordon Research Conferences 2019, 2023, International Xenopus Conference, 2018) and seminars in foreign laboratories.

Between 2018 and 2023, five Master students, six PhD students and two postdoctoral fellows have been trained in the team. All of the PhD ave followed additional training and presented their work on international congress. Concerning the work force, the team recruited a professor and hosted three invited foreign professors. The leader team is also actively involved in teaching and invited in international and national conferences.

Weaknesses and risks linked to the context

One weakness is securing sufficient funding to recruit new postdoctoral fellows and to develop new methodology (e.g., spatial transcriptomic)

Analysis of the team's trajectory

The team's trajectory will continue on the study of the gene regulatory networks controlling the developmental steps of most major vertebrate lineage. Their objective is to define the early molecular events controlling quantitatively vertebrate ectoderm epithelium patterning during development and epithelial-mesenchymal transition. Firstly, they will use different model systems (frog, fish) to study epigenetic and gene co-expression mechanisms inducing transition to EMT state of ectoderm cells in context of physiological development. Secondly, they will study the EMT transition in development and cancer, notably mechanisms of regulation alternative splicing and histone pattern. Indeed, for this, they will collaborate to the Luco's team to use an embryonic organoid model of CCN (cells of crest neural).
Finally, based on first results on single cell transcriptomics (PNAS, 2024), which identify different trajectories driving the state and the destiny of ectoderm, they will focus to explore in more detail these responsible for the acquisition of neural crest stemness and its potential for EMT. In order to realize this project, they will implement an innovative protocol of highly multiplexed spatial transcriptomics to decipher the spatiotemporal dynamics of NC cell transcriptomes upstream and during EMT.
The team's trajectory is ambitious and innovative, using new methodological approaches to continue in their scientific thematic. The implementation of this project will be reinforced by the integration of one researcher in the team of GIRC.

RECOMMENDATIONS TO THE TEAM

The Committee encourages the team to continue to produce excellent science on the field of development and cancer biology. The committee encourages to develop internal collaborations and to continue their international collaborations, maintain its scientific appeal by publishing in highly visible and widely read journals. The committee encourages the team to recruit at least another permanent researcher and at least one postdoc to reinforce the team. This will fuel research, allow broadening of topics, and boost research output. The team should work dedicated to secure new fundings that will allow development of spatial transcriptomics approaches.

Team 7: Signalling and Cancer Progression

Name of the supervisor: Mr. Célio Pouponnot

THEMES OF THE TEAM

The team has focus on paediatric Central Nervous System tumours, mainly medulloblastomas and their response to radiotherapy. The team is interested in the characterisation of group 3 medulloblastoma, specifically the role of NRL and also in the improvement of radiotherapy in two paediatric brain tumours: MB and AT/RT.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations of the last evaluation were to continue publishing in top journals, to improve the scientific visibility of the team through the participation of international meetings in the domain and to attract post-doctoral researchers. The team has taken into account the recommendations
Indeed, the team continue to publish in prestigious journals (Nat. Comm., 2023, 2022, 2021)) and is well recognised in the paediatric tumour field, specifically in medulloblastoma, as attested by invitations to all international meeting and national congress. The team hosted two post-doctoral fellows.

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

CATEGORIE DE PERSONNEL	EFFECTIFS
Professeurs et assimilés	0
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	2
Sous total personnels permanents en activité	**8**
Enseignants chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	2
Doctorants	4
Sous total personnels non permanents en activité	**7**
Total personnels	**15**

EVALUATION

Overall assessment of the team

The team has been productive and successful in the field of paediatric Central Nervous System tumours, with focus mainly medulloblastomas including responses to radiotherapy. The team has excellent visibility, and the scientific production includes several publications in leading journals.

Strengths and possibilities linked to the context

The scientific production is notable and it includes fifteen original articles, five reviews and one patent in 2021. The journals in which the team published are prestigious (Nat. Comm., 2023, 2022, 2021)), visible, widely read,

and pertinent to the team's activities. They published in Cancer Cell (2019, 2018) which is internationally regarded as one of the top cancer research and oncology journals. Since 2021, the team has been labelled by Ligue contre le cancer. The attractiveness is excellent with national (ARC, Cancéropole IDF, INCA) and international grants (H2020-MSCA-ITN-2019) for a total of 2.4 M€. The team is well recognised in the pediatric tumour field, specifically in medullablastoma, as attested by invitations to all the international Medulloblastoma meetings and national congresses. They have also had a strong involvement in the organisation and co-organisation of national and international events which gives them a great visibility, The team has also co-organised several conferences including the international Symposium "Basic Research on Childhood Cancers" (INCa). Members of this team participate in different committees and are involved in research management. The team obtained different fundings from the European community, private companies (Fondation Bristol-Myers Squibb, Janssen Horizon). Since 2018, six members of the team have been promoted (DRCE, DR1, DR2, CRHC and MCU-HC). The team hosted two post-doctoral fellows, four PhD, three permanent staffs (2 assistant professors and 1 technician) and one Research Engineer, during the evaluation period. Four PhDs were defended during this period. Students obtained different prizes such as Fondation l'Oréal/unesco).

Weaknesses and risks linked to the context

No major weaknesses detected.

Analysis of the team's trajectory

The team's trajectory for the next five-years is to focus on pediatric brains tumours and irradiation, promoting new collaborations in the unit. The proposed research will be developed under 3 axis: 1) Development of three new G3 models : implementation of early mouse rhombic lip progenitors (collaboration B.Hassam, salepetrière Hospital, Paris), implementation of cerebellar organoids from IPS cells (collaboration D Passaro, Cochin institute) and development of faithful in vitro G3 tumour organoid models. 2) Studies on the biology of G3 : Decipher the transcriptional network of G3gamma/GSII MB. 3) Understand the mechanism of resistance to Radiotherapy in MB. This project is very well structured, involving solid collaborative network. The team's trajectory is ambitious and the objective is to identify new therapies for the high-risk tumours and provide a better knowledge of its escape to radiotherapy.

RECOMMENDATIONS TO THE TEAM

The Committee encourages the team to continue on the main stream of the research undertaken. The team should develop international collaborations and maintain its scientific appeal by publishing in highly visible and widely read journals.

Evaluation of the SRC Unit

CHARACTERISATION OF THE UNIT

- Name: Signalling, Radiobiology and Cancer
- Acronym: SRC
- Label and number: UMR 3347, U1021
- Composition of the executive team: Mr. Jose-Arturo Londono-Vallejo, Director; Mr. Lionel Larue, Deputy director

SCIENTIFIC PANELS OF THE UNIT

SVE3: Living Molecules, Integrative Biology (From Genes and Genomes to Systems), Cell and Development Biology for Animal Science
SVE7: Prevention, Diagnosis and Treatment of Human Diseases

THEMES OF THE UNIT

The Signalling, Radiology and Cancer Unit (SRC) is a biomedical research unit aiming at understanding the molecular and cellular mechanisms during embryonic development and cancer pathogenesis/progression as well as metastasis to develop new cancer treatments. SRC is currently composed by seven teams and develops its projects along with two major models derived from the neuronal tube, including neural crest and melanocyte/melanoma development (teams Monsoro and Larue), and cerebellum development and the genesis of the medulloblastoma (teams Pouponnot and Seano). These models are studied to investigate the aggressiveness of derived cancers and propose novel radiotherapy treatments with a particular attention to circumvent as most as possible side effects and resistance to therapies (teams Londono and Prezado). Both in vitro and in vivo (mouse, xenopus and zebrafish) have been used as models.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The SRC Unit (CC, CNRS UMR3347, Inserm U1021) is located on the Campus of University Paris-Saclay, on two floors of building 110 and the first floor of building 112.
Originally created in 2010 with the intent to focus research on embryonic development of melanocytes and pathogenesis of melanoma (Teams Monsoro Burq, Larue, Pouponnot and Ayrault). In 2020, the Unit was re-created with some of the former topics and teams and the inclusion of a new team developing radiotherapy research (Team Prezado) as promising therapeutical approach, the team leader of this additional team was laureate of the ERC-Consolidator in 2019. In 2022, A Londono-Vallejo moved from Institut Curie Paris to Orsay and became the new director of the Unit. Within the new direction, the Unit extended the investigation to brain tumour pathogenesis and progression including pediatric brain tumours, such as medulloblastoma and integrated new teams, such as Teams Seano and Prezado.

RESEARCH ENVIRONMENT OF THE UNIT

The SRC unit is part of the Institut Curie, which is a cancer non-profit foundation organised into three entities, namely, Research center, Hospital group and the Head Office. Geographically, the Institut Curie has three sites, including Paris, Orsay and Saint-Cloud. The SRC is at the Orsay site and belongs to the Research Center. As an Institut Curie Unit, the SRC takes advantage of the interdisciplinary research constituted by 88 different teams, spanning from biology to chemistry and state of the art technological platforms.
The SRC unit was part of former domain 1-biology and chemistry of radiations, cell signalling and cancer and composed by seven research teams and an administrative team to support research. SRC possesses different platforms (part of the CurieCoreTech platforms), which are staffed by engineers from the Institut Curie and Inserm. These include cytometry with local usage and FLASH platform of a new prototype of electron linear accelerator for radiation and anticancer therapies. The FLASH platform appears unique in France and has both national and international vocations from different fields of science, including biology, medicine and physics. In addition, SRC has been involved in the installation of the single cell sequencing technology by the cytometry facility.
The Unit is in line with the politics of the Institut Curie by training new generations of scientists, doing interdisciplinary and innovative research, and by always paying attention on gender equality, diversity and inclusion, health and safety regulations and scientific integrity.

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

N.A.

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

GLOBAL ASSESSMENT

The Signalling, Radiology and Cancer Unit (SRC) is a biomedical research center created in 2010, geographically located at the Paris-Orsay campus, and part of the Institut Curie, which is organised in three entities, namely, Research, Hospital, and Head Office. In addition to the Institut Curie, the SRC is endorsed by the CNRS, the Inserm and the University of Paris Saclay. It is a rather small-sised research Unit hosting seven teams and about 75 people (37 permanent positions), including technical and scientist personnel, postdocs and PhD students. Its budget is of about 25 M€ for the past six years (about 8% recurrent funding, 92% external grants), showing therefore a great attractiveness in terms of fundraising and human capital.
The unit mainly focuses its research on development and cancer pathogenesis/progression from the neural crest and brain with a part dedicated to radiobiology and cancer radiotherapy. Radiobiology and radiotherapy are mainly developed by two teams (Y Prezado which was laureate of an ERC-Consolidator Grant in 2019 and A. Londono). Although most of the projects are mainly fundamental/basic science, some teams develop translational/economical projects with both clinical and industrial partnerships and generated 6 patents. However, none of them have been licensed yet.
The attractiveness and visibility of the Unit are overall excellent with an impressive number of competitive national (ANR and INCA, manly, but also ARC, FRM, and LNCC) and European grants (two ERC and a MSCA international training network), three industrial partnerships, 9 scientific prizes, 49 PhD students and 29 postdocs over the past 6 years, demonstrating its competitive position at national and international levels. The SRC Unit has developed state-of-the-art platforms (single cell cytometry and FLASH facility to explore physical and biological parameters for radiotherapy) to support their fundamental and translational research. Both platforms have been used by both internal and external users from academia and industry and have been run by permanent staff from Inserm and the Institut Curie. At the international level, the unit is highly involved in the participation of meetings (>100 presentations including in prestigious Gordon and Cold Spring Harbor conferences) and organisation more than 30 of national and international meetings of their specialities (such as melanocytes and genetics of melanoma in Spain and immune-oncology workshop in Japan).
The scientific production of the unit is overall excellent. The amount of publication is in agreement with the size of the unit: 230 scientific publications including 80 signed in first/last position, with excellent discoveries of new molecular and cellular mechanisms involved in cancer, development and radiobiology published in good journals of speciality (Development, Cancer Res, etc) or general large audience journals (Nature Comm, Commun Biol, Cancer Cell, Nature Prot, and Sci Adv, etc).
All the teams are very active in teaching, notably at the University Paris Saclay. One team has organised a European course.

The interaction with the non-academic sector is very good for the seven teams. The unit is active for the development of radiotherapy from their translational research in brain- and neural crest-derived cancers. The valorisation stemmed from their research findings is excellent, with 6 patents and a partnership with a start-up company (teams 2-L Larue; 3-C Pouponnot; 6-A Londono- Vallejo; 7-Y Prezado). Two industrial Cifre and other contracts have been made for PhD students, postdocs, and engineers. The unit is also involved in Carnot institutes. However, no patents have been licensed yet. The unit has implemented relevant outreach actions and means to communicate on their research activity with targeted communities (patients and donors) and the public.
In conclusion, the SRC is an excellent biomedical research unit well positioned at both national and international levels. Although the Unit will close at the end of 2025 for the retirement of many team leaders, including the current director Dr Londono-Vallejo, this Hcéres committee would like to acknowledge the outstanding and innovative work that has been done by all past and current personnel of the SRC and their involvement in teaching activities.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Previous report recommended increasing the impact of the publications, the interaction with other Units of the Orsay site, and strengthening the research on radiobiology. These recommendations have been successfully addressed by the SRC. Indeed, some work of the unit has been published in Nature Comm, Cancer Cell, Nature Prot, and Sci Adv, etc. Meetings and international seminars have been held in collaboration with other Units. Finally, the radiobiology research has been reinforced by the recruitment of one new team headed by Y Prezado (ERC consolidator).

B - EVALUATION AREAS

Guidelines for all areas of evaluation (1, 2, 3 and 4): Considering the references defined in the unit's evaluation guidelines, the committee ensures that a distinction is made on the outstanding elements for strengths or weaknesses. Each point is documented by observable facts including the elements from the portfolio. The committee assesses if the unit's results are consistent with its activity profile.

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

Assessment on the scientific objectives of the unit

The scientific objectives of the unit are excellent. The unit develops competitive research in brain and neural crest-derived cancers including pediatric cancers, with potential biomedical and therapeutic valorisations. They focus on uncovering novel mechanisms of cancer pathogenesis and normal physiology of neural development, and find new therapeutical interventions with radiation, which are timely and clinically relevant.

Assessment on the unit's resources

The SRC can be rated excellent on this criterion. The unit has secured all the resources needed for its research during the past mandate. Human resources are reasonable with both permanent staff scientists and technical staff. Many PhD students and postdocs were also present in the unit. The external funding is outstanding, which allowed the development of state-of-the-art platforms and original research. However, it appears that few teams do not have permanent technical staff.

Assessment on the functioning of the unit

The functioning of the unit is also excellent, with the composition of seven research teams. The Unit successfully implemented relevant actions to comply with regulations in terms of human resources and technological platform management, health and safety, gender equality, scientific communication, etc... However, no clear action appears from the document about informatics security, cold data storage and protection of both clinical and scientific data.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

SRC aims at developing innovative and competitive research projects in cancer cell heterogeneity and response to therapies, which represents a major public health concern. In this context, each team uses modern

strategies that span from omics and single cell approaches for both normal and pathological events of neural crest- and tube-derived cell development and transformation, as well as response to radiation therapy. Notably, they combine such high-throughput approaches with physiological, preclinical models and patient samples, to understand the mechanisms of cancer pathogenesis/progression and resistance to therapies. They also aim at identifying innovative therapeutic intervention, with a focus on radiation.
The unit takes advantage of the synergy and complementarity of their own teams to achieve ambitious projects. The projects involve the participation of the teams in some scientific medical programmes, such as Medico-Scientific Programme, radiobiology, and paediatric tumours. Finally, SRC is also involved in scientific communication and outreach activities.

Weaknesses and risks linked to the context

No major weaknesses

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

SRC possesses sufficient human resources to ensure its research activity. About half of the personnel have permanent positions, with the CNRS as the main employer. It currently hosts 24 permanent and non-permanent engineers and technical staff. In addition, nineteen researchers and engineers hold permanent positions. It welcomed 49 PhD students and 29 postdocs in the last six years. Each team trained quite a lot of master students as well.
The unit secured about 150 external grants in the past mandate plus the internal financial resources coming from the following Institutions, Institut Curie (about 185 K€ per year), CNRS (about 85 K€ per year), Inserm (about 54 K€ per year) and University Paris Saclay (about 34 K€ per year). Together with the external grants the total amount raised by SRC is about 25 M€ for the past six years to ensure common consumables, chemicals, small equipment, run facilities, stimulate the use of new technology (such as single-cell sequencing) and develop scientific projects within each team. All teams have reasonable financial means to support their own research projects and activities.

Weaknesses and risks linked to the context

None has been identified.

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

SRC has implemented specific actions to fulfil the regulation governing human resources management, psychosocial risks, ethics (animal work and scientific integrity), gender equality, safety, environment, and protection of scientific heritage, for instance, all new incomers must follow a training class of health and safety gestures upon 15 days from arrival.

Weaknesses and risks linked to the context

From the document, it seems that there are no structured actions for informatics security, cold data storage and protection of both clinical and scientific data, back-up system, or central server(s) for calculation.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of SRC is excellent, with many competitive national (ANR and INCA, mainly, but also ARC, FRM, and LNCC) and European grants (two ERC and a MSCA international training network), three industrial partnerships, nine scientific prizes, 49 PhD students and 29 postdocs over the past six years demonstrating its competitive position at national and international levels. The unit is also highly involved in national and international meetings. Although the Unit will stop at the end of 2025, the two excellent platforms will be still in place at the Orsay site of the Institut Curie.

Strengths and possibilities linked to the context

SRC group leaders and scientists of each team presented their work in different national and international meetings, including in some prestigious ones, such as Gordon and Cold Spring Harbor conferences. Overall, they have disseminated and communicated their research findings via their participation to about a few hundred international conferences, seminars, oral and poster presentations. SRC teams have organised more than 30 meetings (such as melanocytes and genetics of melanoma in Spain and immune-oncology workshop in Japan). SRC successfully obtained European research applications, including ERC and MSCA international training network and national grants such as the LNCC, ANR, ITMO Cancer, etc. nine scientific prizes and various prestigious assignments have been given to PIs and staff scientists during this contract (e.g. FRM, Robert Arceci Innovation Award, Washington DC, National Academy of Science). Some members are also present in various national and local scientific and university councils. Young and senior researchers act as reviewers and editorial board members of some international and national journals in the fields of cancer, development, neurology, skin, and medicine. Their participation as editors in all these discipline journals is in perfect harmony with the topics developed at the SRC.
49 International and national PhD students as well as 29 post-doctoral fellows worked or are still working in the center and obtained some competitive fellowships by international, foreign or national fellowships or programmes, including the MSC research fellowship. SRC organizes internal seminars in which students and post-docs present their work.
All the teams are very active in teaching, notably at the University Paris Saclay. One team has organised a European course.
As aforementioned, in addition to its own recuring funds from the Institut Curie, CNRS, Inserm and Paris Saclay University, which represent about only the 8% of the budget of the Unit, SRC is very active in applying and obtaining external grants, including the ERC, ANR, INCA, ARC ATIP, FRM, industrial contracts, Carnot Institute, and many more… for a total of 25 M Euros for the past six years. INCA and ANR are the major sources of external funding with almost of them coordinated by team leaders of the Center. 2 ERC have been received by Team 7 (Prezado) as consolidator and Team Seano as starting one, as well as a Marie Curie contract by A Ballestin (Team Seano). Three industrial partnerships have been also set up by Onxeo with Team Londono-Vallejo and Varian-Siemmens with Team Londono-Vallejo and team Prezado.
The Unit possesses two platforms, including the FACS facility dedicated to single cell analysis, which is also part of the CurieCoreTech cytometry platform and the FLASH facility to explore physical and biological parameters for radiotherapy. Both platforms have been used by both internal and external users from academia and industry. Both platforms have been run by permanent staff from the Inserm and the Institut Curie.

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

None.

AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

Altogether the scientific production of the SRC is excellent with 230 scientific publications including about 80 signed in leading position. The Unit generated numerous illustrative contributions in the field of cancer, development and radiotherapy published in some of the best journals of the specialities (Development, Cancer Res, etc) or general prestigious journals (Nature Comm, Commun Biol, Cancer Cell, Nature Prot, and Sci Adv, etc), demonstrating the scientific excellence and competitiveness they are capable of.

Strengths and possibilities linked to the context

The SRC has generated a total of 230 publications, including peer-reviewed research articles, reviews and preprints BioRxiv among which, 38% were signed as first or last author. These articles were published in both multidisciplinary Journals, including Nature Comm, Commun Biol, Cancer Cell, Nature Prot, and Sci Adv, and specialised Journals focus on Cancer, development or radiobiology.
The scientific production per team is well balanced and proportionated to the human resources of each team with technical staff always associated with publication. In average 3.3 paper per member of each team has been produced in the last mandate. At the central level, PI are encouraged to share corresponding positions with their postdocs, if possible.
Both scientific integrity and ethics are in line with European and National legislations with a particular care about the accuracy and precision of the laboratory notebooks and the use of validated and updated protocols. The animal experiments are minimised as much as possible (three R rule). Open science is also promoted and recommended.

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

None of the projects developed at SRC have been published in highly prestigious generalist Journals during the mandate. It appears that the institute has no clear strategy for long-term storage management of produced data.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The interaction of the Unit with the economic sector is very good for 3 teams and excellent for the team Prezado. One team also collaborates with a start-up company on single cell technology. This transfer activity has not been valorised with licenses yet. The unit has implemented relevant outreach actions and means to communicate on their research activity with targeted communities (patients and donors) and the public.

Strengths and possibilities linked to the context

SRC promotes non-academic partnerships with hospitals and industry and generated six patents in the past 6 years. These partnerships supported clinical and industrial projects by Cifre and post-doctoral/engineer contracts. Team Prezado is the most active team in economical valorisation with three patents in the current mandate.
All PIs have outreach activities through roundtables with the public, patients and donors, as well as audience on radio and video broadcasts, public conferences, and school visits. Major publications are submitted for press released through CNRS INSB.

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

It appears that none of the patents generated by the SRC have been licensed, although some interest has been shown for one of the patents generated by Team7.

ANALYSIS OF THE UNIT'S TRAJECTORY

None, since the Unit stops at the end of 2025. In addition, the following teams will not be reconducted for the next period because the team leader(s) are retiring, including Team Larue and Team Londono.
In 2025, Team Ayrault will join the new Oncopediatric Unit (Concert) in Paris and team Seano will join the new Unit of Chemical Biology of Cancer in Orsay site, and for the Team Prezado, the leader, has accepted a professor position at the Univ. of Santiago de Compostela. On the other hand, the Team Monsoro-Burq and the Team Pouponnot will join the GIRC Unit. Thus, the evaluation of their past activities and the analysis of their trajectory are detailed in the GIRC Unit.

RECOMMENDATIONS TO THE UNIT

N.A.

TEAM-BY-TEAM OR THEME ASSESSMENT

Part to be duplicated for each team according to the organisation of the unit, be sure to use the nomenclature used by the unit (teams, axes, themes, etc.).

Team 8: Normal and Pathological Development of Melanocytes

Name of the supervisor: Mr. Lionel Larue

THEMES OF THE TEAM

Cutaneous melanoma incidence is steadily rising in France and Western countries. The objective of the team is to build a comprehensive understanding of the molecular and cellular mechanisms underlying both normal melanocyte development and melanoma progression. The team has developed genetically rational, immunologically coherent, and relevant in vivo and in vitro melanoma models tailored for use in a pharmaceutical preclinical pipeline. They develop five complementary axes, Establishment of the melanocyte lineage, Melanocyte function, Renewal of the melanocyte lineage, Melanoma initiation and progression, preclinical models and Therapeutics.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has intensified its attempts to publish in top level generalist journals such as Nat Com, Genes & Dev and one manuscript submitted in BioRXiv which is under evaluation in Nature.

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

EVALUATION

Overall assessment of the team

Team members were strongly involved in teaching. The team made remarkable scientific productions reflecting the excellence of the research conducted with 46 articles (16 as last authors in high-ranking journals); seven reviews and eighteen also in prestigious journals for collaborations, one patent. In addition to the track records, activities of the team members gave a high international visibility, visiting Professor at the University of Tsukuba (Jp), 45 invitations at international conferences and seminars. Remarkably the team organised twelve meetings. Important competitive grants allowed to sustain the program.

Strengths and possibilities linked to the context

The team is a rather small size team, composed of six members. However, the production is excellent since they have published 46 articles and secured one patent. Members of the team are last authors for sixteen of these original articles. They are published in high-ranking journals like Nature Com, Genes & Dev, J Invest Dermatol. They also authored seven reviews and collaborated on eighteen original articles in high-ranking journals. They have trained six PhD students and five postdocs.
The team was very successful in grant applications gathering 2.2 M€ from national agencies or associations (INCA, ARC). The team got the competitive label FRM in 2021.
Most of the team members have been involved in teaching activities at various universities in France and abroad. In 2019, the team organised a European course. The team leader taught 130 hours per year until 2019, and 24 hours afterward. Since 2016, he was a visiting Professor at the University of Tsukuba (Japan). The international visibility of the team is high as reflected by 35 and 10 invitations as speakers at conferences and seminars worldwide. Remarkably, the team organised twelve meetings, some of which had over 1000 attendees.

Team members were involved in Scientific councils and regularly evaluated French and international grants (estimated at 80). They were also reviewers for about 200 publications in journals such as Cancer Cell, Cancer Res, Cancers, Cell Reports, Dev Cell, eLife, JCB, NAR, Nature Com, Oncogene, Scientific Rep., and Sci Trans

Med. They were also associate editors for different specialised journals such as J Invest Dermatol, PCMR, Exp Derm, and PPS.

The team have made significant contribution in the field through development of genetically rational, immunologically coherent, and relevant in vivo and in vitro melanoma models tailored for use in a pharmaceutical preclinical pipeline. They have generated vital insights into the establishment of melanocytes from melanoblasts during development and the renewal of melanocytes from melanocyte stem cells, particularly crucial during aging. They have deciphered signalling pathways involved in melanoma initiation (proliferation and evasion of senescence) and progression (invasion and formation of metastases) using both in vitro and in vivo approaches.

Weaknesses and risks linked to the context

The team spent a lot of time to generate mouse models and implement novel protocols with a quite reduced manpower.

The team collaborated with clinicians and pathologists outside of Institut Curie but did not interact strongly with dermato-oncologists at the Curie Hospital, where cutaneous melanoma is not a priority

Analysis of the team's trajectory

N.A.

RECOMMENDATIONS TO THE TEAM

None, since the team stops at the end of 2025.

Team 9: DNA Repair, Radiations and Innovative Cancer Therapies

Name of the supervisor: Mr. Arturo Londono

THEMES OF THE TEAM

The team developed strategies to improve the therapeutic window of radiotherapies. The aim is to implement physical and/or chemical approaches that protect healthy tissue while being as effective against cancer cells. Four main axes were followed: dissecting the molecular mechanisms responsible for radioinduced pulmonary fibrosis, characterising the effect of irradiation delivered at a high dose rate (the FLASH effect) and studying the mechanisms of radiosensitisation/radioprotection induced by the repair inhibitor Dbait (now known as AsiDNA), identifying the role of Hedgehog signalling on DNA repair in tumour cells.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The actual PI joined the Orsay site to head the unit, and as well as to head the team after the PI retirement. Importantly, this team allowed to extend the research to other cancer locations such as brain tumours (medulloblastoma, glioblastomas, retinoblastoma), through research projects developed in several teams. This answered perfectly well to the recommendations suggesting to increase the collaborations between the teams of the unit.
Several collaborative works between team's unit were produced. Notably, the teams showed that ASIDNA, a molecule developed in the team, is a radiosensitiser in medulloblastoma with no added toxicity (Clin Cancer Res, 2020). They also improved RT treatment in two paediatric brain tumours, MB and AT/RT, including a specific modality of therapy, named FLASH, discovered in Institut Curie.

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

EVALUATION

Overall assessment of the team

The scientific production of the team was excellent with 26 articles in specialised journals or more generalist journals such as Nat Commun, Nat Aging, eight reviews and book chapters, and 1 patent. The team trained 11 PhD students. The team co-organised the International Symposium on Innovative Radiation Therapies and team members were invited at sixteen international conferences. The projects are sustained by strong and regular grants. The team manages a unique prototypic device for FLASH electron radiation that is open to all, an equipment that confers to the team a high international recognition.

Strengths and possibilities linked to the context

The current PI joined the Orsay site to head the unit and as well as to head the team after the PI retirement. Importantly, this team allowed to extend the research to other cancer locations such as brain tumours (medulloblastoma, glioblastomas, retinoblastoma), through research projects developed in several teams.
Over the period, the team has obtained ~1.5 M€ from international programmes (European Euramet – UHDpulse, International Network for Training and Innovation in Therapeutic Radiation), national agencies or associations (ANR, La ligue, Fondation EDF) and from industrial contract (Onxeo).

The team has a long-standing experience in the development of radio-sensitising molecules, which are in clinical trial and licensed by a biotechnology company. The team has generated an interactive atlas of the lung responses to radiation (https://lustra.shinyapps.io/Murine_RIPF_Atlas/), opening the door for further detailed exploration of the spatio-temporal dynamics of mechanisms leading to radiation toxicities. The team demonstrated that a radio-sensitising molecule can be also a radio-protector, opening the route to the development of bi-functional molecules that can improve the well-being of patients treated with radiotherapy.

The team has contributed to the organisation of the "International Symposium on Innovative Radiation Therapies", held in Orsay and organised by the European research consortium Theradnet and the interdisciplinary center for cancer therapies based on radiations and nanoparticles, iNANOTHERAD, which is an interdisciplinary program of University Paris-Saclay.

The scientific production of the team was excellent, reflecting these activities. They published, 26 original articles in specialised journals or more generalist journals such as Nat Commun, Nat Aging, eight reviews and book chapters, and one patent. The team trained eleven PhD students and is involved in teaching. The team co-organised the International Symposium on Innovative Radiation Therapies (Insirt) that was held in Orsay October 5-7, 2023 and the team members were speaker invited at 16 international conferences. Team members are regularly reviewers for journals such as Applied Sciences, Cells, Cancers, Plasma & Plasma Biopolymers, Biomedicines, PPS. The projects are sustained by strong and regular grants. Thanks to the presence of permanent personnel highly specialised in medical radio-physics, the team manages a unique prototypic device for FLASH electron radiation that is open to all, an equipment that confers to the team a high international recognition.

Weaknesses and risks linked to the context

Despite broad advertisement, the team has failed to attract excellent post-doctoral fellows/research associates with exceptional CVs that could allow them to compete in national calls to obtain permanent research positions.

Analysis of the team's trajectory

None, since the Unit stops at the end of 2025.

RECOMMENDATIONS TO THE TEAM

None, since the Unit stops at the end of 2025.

Team 10: New Approaches in RAdiotherapy

Name of the supervisor: Ms. Yolanda Prezado

THEMES OF THE TEAM

The team was pioneering the conception and development of innovative Radiation therapy (RT) techniques to drastically reduce normal tissue toxicities. The team was interdisciplinary with physicists, biologists, bioinformaticians and medical doctors, with a translational vision. It focused its research on optimising Spatial and temporal dose modulation: spatial fractionation of the dose in radiation therapy, particle type and energy and developed new accelerator concepts.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The Hcéres committee recommended to strengthen the radiobiology research activities. The CNRS group leader, a radiophysicist, awarded by a consolidator ERC grant, and who has developed spatial fractionation strategy to make radiotherapy more efficient and less toxic was recruited in 2019.
The PI was promoted Senior principal investigator by the international Scientific Advisory Board of the Institut Curie.

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

EVALUATION

Overall assessment of the team

The team developed news approaches on radiotherapy. The team leader was laureate of the ERC-Consolidator call (2019) and of the award from French Academy of Sciences. The team made a remarkable contribution with the conception and development of innovative radiation therapies using distinct dose delivery methods such as minibeam radiation therapy and FLASH. The scientific production and international recognition were remarkable with 45 research articles, six invited reviews, four invited book chapters and 43 invitations to international conferences.

Strengths and possibilities linked to the context

The team developed news approaches on radiotherapy. The team leader was laureate of the ERC-Consolidator call (2019) and of the M and Mme Peyre French Academy of Sciences, 2021. She was recognised in March of 2023 as a senior group by the international Scientific Advisory board of Institut Curie, following positive evaluation by an AdHoc Committee on April, 2022.

The team composed one permanent senior scientist (DR2) and 2 permanent ITAs has pioneered the concept and development of innovative RT able to reduce normal tissue toxicities. It has trained nine PhD students, eight post-docs, three M2 students and one M1 student. Its contributions to socio-economic and cultural development are demonstrated by 3 patents applications and several industrial collaborations. The team is also internationally renowned as demonstrated by the high number of invitations (43), it attracts international sabbatical professors and students, has been awarded an ERC consolidator grant and won several prizes (.ie. prize of the French Academy of Sciences.
The project is supported by highly competitive grants with more than 5 M€ attracted and 1 ERC consolidator grant.
The scientific production is remarkable with 45 research articles, six invited reviews, four invited book chapters including one as a selected article, Evaluation of the role of the immune system response following minibeam radiation therapy. IJROBP. 115, 426-439 (2023).

A remarkable contribution of the team in the field was the conception and development of innovative radiation therapies using distinct dose delivery methods such as minibeam radiation therapy and FLASH. This strategy showed a remarkable reduction in side effects of the radiation.

Weaknesses and risks linked to the context

The team had only one senior scientist during the period (the PI), which limits the development of some further activities regarding teaching and outreach.

The recruitment via CNRS or Inserm is difficult since there is a limited number of young radiobiologists both in France and internationally, and the recruitment panels at CNRS or Inserm not always understand the specificities of the CV and publications in this domain.

Analysis of the team's trajectory

None, since the Unit stops at the end of 2025.

RECOMMENDATIONS TO THE TEAM

None, since the Unit stops at the end of 2025.

Team 11: Signalling, development and brain tumours

Name of the supervisor: Mr. Olivier Ayrault

THEMES OF THE TEAM

The main team's research interest is the study of medulloblastoma formation and progression, the most common paediatric tumour arising in cerebellum. In particular, the team has focused on both normal cerebellum development and medulloblastoma formation using an interdisciplinary approaches and mouse models.

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CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has achieved recommendation of criterion 1 by generating major breakthrough in the field, not achieved recommendation of criterion 2 to secure a stronger permanent workforce, and has achieved criterion 3 by generating a secure niche in the field, further developing developmental aspects of the research and by developing strong interactions with related teams

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

CATEGORIES DE PERSONNEL	EFFECTIFS
Professeurs et assimilés	2
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	0
Sous total personnels permanents en activité	**1**
Enseignants chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	3
Doctorants	3
Sous total personnels non permanents en activité	**6**
Total personnels	**7**

EVALUATION

Overall assessment of the team

In the five-year period the Team has published four research articles as main contributor in highly reputed journals, 30 research articles as collaborative work and three reviews. PhD students and post-doc signed as first or co-first authors articles as for team's main contributions, and several articles as co-authors in collaborative work. The PI has also coordinated and associated an international study bringing together the largest centres working in the field. Further, the Team has participated in several important studies and discoveries in the field published in top journals.

Strengths and possibilities linked to the context

The PI is internationally recognised and is a main figure in the field of medulloblastoma research. The team benefits from a large spectrum of international collaborations. The scientific production of the team consisted

in 30 original articles (Dev.Cell, Nature Comm, EMBO Mol Med,) and three reviews (e.g. Nature Review Medecine). Among the ten original publications as main contributors, four were published in large audience journals (Nature, Cancel Cell)) as main contributors. The team has obtained exceptional funding (5.5 M€) from national agencies and associations (INCA, ARC, La ligue), international charities associations (Brain Tumour Charity grant (UK), St. Baldrick's Robert J. Arceci Innovation Award" (USA), Alex's Lemonade Stand Foundation for Childhood Cancer (US)) and the European H2020 programs.
The team members have organised international meetings (- SIOPe embryonal Brain Tumour Group meeting in, Hamburg (Germany), Cancer Research UK, Brain Tumour Conference, London, (UK))

Weaknesses and risks linked to the context

Absence of permanent researchers in the Team. Need of personnel dedicated to GDPR compliance as human sample declarations and policy proposals. PhD students and post-doc largely involved in collaborative work in addition to be dedicated to their specific topic. Articles published as main contributors include a large number of authors.

Analysis of the team's trajectory

The team trajectory was analysed in the context of its new unit, last year.

RECOMMENDATIONS TO THE TEAM

N.A.

Team 12: Tumoural Microenvironment

Name of the supervisor: Mr. Giorgio Seano

THEMES OF THE TEAM

Since 2018, the team has focused on brain tumours and has specialised in tumour plasticity, resistance mechanisms, and tumour microenvironment. The lab investigates the effects of each of the conventional therapies on cell and microenvironment plasticity. Their model system to test the involvement of tumour plasticity during therapy is glioblastoma (GB), a highly plastic, resistant, and deadly brain tumour.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

N/A

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

N/A

EVALUATION

Overall assessment of the team

In the 2018-2023 period, the team published eighteen articles and seven reviews, of which a main research article that the PI signs as corresponding author (Nature Comms), two articles as first author (from post-doc work), one methods article (Nature Protocols) and several collaborative articles in reputed journals signed by PhD students and post-docs. The team secured highly competitive national and european grants (ERC, INCa). The attractiveness is good, witnessed by recruitment of personnel with european funding, invitation to national and international conferences and securing an ERC grant.

Strengths and possibilities linked to the context

The scientific production of this team is excellent in quality involving publications in highly reputed journals, demonstrating scientific excellence and competitiveness. The team has an excellent national and international visibility. Between 2018 and 2023, three PhD students and two postdoctoral fellows have been trained in the team. The attractiveness and visibility of the team is overall excellent with a number of competitive national (ATIP avenir, INCa) and European grants (ERC StG, Marie Curie postdoc fellowship). Overall, the team collected during this period over 5 M euros.

Weaknesses and risks linked to the context

From the information provided, it is unclear what the workforce of the Team will be for the next five-years period. Given the large amount of funding obtained, the specific scientific production relative to the main research themes appears modest (only one article as corresponding author published in Nature Communications). Need to secure funding from 2025 onwards (only two contracts ending 12/25).

Analysis of the team's trajectory

The team trajectory was analysed in the context of its new unit, last year.

RECOMMENDATIONS TO THE TEAM

The committee recommends to continue on this stream, and consolidate both the workforce and the publication record.

CONDUCT OF THE INTERVIEWS

On-site visit

Date

Start: 29 November 2024 08:00 A.M.

End: 29 November 2024 07:00 P.M.

On-site

INTERVIEW SCHEDULE

No interview was scheduled with the director of the Unit.

However, a meeting with the committee was expressly asked by the technical and engineering staff PAR and therefore setup during the on-site visit. Since the Unit is closing at the end of 2025, the PAR also must move along with their own teams. Some of them will follow the team they work with while some others wish to change team for several personal or scientific reasons. In addition, the PAR working in teams that close need to find a new team and Institute.
During this meeting, the PAR from the Inserm and the CNRS, who will not join the GIRC Unit for the next mandate, showed very stress because they do not feel well accompanied during this transition by their own employers. In particular, they mentioned a lack of clear and transparent procedure to move to another Research Center, and sometime contradictory answers from the Human Resources Dept. Overall, this generates an uncomfortable working condition with unnecessary stress and incertitude for the near future. In total five PAR from CNRS and two from Inserm are concerned.
No issue was mentioned for the technicians/engineers who will join the GIRC Unit (2 from the CNRS and 1 from the Inserm) nor for those who have the Institut Curie as employer.

Program of the Hcéres visit of GIRC

"Genome Integrity, RNA and Cancer"
UMR3348, Director: Stefan Vagner

NOTE: No observer during the private sessions (in red below)

8:00 – 8:15	Preliminary meeting of the expert committee (closed hearing) , (Private Link)
8:15 - 8:30	Presentation of the Hcéres evaluation to the unit (SO/SVE3) (CS: C. Etchebest)
8:30 – 9:00	Unit main outcomes (15'+ 15' Q/A) (Unit Director: S. Vagner) (all unit members present)
9:00-9:30	Unit trajectory (15'+ 15' Q/A) (Unit Director: S. Vagner) (all unit members present)
GIRC TEAMS PRESENTATION	
9:30:10:05	Team) 1 RNA Biology, Signalling and Cancer (S. Vagner, 15'+ 15' Q/A +5' PI alone)

10:05-10:40	Team 2 DNA Recombination, Replication and Genome Stability (S. Lambert) (15'+ 15' Q/A +5' PI alone)		
10:40-11:10	Short Debriefing/Break		
GIRC TEAMS PRESENTATION (CONTINUING)			
11:10-11:45	Team 3 Controlling Microtubule Dynamics and Function with the tubulin code (C. Janke) (15'+ 15' Q/A +5' PI alone)		
11:45-12:20	Team 4 Chromatin and RNA splicing (R. Fernandez de Luco) (15'+ 15' Q/A +5' PI alone)		
12:20-12:35	Team 5 ARN, microenvironnement tumoural et métastase (A. Navickas) (10' P+10' Q/A+ 5' PI alone)		
12:35-14:00	Short Debriefing / LUNCH		
14:00-14:35	Team 6 Signalling and Neural Crest Development (A. Monsoro-Burq) (15'+ 15' Q/A +5' PI alone)		
14:35-15:10	Team 7 Signalling and Cancer Progression (C. Pouponnot) (15'+ 15' Q/A +5' PI alone)		
GIRC SPECIFIC MEETINGS (PRIVATE)			
15:20-15:50	Meeting with technical and administrative staff	Meeting with PhD students and post-docs	Meeting with researchers and teaching-researchers
15:50-16:00	Short Debriefing		

[1]

[1] Follow next page

Program of the Hcéres visit of SRC

"Signalling, Radiobiology and Cancer" UMR3347, Director: Arturo Londono

16:00-16:20	Unit main outcomes (Arturo Londono) (10'+10'Q/A)		
16:20-16:40	Team 5-SRC: Tumour Microenvironment –(G. Seano, 10'+10' Q/A) Past (Saida)	Team 4-SRC: Signalling in Development and BrainTumours (O. Ayrault 10'+10' Q/A); Past (Claus, Domenico)	Meeting with technical and administrative staff (in French) SRC (Olivier, Sandrine, Michele, Cathy)

GIRC VISIT (CONTINUATION)

16:40-17:10	Meeting with supervising bodies
17:10-17:40	Break / Short Debriefing (Private Link)
17:40-18:10	Meeting with the head of the unit/deputy director (UD only)
18:10-18:40	Committee meeting/ final debrief: overview of all teams, Unit Trajectory update of the reports etc..

PARTICULAR POINT TO BE MENTIONED

Regarding the PAR from the CNRS and the Inserm who will not join the GIRC Unit, it is strongly recommended to act, as quickly as possible, to alleviate the feeling of incertitude and stress and accompany them to a transition as smoothly as possible.

PARTICULAR POINT TO BE MENTIONED

Regarding the PAR from the CNRS and the Inserm who will not join the GIRC Unit, it is strongly recommended to act, as quickly as possible, to alleviate the feeling of incertitude and stress and accompany them to a transition as smoothly as possible.

GENERAL OBSERVATIONS OF THE SUPERVISORS

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Objet

General comments to the HCERES evaluation report of
Genome Integrity, RNA and Cancer (GIRC) &
Signalling, Radiobiology and Cancer (SRC)
DER- PUR260025164 - EV 0753172R (common report)
Evaluation campaign 2024-2025 / Group E

HCERES
For the attention of Mr Stéphane Le Bouler, Interim President and of the Members of the Expert Committee chaired by Mr Claus Storgaard Sorensen.

Paris, on 7th March 2025

Dear All,

We would like to thank the members of the HCERES Expert Committee for their time and extensive works resulting in the positive evaluations of UMR3348 and UMR3347-U1021.
Factual modifications will be listed in a separate document for both units.

Concerning the Unit 3348:
We appreciated the fact that the report recognized the scientific excellence but also the human and organizational dynamics of UMR 3348. We have considered the recommendations and will take them into account moving forward.

Regarding the renovation needs, this point has already been addressed and is part of the renovations across all the old buildings of the Institut Curie in Orsay dedicated to research. Some renovations have already taken place or are ongoing, and the others will be part of an upcoming comprehensive program.

Regarding informatics security, cold data storage and protection of both clinical and scientific data, it should be noted that the Unit benefits from the environment of its governing bodies, especially Institut Curie that provides an IT department and a DATA department to help the researchers and administrative staff, notably for the management and storage of data.

Concerning the Unit 3347-U1021:

We need to point out that all teams could benefit from permanent technical staff, contrary to what is mentioned in the weaknesses linked to the context (resources).

Also, regarding the "PAR" members of the teams that will be closing, they have been supported by their governing bodies and solutions of relocation in other teams have been found with them.

We hope that our comments will provide a better understanding of the situation for the HCERES expert committee.

Yours sincerely,

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