Research evaluation

# EVALUATION REPORT OF THE UNIT

SGCSR - Stabilité génétique, cellules souches et radiations

## UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université Paris - Saclay,
Commissariat à l'énergie atomique et aux énergies alternatives - CEA,
Université Paris Cité,
Institut national de la santé et de la recherche médicale - Inserm

**EVALUATION CAMPAIGN 2024-2025**

GROUP E

Rapport publié le 08/04/2025

In the name of the expert committee :

Mr Lucas Jacques Waltzer, 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 Lucas Jacques Waltzer, Centre national de la recherche scientifique – CNRS, Clermont Ferrand |
| **Experts:** | Mrs. Muriel Barberi-Heyob, Université de Lorraine (representative of CNU)<br>Mrs. Susan Chan, Institut national de la santé et de la recherche médicale – Inserm, Illkirch<br>Mr Olivier Feraud, Inserm, Créteil<br>Mr Antonin Morillon, CNRS, Paris<br>Mrs. Miria Ricchetti, Institut Pasteur Paris (representative of CSS Inserm) |

## HCÉRES REPRESENTATIVE

Mrs. Marie José Stasia

## REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Mr. Reiner Veitia, CEA
Mrs. Anne-Paule Roqueplo, Université Paris Cité
Mr. Mehran Mostafavi, Université Paris-Saclay
Mr. Alain Eychene, Inserm

# CHARACTERISATION OF THE UNIT

- Name: Stabilité génétique, cellules souches et radiations
- Acronym: SGCSR
- Label and number: UMR-E 008 | U 1274
- Composition of the executive team: Mr. François Boussin

## SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement
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

The joint research unit "Genetic Stability, Stem Cells and Radiation" (SGCSR) studies the molecular mechanisms of DNA repair and genome stability, as well as the biology of normal (germinal, haematopoietic and neural) and cancer stem cells.
Its research encompasses several fundamental aspects of genome maintenance (non-homologous end joining, homologous recombination, base excision repair, telomere biology, double strand break repair, oxidised based repair…), the characterisation of cellular and molecular responses to ionising radiation, the study of reproductive biology (gonad development, meiosis, germ line stem cells, testicular cancer, endocrine disruptors…), haematology (leukaemic cell chemoresistance, interactions with the bone marrow microenvironment, haematopoietic cells response to irradiation…) and neurobiology (neurological pathologies, neural stem cells, brain organoids, gliomas, strategies against radiation-induced brain injury…). One of the major goals is to propose new strategies to improve cancer treatment by increasing the efficiency of radiotherapy and preserving healthy tissues.
The unit relies on the use of several model systems (Saccharomyces cerevisiae, Helicobacter pylori, human cell lines and primary cells isolated from human tissues) and preclinical models (organoids, mice).

It is currently composed of six teams:
- Team 1: DNA Repair and Chromosome Stability (ERSC)
- Team 2: Niche and Cancer in Haematopoiesis (ENCH)
- Team 3: Neurogenesis, Repair and Cancer (ENRC)
- Team 4: Differentiation of Germ Cells (EDG)
- Team 5: Genetic Instability (ERIG)
- Team 6: DNA replication and genome stability (ATIP-Avenir 2023)

## HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The SGCSR was created in 2019 following the fusion/restructuration of two previous research units created in 2009 (UMR967, "Genetic stability, Stem cells and Radiation") and in 2022 (UMR566, "Gametogenesis and Genotoxicity"). A CEA Director of Research was appointed as director of the unit, with a deputy director who is an Inserm - Director of Research.
The unit is located in one building of the Institute for Radiation Protection and Nuclear Safety (IRSN) site of Fontenay-aux-Roses.

## RESEARCH ENVIRONMENT OF THE UNIT

The SGCSR is a joint research unit (UMRE008-U1274) affiliated to the French Atomic Energy and Alternative Energies Commission (CEA), the National Institute of Health and Medical Research (Inserm), the University Paris-Saclay (UPS) and the University Paris-Cité (UPC). Both universities benefit from an IdEx. The teams of the unit are affiliated to five doctoral schools in life sciences from these two universities.
The SGCSR is deeply embedded in the CEA, which is the principal employer of its staff. It is the main component (~85% of the staff) of the Cellular and Molecular Radiobiology Institut (IRCM, directed by the actual director of the SGCSR unit). The other constituents of the IRCM are located in Bruyères le Chateau and Evry, working respectively on radiotoxicology and skin integrity. The IRCM itself is one of the three departments of the François Jacob Biology Institut (IBFJ, directed by one of the PI of the SGCSR unit), an institute attached to the CEA Direction of Fundamental Research. The other two departments of the IBFJ work in the field of infectious disease & autoimmunity or develop preclinical models for the detection and treatment of human diseases.
The unit/IRCM hosts 9 platforms under the CEA umbrella, one of which (PARi- an high-throughput RNAi screening platform) has an IBISA label.

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

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 3 |
| Maîtres de conférences et assimilés | 2 |
| Directeurs de recherche et assimilés | 19 |
| Chargés de recherche et assimilés | 18 |
| Personnels d'appui à la recherche | 34 |
| **Sous-total personnels permanents en activité** | **76** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 7 |
| Personnels d'appui non permanents | 5 |
| Post-doctorants | 0 |
| Doctorants | 19 |
| **Sous-total personnels non permanents en activité** | **31** |
| **Total personnels** | **107** |

## 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 |
|---|---|---|---|
| CEA | 0 | 33 | 27 |
| Inserm | 0 | 4 | 3 |
| U PARIS-CITE | 3 | 0 | 4 |
| U PARIS SACLAY | 2 | 0 | 0 |
| **Total personnels** | **5** | **37** | **34** |

# GLOBAL ASSESSMENT

This medium-sized unit (~110 persons) conducts research in the fields of DNA repair and stem cell biology to reveal radiation-induced pathogenic pathways, increase the efficiency and safety of radiotherapy and develop new therapeutic approaches for fighting cancer. Its lines of research are clearly defined, relevant in terms of fundamental and translational research, and internationally competitive. The unit benefits from an excellent level of resources, with an important support from the CEA in term of permanent staff and a high level of external funding, which allow the development of innovative projects. The unit's organisation is sound and generally very functional, but suffers from a complicated interweaving of various scientific/administrative layers. Still, the unit has created and maintained an excellent working environment with various state-of-the-art platforms, some of which provide quite rare services (e.g., for irradiation or cell-based high-throughput screening). The unit is strongly integrated within the CEA DRF, but its links with the higher education system and clinical research could be strengthen.

The unit has attracted a high number of new staffs coming from neighbouring CEA labs (6 researchers and 5 support staff) but also thanks to the recruitment of five support staff and seven researchers, including one new ATIP/Avenir team. The teams are very well funded thanks to their success in competitive calls mainly from French funding agencies or charities. The unit has a very good scientific animation policy and some PI have an excellent international visibility. The unit is active in training PhD (56 joined the unit during this period) and has set up sound actions to promote career development of its trainees and staff.

The scientific production of the unit is excellent, with more than 200 publications, including 85 research articles as main authors, essentially in very well-established international journals. Important discoveries were made in all the teams across the range of topics covered by the unit (DNA repair, telomere biology, natural transformation

by H. pylori, cell stemness/differentiation, haematopoiesis, neurobiology cancer, radiation biology…). Team members have also published a very good number of papers of interest in collaboration with international laboratories. These discoveries lay a solid foundation for the continuation of their ambitious research programs and the development of translational-oriented projects.
The unit has obtained significant support from EDF and pharmaceutical companies, demonstrating strong interaction with the economic world. Their research also has a strong potential for clinical developments, which are taken into consideration by most of the teams. Some members of the unit are well involved in outreach activities and science dissemination to the general public.

# DETAILED EVALUATION OF THE UNIT

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

The previous committee recommended strengthening the links with the medical world.
Effective efforts in that direction have been done by some teams, as illustrated by the participation to the Institut Carnot Opale or the association to the SIRIC Paris-Kids-Cancer.
It also encouraged the unit to strengthen its link with the university and increase the number of PhDs.
Accordingly, the unit was involved in development of new master "Genome Stability and Epigenome" at the UPC and several researchers contribute to teaching at the M1 and M2 level. On the other hand, two assistant professors left the unit during this period.
As recommended, a mentoring system has been set up to accompany temporary staff (students, post-doc...) in their career.
As recommended, research teams tried to establish a "stop and go" strategy to focus their efforts on their most promising projects.
As recommended, training in bioinformatics was reinforced. For instance, six members of the IRCM received training from Artbio (IBPS) thanks to support from the CEA and several unit members benefited from bioinformatics training session organised at the IBFJ in 2023 and 2024.
As recommended, genuine efforts were made to reorganise lab space. Notably all the members of Team 1 are now located on the same floor. Only Team 3 remains spread across different floors and a meeting room is still lacking due to space and financial constraints.
Also, the unit created a website and a platform steering committee was set up, which holds regular meetings and consults the users.
Altogether the unit responded very well to the recommendations of the previous Hcéres committee.

## B - EVALUATION AREAS

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

#### Assessment on the scientific objectives of the unit

The SGCSR has set itself clearly defined and relevant scientific objectives, which are well aligned with its supervising bodies policy. The different teams develop very strong lines of research in competitive fields pertaining to DNA repair, radiobiology, oncogenesis, haematology, neurobiology or germ cell development. Despite the underlying thematic diversity, their research is well interconnected and brings novel insights into fundamental and health-related biological processes. However, the unit's ambitions in terms of clinical transfer do not appear to be fully realised.

#### Assessment on the unit's resources

The unit benefits from an excellent level of resources. Overall the teams are very well funded as they have been very successful in obtaining external contracts, essentially at the national level. The various platforms provide a strong support, but many equipments start to be old and the pooling of financial resources could be increased. The human resources are very strong, with a high ratio of support staff and numerous experienced CEA researchers, which could advocate for the implementation of higher-risk projects. Recruitments and arrivals of new staff have more than compensated for external mobilities/departures and brought new expertise to the unit.

## Assessment on the functioning of the unit

The functioning of the unit is very good to excellent. The management of the unit is very well structured but the entanglement of the unit within the IRCM, the IBFJ and the CEA creates a complex (and sometimes detrimental) administrative and operational multilayer organisation. Meetings between the direction and the group leaders, the unit council or the whole unit are regularly organised. Sound measures are in place to ensure that the unit complies with its institutional requirements. The unit makes significant efforts to sustain an active scientific life and animation.

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

#### Strengths and possibilities linked to the context

The unit has identified ambitious and relevant scientific objectives of fundamental and applied significance. The scientific strategy of the unit is defined by the director in coordination with the team leaders and it is regularly discussed at the level of the PIs and of the whole unit.
Their research aims at understanding both basic mechanisms of DNA repair and stem cell biology to reveal radiation-induced pathogenic pathways, increase the efficiency and safety of radiotherapy and develop new therapeutic approaches for fighting cancer, infertility or certain neurological pathologies. These objectives fit very well with the general mission of the Inserm and were in line with the CEA flagship program in radiobiology, which benefited from specific support until 2021. They are also well connected with the universities, with important contributions of the unit for the creation of a Research Federation in haematology at UPS or the establishment of the Master degree "Genome stability and epigenome" at UPC.
The unit scientific objectives are clearly articulated around the activity of five relatively large teams which develop distinct but connected projects of high quality. Three of those teams (ERSC, ENCH, ENRC) are accredited by Inserm. In addition, a new group leader with complementary expertise in replication stress was recently recruited on an ATIP/Avenir program. The interconnection between the teams is illustrated by joint funding, notably within the CEA or EDF programmatic actions, and co-publications of a dozen research articles.
The teams use a good range of model systems (Saccharomyces cerevisiae, Helicobacter pylori, human cell lines and primary cells isolated from human tissues) and preclinical models (organoids, mice). The implementation of their projects is supported by nine technological platforms shared with the IRCM and headed by a SGCSR researcher.

#### Weaknesses and risks linked to the context

Although the strategy of the unit is generally well shared, the overarching ambition to translate their findings toward clinical application is not realised by all the teams.
While the unit has recently renewed its scientific advisory board (SAB), it did not seem to regularly involve the SAB in the definition of its scientific policy or in the recruitment of new talents during this contract.
The CEA has not renewed its research program in radiobiology beyond 2021. This raises questions about the unit's position in the future policy of the CEA.

### *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

This medium-sized unit hosts around 110 persons, with a large majority (~75%) of staff on permanent positions which bring a strong and rather stable core of human resources to fulfil its ambitions. Most of the permanents (60) are employed by the CEA, while the remaining are employed by the Inserm (7), UPC (7) and UPS (2). One strength of the unit is the relatively high ratio of support staff to researchers (0.8), which allow to bring long-term technical support both to the teams and the platforms. Accordingly, except for the new ATIP/Avenir team, all the teams are constituted by a good number of permanents (≥8). The unit is also reinforced by nineteen PhD students and a few postdocs (5) and technical staff (4) on fixed-term contracts. Overall, the number of persons in the unit has increased during the current period of evaluation (+9), the flux of incoming staff (+24) being superior to the departing ones (-15).
The unit benefits from a substantial level of recurrent support from its supervising bodies (Inserm, UPS, UPC CEA) representing ~230k€/year. 80% of this budget is reallocated to the teams and the rest is used for shared expenses and equipment maintenance. Moreover, the unit obtained specific grants from Inserm to buy a spectral

cytometer (2021, 120k) and a spinning disk microscope (2023, 75k€). Besides, the teams of the unit obtained a very high level of funding through competitive calls (~2.5M€/year, but with important yearly fluctuations). Of note, the unit's radiobiology research has also been supported by specific grants from the CEA and EDF for equipment or collaborative research programs, contributing for ~2M€ to the unit's budget since 2017.
Of note, the IRCM also benefits from recurrent funding from the CEA (mostly used to pay CEA staff salary), incomes from its technological platforms and overheads on some contracts, which allow to support the cost of the platform and invest in new equipment. Part of the unit/IRCM budget is used to support new teams / researchers.

### Weaknesses and risks linked to the context

The reallocation of a major part of the recurrent budget (80%) to the teams and the limited contribution of the teams (overheads on some grants + fees on the use of common platforms) to the constitution of the common budget makes it difficult for the unit to conduct a strong incentive policy, to programme equipment renewal or to invest in new technologies.
As mentioned above, the CEA has not renewed its research program in radiobiology. This may lead to an important decrease in funding for the unit.
The financial relationships between the unit, the IRCM and the CEA are not straightforward and may hamper the unit capacity to mobilise its resources.
Along the same lines, the ordering system and financial overseeing for CEA-managed contracts are not well organised. The lack of a dedicated financial officer leads to a loss of time for numerous employees.

## *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 overall management of the unit is well structured. The director is helped by a deputy director and they work in close collaborations with the other group leaders (heads of CEA teams and laboratory) thanks to weekly meetings. Platforms' managers are also associated with these meetings every month. There are regular encounters of the unit council (quarterly meetings) or the whole unit (twice a year).
The unit director is also the head of the IRCM since 2022 (an important point for the smooth administrative and scientific management of the unit), and two members of the unit stand as deputy director of this structure, which certainly facilitates the interactions with the SGCSR.
A mentoring system has been set up to accompany temporary staff (students, post-doc...) in their careers. Since 2022, a transparent procedure for awarding promotions and bonuses to CEA staff has been set up by the IRCM.
Two committees have been set up, committed respectively to parity and professional equity and to eco-responsible approaches.
Sound measures are in place to ensure that the unit complies with its institutional requirements. Notably, the unit has a safety manager and works in compliance with good laboratory practice and legislation for the handling of GMOs, the use of human samples and radioactivity, and the disposal of biological waste.
The unit members follow the quality management procedures set by the CEA DRF, with local correspondents in the unit that inform the newcomers about the rules and usage of the lab notebook.
The IT network and the access to the buildings are run under the strict regulations of the CEA.
Overall, the vast majority of the different categories of personnel expressed their satisfaction with working in the unit.

### Weaknesses and risks linked to the context

The entanglement of the unit within the IRCM, the IBFJ and the CEA creates a complex and sometimes detrimental administrative and operational organisation. Notably, the management of the CEA budget by the IBJF rather than the unit or the IRCM complicates the definition of an annual budget for the unit scientific policy.
The subdivision of the research teams into Inserm teams and CEA laboratories is not very clear. The lab website does not reflect well the current organisation of the unit.
The direction had to deal with serious behavioural problems with one person of the unit, but this issue was treated adequately, with the help of the relevant CEA and Inserm human resource department.
The unit lacks visibility in terms of human resources as there is no advance planning for CEA recruitment and many retirements are expected in the coming years.
The premises of the unit are not very well maintained and lead to a sub-optimal functioning even for safety-related issues (e.g., delayed fume hoods repairs). Some refurbishments are clearly required- which sometimes comes as a direct cost for the unit or cannot be performed swiftly.

While the management of the unit has made significant effort to implicate all the staff in the life of unit, there is still room for some improvement, for example concerning the timely diffusion of meeting reports, the use of English in addition to French in internal communications or the redaction/diffusion of the unit's "règlement intérieur".
The level of IT support for data storage, computing power or computer workstation management is not sufficient to meet the unit's needs.

## EVALUATION AREA 2: ATTRACTIVENESS

### Assessment on the attractiveness of the unit

The unit has an excellent level of attractiveness. It benefited from the arrival of many permanent staff and the recruitment of five PAR and seven researchers, including a new ATIP/Avenir group leader. It also hosted 56 PhD and 23 postdocs over this period, including from other countries (27/79). The unit obtained substantial funding (~2 to 2.5M€/year) through competitive calls mainly at the French level. They contributed to the organisation of international meetings and had an active scientific animation policy. Unit's members are involved in various national committees and involved in science evaluation. Its platforms are well equipped, notably for irradiation, imaging, cell sorting, screening and phenotyping. Valuable actions to promote internal career development are in place.

### Strengths and possibilities linked to the context

The unit attracted a high number of new staff coming from neighbouring CEA labs (6 researchers and 5 support staff) but also thanks to the recruitment of five support staff (4CEA, 1UPC) and seven researchers (4 CEA and 3 Inserm). Among them, one obtained an ATIP/Avenir to set up her own team and she received further support for the unit and IRCM (50k€ + free access to platforms for 2 years + priority for a CEA doctoral fellowship). Of note, the unit also dedicates a 10k€ allowance to newly hired researchers to help them develop their project. The unit also attracted a total of 56 PhD (14 foreigners) and 23 postdocs (13 foreigners). A voluntary mentoring program is offered to all temporary staff. In addition, the unit supports the career development of its staff: it encourages the emergence of researchers as group leader in the unit, and a fair procedure has been set up for awarding promotion/bonuses to CEA staff.
The unit was very successful in competitive calls for projects. It obtained ~15M€ of grants over the 2018-2023 period. These include: seventeen ANR-supported projects (9 as coordinator), eleven EDF "Grand Accord", nine INCa grants, one FRM and one LNCC team labels, one European consortium contract as well as numerous other contracts. Overall, 75% of these resources come from national agencies or charities, 16% from technological transfer and industrial collaborations, 7% from international grants and 2% from local/regional sources.
Members of the unit contributed to the organisation of some conferences, such as the first international meeting on Non-Homologous End Joining (which took place in Fontenay-aux-Roses in 2023), the meeting of the Société d'Andrologie de Langue Française – SALF, or the Société Française de Radioprotection and the French "3R" meeting (DNA Repair, Replication and Recombination). They were invited to present their work to ~90 conferences or seminars, including in a few important events in France (Congrès SFH, SALF, GynFoch, Dingo…) or at the international (EMBO Conference on Chromatin Dynamics, International Workshop on H. pylori, International meeting on Laminopathies/Nuclear envelope conference, Mitotalk, Tritium 2019…). Thirteen scientists or PhD students obtained an award at conferences. In addition, the unit proposes weekly internal or external (~15/year) seminars to increase its visibility and favour scientific exchanges with its scientist and trainees. The unit's reputation is also attested by a very good number of collaborations, including with leading institutions (e.g., Institut Curie, Institut Pasteur, Crick Institute, Erasmus Medical Center, Harvard Medical School…). Moreover, one team is part of two European consortia (Counteracts, Eura-Net Strokes) and is affiliated to the Institut Carnot Opale.
Members of the unit also actively contribute to science evaluation and organisation. Notably, ten scientists of the unit stand in supervising bodies or evaluation committees (e.g., Inserm CSS 1, University CNU 65, ARC CN2, CSS Bio Inrae…) as well as in learned societies (Agence de Biomédecine, CHO, EFS, GDR Repro, Gircor, SALF, SFG, Lady Tata Foundation…).
The unit hosts nine platforms of the IRCM dedicated: animal facility, animal experimentation, irradiation, microscopy, flow cytometry & cell sorting, genetic engineering & protein expression (CiGex), High-Throughput and High-content Screening (PARi), Multiplex immunochemistry, and Cytogenetics. Four of these platforms were created since 2019 and one of them (PARi) benefit from an IBISA label. The CiGex, Irradiation and PARi platforms are particularly attractive to external teams (respectively 28, 14 and 12 external teams between 2019 and 2023). The platforms cover the main needs of the unit and provide access and formation to state-of-the art technologies, notably for high content live imaging, confocal imaging, single cell genomics, cell sorting,

engineering and phenotyping, or mouse irradiation and (xeno)grafts. They are run by a steering committee under the direction of K. Dubrana, with a well-established pricing policy.

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

With ~30 scientists holding an HDR, the unit could welcome more PhD students. A number of postdocs were hired for a very short time. Many scientists (3 support staffs, 6 researchers and 3 assistant professors) left the unit.
The unit's involvement in European consortia and its internal funding could be improved.
Some equipment on its platforms is aging and will require replacement to keep up with modern standards and maintain a good level of service. However, the unit has a clear strategy in terms of investment/renewal.
The fees to access some platforms do not properly cover their costs.
Some platforms appear understaffed or overbooked, leading to delay in access and limited capacity of support for the acquisition of expertise by newcomers (e.g., for image analysis, bioinformatics).

## EVALUATION AREA 3: SCIENTIFIC PRODUCTION

### Assessment on the scientific production of the unit

The unit has an excellent level of scientific production, with more than 200 publications, including 163 research articles (50% as lead author), mainly in well-established journals, during this period. Important discoveries have been made in all teams. This output is commensurate with the unit's workforce (~45 researchers & professors) and the contribution of the different categories of staff is well taken into account. The unit complies with the principles of research integrity and ethics, and it follows the guidelines of its governing bodies.

### Strengths and possibilities linked to the context

During this period, members of the unit produced 215 publications, including 163 research articles, 32 review or comment articles as well as a few book chapters or monographs. The production is generally of very high quality, with most research articles in well-established journals corresponding to the unit's fields of research. Around 50% of the publications are signed a first and/or last author. This includes articles in Blood Advances, Cell Death & Differentiation, Cell Reports, DNA Repair, eLife, EMBO J, Environmental Pollution, Molecular Cell, Nature Communications, Nucleic Acids Research, PLoS Genetics, Science Advances or Stem Cell Reports. Important findings were made in all the teams (cf. team reports) across the range of topics covered by the unit (DNA repair, telomere biology, natural transformation by H. pylori, cell stemness/differentiation, haematopoiesis, neurobiology cancer, radiation biology…). Besides, members of the unit presented their results orally at ~130 events (invited seminars, national or international meetings) during the period.
Considering the field of research, the publication rate is proportionate to the unit's work forces (respectively 3.5 or 1.8 publications per researcher or professor over the period). Members of scientific platforms are well associated with the publications: they co-signed 51 research articles. The unit encourages an adequate publication signature policy to establish the position of authors, taking into account their contribution as well as career development aspects.
The unit applies the recommendations of the CEA DRF, including clear procedures for the use of laboratory notebooks, and there is an automated data archiving on a dedicated CEA server. The unit also complies with the regulations relating to animal research, GMOs and human biological samples. All doctoral students and most staff members have attended research integrity courses. An integrity correspondent is present on site.

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

Given the composition of the team (relatively high number of researchers and support staff), the publication record could be further improved.
Only a dozen publications are shared between teams of the unit, reflecting a level of internal collaborations that could be increased.
One important research publication had to be retracted.

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

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

The unit contribution to society is very good to excellent. It has obtained several grants with private companies and two patents were registered. Some teams are involved in translational clinical research. Some unit members are involved in outreach activities and dissemination of science to the general public.

### Strengths and possibilities linked to the context

Most teams of the unit benefited from grants with EDF and some of them had contracts with biotech/pharma companies (Sanofi, Servier, BiovelocITA, SmartImmune), reflecting strong links with the economic world. One PhD benefited from a Cifre fellowship. The unit can take advantage of IBFJ "cellule delta" to develop valorisation projects. Two patents were registered for evaluation and one project was deposited for "prematuration" with Université Paris Saclay SATT. Besides, the unit platforms are open to private companies and occasionally work with them.
Some teams (esp. ENCH, ENRC, EDG) have strong links with clinicians, notably in the field of haemato-oncology, brain cancer, radiobiology and reproductive biology.

The unit welcome every year a number of fourteen-year-old school children and various team members contributed to interviews or YouTube videos for the general public to raise awareness about scientific research and health-related issues.

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

The implication of the unit in outreach and its contribution to the dissemination of science in the society is relatively limited and not formally organised at the unit level. It is also hampered by the strict regulations of the CEA concerning public access to its premises.
Given its activity profile and stated ambition, the translational potential of SGCSR research is not fully achieved.

# ANALYSIS OF THE UNIT'S TRAJECTORY

The trajectory of the unit is scientifically sound and in line with the former contract. Accordingly, the unit's scientific objectives will continue to revolve around to main goals: (i) gain new knowledge on fundamental biological processes centred on genome stability and cell stemness, and (ii) propose new strategies to improve the treatment of cancerous and non-cancerous pathologies, with a non-exclusive focus on radiotherapy. While the unit has been very successful along its first objective with all the teams contributing actively, its second objective seems both less shared and more difficult to achieve. This is probably due in some cases (1) to the models used by some teams, (2) a focus on fundamental questions not linked to a specific disease or at the expanse of more translational aspects, and (3) still limited interactions with clinicians. Nonetheless, the scientific directions are well identified and fully relevant and the unit appears to be in an excellent position to continue to perform high-level science.

For the next contract, four of the teams currently present in the unit wish to be renewed or created without major modification (ERSC led by the future unit director; ENCRH led by the deputy director; EDG; ATIP/Avenir). It is proposed that (1) the ENRC team splits in two, ENRC headed with a new PI and an independent team headed by a new PI 2, (2) that one of the leader of Erig emerge to form a new team, and (3) that the team working on skin regeneration (belonging to the IRCM and located both in Evry and Fontenay) joins the unit. Thus, the new unit would be composed of nine teams, among which six will apply for Inserm accreditation. In addition, the unit anticipates that it will regularly open call for new researchers or team leaders. The arrival of the team on skin regeneration in the unit will strengthen its position in the field of stem cells and cell therapy, with a very strong potential in terms of valorisation and a good fit with radiobiology-related questions. However, its dual location in Evry and Fontenay may limit its integration and the synergies with other teams. Besides, the recruitment strategy & access to leadership position within the unit would certainly benefit from the advice of a SAB (as proposed for the next contract) to ensure a good equilibrium between internal promotion and the arrival of new blood as well as to reinforce the scientific ambition of the unit.

Concerning the governance of the unit, a new director will be appointed (the current head of Team 1), who will work in coordination with the current deputy director. The unit will remain associated to the CEA as a main constituent of the IRCM. It will also try to maintain its Inserm accreditation and to strengthen its links with the universities of Paris Cité and Paris Saclay, which is an important factor to raise the unit visibility among students. Several challenges (scientific, operational or societal) facing the unit have been identified by the future director, who seems committed to tackling these issues head-on. Notably, the proposal to have dedicated PhD fellowships for joint projects within the unit may help bridge the gap between thematic and bolster synergies.

# RECOMMENDATIONS TO THE UNIT

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

The administrative relationships between the unit, the IRCM, the IBFJ and the CEA could be streamlined. Along the same lines, the intermingling of teams, CEA-accredited laboratory and Inserm-accredited teams could be simplified.

The unit should identify new means to invest in its platforms and maintain state-of-the-art equipment fitting its scientific activity / long-term strategy.

The unit is encouraged to further increase scientific animation between teams and with external seminars.

## Recommendations regarding the Evaluation Area 2: Attractiveness

The unit should work in closer association with its SAB to obtain external advice on new team recruitment/arrival and internal (re)organisation, notably for team emergence or change in the group leader.

The unit should have a clearly defined strategy in terms of human support for new teams. It is also encouraged to formalise its mentorship program and to extend it to new PIs.

The PI should try to obtain more funds at the international level and to attract more postdoctoral fellows.

The members of the unit should try to increase their participation to teaching at the university.

The SGCSR web site should be regularly updated to increase the unit's visibility.

## Recommendations regarding Evaluation Area 3: Scientific Production

Keep the excellent level of production and, as always, try to bring it to even higher levels.

The unit should try to increase the synergies between teams to develop shared projects leading to breakthrough research.

Given the composition of the unit, with a large number of permanent scientists, more high risk/high gain projects could be undertaken.

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

The unit could have a more proactive role in the organisation of activities toward the general public.

The unit could be more ambitious in developing translational research and tightening its link with clinicians.

# TEAM-BY-TEAM OR THEME ASSESSMENT

**Team 1:** DNA Repair and Chromosome Stability (ERSC)

Name of the supervisor: Mr. Stéphane Marcand

## THEMES OF THE TEAM

Team 1 is studying DNA repair and chromosome biology in the budding yeast Saccharomyces cerevisiae. To get a better understanding of the fundamental mechanisms governing genome maintenance, they address three important outstanding questions: how chromatin structure impacts DNA repair, how ionising radiation challenges NHEJ repair accuracy, and how telomeres promote chromosome folding and segregation in mitosis. The three subgroup leaders join efforts and collaborative activities to dissect the molecular mechanisms and reveal an integrative vision of these threeDNA maintenance events.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

3 recommendations were previously made:
1) The three former teams are encouraged to maintain their excellent scientific output and even further increase the impact of their publications by focusing on a limited number of flagship projects.
This was achieved with numerous milestone publications in the field.
2) The team should be reunited in an adjacent space with more office spaces and welcome more postdocs.
This needs to be addressed both at the postdoc recruitment level and joint space.
3) Increase interactions with other teams in the unit and integrate radiobiology aspects in the scientific strategy.
The team successfully managed to integrate completely the three subgroups with shared scientific activities and outputs. Next term would be more productive in interacting with other members of the unit. Radiation aspects were studied with an important publication on ionising radiation (NAR 2021).

## 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 | 4 |
| Chargés de recherche et assimilés | 2 |
| Personnels d'appui à la recherche | 5 |
| **Sous-total personnels permanents en activité** | **11** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 1 |
| Post-doctorants | 0 |
| Doctorants | 5 |
| **Sous-total personnels non permanents en activité** | **6** |
| **Total personnels** | **17** |

# EVALUATION

## Overall assessment of the team

The team has an excellent to outstanding scientific production with a total of eighteen accepted publications (12 research articles including 7 as main authors, as Plos Genet 2023, EMBOJ 2022, NAR 2021, Nat Comm 2021, Cells 2021, Mol cell 2019, Elife 2018). The visibility is excellent with four new permanent staff (2 CR, 1 engineer, 1 tech) and six PhD students recruited as well as a regular capacity to attract funds with over 1,8 M€ (incl. five ANR grants and one "FRM team" grant). The non-academic activity remains very good with outreach dedication (women in sciences promotion, "scientifique toi aussi").

## Strengths and possibilities linked to the context

The team focuses on DNA repair and chromosome biology in the budding yeast Saccharomyces cerevisiae and is highly visible in the field, being a leader in developing approaches and understanding fundamental mechanisms. Three main questions are addressed around how chromatin structure impacts DNA repair, how ionising radiation challenges NHEJ repair accuracy, and how telomeres promote chromosome folding and segregation in mitosis. Eight main contributions have emerged combining the expertise of the three subgroups over the past period.
The scientific production is excellent to outstanding with eighteen publications (12 research including 7 as the main author and 6 reviews) in the best journals for the field (Plos Genet 2023, EMBOJ 2022, NAR 2021, Nat Comm 2021, Cells 2021, Mol cell 2019, Elife 2018).
The attractiveness and visibility of the team are excellent with numerous conferences in international meetings (incl. 27 international; e.g., EMBO Workshop, 3R meeting), and recruitment of four permanent staffs (2 CR in 2019 and 2023, 1 engineer in 2021 and 1 tech in 2018) as well as six PhD students graduated over the period. The recognition of the team is visible throughout their capacity to attract fundings (5 ANR, 1 FRM-team grants to reach over 1.8 million euros over the period).
Finally, the outreach activity is very good with special focus on young people training or research activity incentive for women (women in sciences, "scientifique toi aussi").

## Weaknesses and risks linked to the context

The team has no major weakness, but given its excellence is lacking of an international funding such as ERC or HFSP to secure postdoc contracts. Also, the team hired no postdoc over the period. This might affect the continuity of further permanent recruitment of CR in the coming years. The outstanding research remains limited to budding yeast and might benefit of diversification towards mammalian models to address more complex chromatin contexts for DNA repair. The valorisation and outreach activities are not at the highest level for such an excellent team.

## Analysis of the team's trajectory

The team is aiming at continuing to study genome biology through seven main axes:
1-Deciphering the End protection at telomeres vs DSB repair at subtelomeres by addressing Rap1 and Rap1-independent mechanisms both using molecular, cellular, biochemical approaches and in vitro assays (collab. With a PI of IRSN).
2-Understanding the link between homologous recombination and the regulation of Rad51 nucleofilament, by performing structural studies (collab. CEA, I2BC, Saclay) followed up by functional analyses (collab. I Curie) and finally by exploring human homologs (collab. with a PI at I2BC).
3-Defining the coordination of DNA repair and replication by first addressing the molecular basis of Rad51 filament toxicity (collab. Institut Curie), or using ChIP-seq and DNA gaps repair assessment and finally by extending to mammalian cells (collab. Pi of the ATIP Avenir). The second part will be dedicated to the Rad51 paralogs Rad55 and Rad57: their roles in gap accumulation and G2 cell arrest.
4-Understanding why DSB can induce firing of replication origin by identifying the cis- and transacting factors that trigger replication firing using genetic screens and candidate approaches (chromatin modifiers).
5-Further exploring how the mechanisms protecting telomeres against fusion and resection act during replication and contribute to telomere length homoeostasis by characterising the roles of Ku interactions with DNA:RNA hybrids at telomeres (collab. two PI of Institut Curie). and by studying the maintenance of the telomere protection in a physiological dynamic context (collab. PI of team 6). Finally, understanding how homologous recombination is tuned at telomeres will be explored combining in vivo and in vitro approaches (collab. with the PI of the skin regeneration team).

6-Exploring the SMC complexes at chromosome ends and at broken ends using in vivo signals of condensin refolding at the end of mitosis multiplying various parameters, and by ChIP-Seq. In addition, mechanisms of the DNA damage induced cohesion will be addressed through biochemical, microscopy approaches and proteomic/genetic screens.
7-Studying NHEJ in response to radiation-induced DSB by capturing NHEJ-dependent chromosome rearrangements and in vivo genetic approaches both in yeast and human cells (a PI of I2BC and a PI of IRSN).
The trajectory is sound and robust and capitalised on the expertise of the team and the actual collaborations. The ambitious aims and their number would need strong and large midterm funding schemes.

## RECOMMENDATIONS TO THE TEAM

The team members should certainly continue the outstanding and rigorous science that they produce, they should also try to accommodate more valorisation of their research (protecting some methodologies), but the most important recommendation would be to recruit more young scientists in the team with postdocs to renew and secure the future of the team. Such recruitments could be supported by an international funding, an excellence label that the team has proven already. On this aspect, a high risk high/high gain project could be to propose a research program using mammalian models, with higher(epi)genomic complexity.

**Team 2:** Niche and Cancer in Haematopoiesis (ENCH)

Name of the supervisor: Ms. Françoise Pflumio

## THEMES OF THE TEAM

The team is composed of two groups that study normal and pathological haematopoiesis affected by: 1) irradiation, and 2) interactions with the bone marrow microenvironment.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

"Increase interactions with clinicians to maximise the potential for outstanding current models to generate hypothesis-generating research, and increase public outreach activities, if possible, driven by trainees as a teaching opportunity."
These are ongoing actions and could still be stronger.

"Increase specific career mentoring of postdocs from an early stage."
It is unclear how this recommendation was addressed.

"Prioritise projects with high visibility. The team should identify, every one to two years, one flagship project with potential for high impact publication, define go/no-go experiments and allocate the necessary resources to make it a success."
The team pointed out several research highlights that were achieved. It obtained sufficient funds to support most of the projects. It is unclear if further actions were taken.

## 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 | 4 |
| Personnels d'appui à la recherche | 2 |
| **Sous-total personnels permanents en activité** | **9** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 3 |
| Personnels d'appui non permanents | 2 |
| Post-doctorants | 0 |
| Doctorants | 2 |
| **Sous-total personnels non permanents en activité** | **7** |
| **Total personnels** | **16** |

# EVALUATION

## Overall assessment of the team

This large team, made up of two formerly separate once, and composed of eighteen permanent staff had an excellent scientific production: the team published seventeen papers as first or senior authors in well-regarded general and speciality journals (e.g., Sci Adv, Cell Rep, PLoS Genet, Blood Adv, Leukaemia, Haematologica). Visibility is excellent. The team leader is deputy director of the unit. The team obtained>2.5M€ in this period, which included national grants (ANR, INCa) and charities (Ligue, ARC, labelled team), European consortiums x2 (partners), as well as smaller grants. The socio-economic contribution is excellent, as attested by contracts with pharma companies, translational research projects, interaction with charities and outreach activities.

## Strengths and possibilities linked to the context

This is a large team made up of two formerly separate teams, which merged during the 2018-2023 period. It is made up of eighteen permanent staff, with two PIs (Inserm), one for each "lab", and seven-nine researchers and ITA per lab. The majority of the researchers/ITA are CEA-funded staff. The research is divided in sub-projects which are developed by the different researchers of the team, in a semi-independent or independent manner, with backup supervision by the PIs. Several publications are signed (senior, corresponding) by the researchers and not the PIs. As of the end of 2023, the team is composed of ten persons. One PI (not the team leader) will retire in 2025.

The team's research is closely aligned with the scientific orientation of the UMR1274. The team has studied the response of haematopoiesis and the gastrointestinal tract to different doses of irradiation, such as tissue regeneration, bone marrow macrophage function, ROS-dependent haematopoietic defects. It has studied the interactions between leukaemic and normal progenitor cells in the bone marrow microenvironment, particularly in terms of hypoxia and cell plasticity. Several of the projects were the continuation of long-term studies that have spanned several evaluation periods, indicating the determination of the team to pursue deep mechanistic dissections.

Scientific production is excellent for the size of the team. The team published>50 articles, including seventeen as first and/or senior authors in well-regarded general and speciality journals (e.g., Sci Adv, Cell Rep, PLOS Genet, Blood Adv x2, Leukaemia, Haematologica x2) and 2 in the pipeline (bioRxiv). Its willingness to network and share expertise/reagents are clear from the high number of productive collaborations (Haematologica, Nat Commun, Cancer Discov, Blood, Nat Immunol). The team has published ten reviews/book chapters.

Visibility is excellent. The team leader is deputy director of the unit. The team obtained>2.5M € in this period, which included national grants (ANR x3, 1 as coordinator; INCa x3, 1 as coordinator; Institut Carnot) and charities (Ligue Contre le Cancer, Fondation ARC, both as a labelled team), European consortiums x2 (partners), as well as a host of smaller grants. Team members regularly gave oral presentations internationally (European Hematology Association x6). The team leader and team members were active in numerous committees, at the national (e.g., Club Haematopoiesis and Oncogenesis, Institut Carnot, Inserm CSS x2) and international (Lady Tata Fund Board) levels.

Training is excellent. Five researchers obtained their HDR to mentor students. The team hosted eight postdocs, four from outside France (Japan, India, Spain, Lebanon). Seven PhD students were trained, with more ongoing. Many were funded by the national MENRT fellowship, attesting to the quality of the students. Other were funded by the Ligue Contre le Cancer. One was supported by a Cifre fellowship that supports projects between academic and companies. Almost all of the PhD students published at least 1 paper as the first author. Team members regularly participated in thesis and HDR committees.

The team is excellent in its contribution to society. It received a grant from the Smart Immune biotech company, as well as a Cifre PhD fellowship for a project in collaboration with them. The team conducted a SATT-funded prematuration project on the use of Muse cells in the treatment of lethal gastrointestinal syndrome. It participated in outreach activities with charities (The Hope of Princess Manon, Société Française Cancers Enfant, Fondation ARC) and public schools.

### Weaknesses and risks linked to the context

The team leader was not co-senior or co-corresponding author on a number of the papers. The two parts of the team do not seem to publish together, suggesting parallel visions and use of resources. Some team members have low publication records. Few (only 2) postdocs published. Ten of the permanent researchers/ITA left the team during this period.
One important paper was retracted in this period; this problem seemed to have been treated adequately.

### Analysis of the team's trajectory

In the next period, the current team (6 researchers, 1 engineer, 1 PhD student in 2024) will be joined by a group from the OncoHematology team in the CEA/FAR Centre (2 researchers, 4 clinician scientists). The team leader will be the only PI. The scientific strategy will be to pursue only the funded projects. The projects are a continuation of the previous research. Collaborations with clinicians, companies and other labs will continue. The integration of the Onco-haematology researchers/clinician scientists, who study abnormal haematopoietic cells and their interactions with the bone marrow microenvironment will add new experimental models and include more interactions with clinicians.

The three main objectives are:
1) Radiobiology: finding strategies to protect humans from acute radiation syndrome
2) Interactions between the BM microenvironment and pathological cells in haematopoiesis
3) Development of preclinical strategies in acute lymphoblastic leukaemia and haematopoietic reconstitute post-transplant

Each objective has two-three independent aims which are complete projects in themselves. The aims have been funded by various sources or are under review for funding.
The project is ambitious and may need to be more focused/streamlined. However, it is well matched to the expertise of the team, and aligned with the overall goal of the unit. It is an added value that the new team will have clinician scientists.

## RECOMMENDATIONS TO THE TEAM

The team leader and team members should find a better middle ground, where the researcher gains independence and visibility, and the team leader receives credit for her important leadership role. Whenever it is appropriate, the team leader should be co-corresponding or co-senior author in the team's papers.
The team should take advantage of the important turnover of staff to develop their new avenues of research.
The team can further increase its international visibility by attending more meetings abroad.

**Team 3:** Neurogenesis, Repair and Cancer (ENRC)

Name of the supervisor: Mr. François Boussin

## THEMES OF THE TEAM

The team of neurobiologists and radiobiologists carries out fundamental research focusing on the response to DNA damage and its repair in the context of the normal brain and glioma. The ENRC team brings together two previous teams, LRP and LREV.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Answers to the recommendations from the previous report:
"Better visibility in the medical world could facilitate the recruitment of PhD students (MD, foreigners) and the success of grant applications; particularly as far as European or international grants are concerned. The team should make efforts to attract major grants in addition to the multiple small grants from charities which they get regularly."
The team is well funded and succeeded in competitive grants. The team was funded from four different sources: 1) recurrent grants from Université Paris-Saclay, Université Paris Cité and Inserm, 2) by an internal CEA program (IrBio), 3) by grants from public, charitable and private organisations, such as grants from ANR, INCa, Sanofi and Servier and, 4) by executing service contracts (BiovelocITA and Sanofi).

"Owing to the importance of the Public Health of some of their studies, they could aim at publishing in higher impact journals."
The improvement of the quality level of publication must be pursued.

"The team lacks some connections with the clinics while its research may have clear development in patients and in the general population as well. It may also broaden the possibilities to fund the research. They should aim for a communication plan for the future, both towards the medical field and the non-scientific public."
The team has developed valuable interactions with clinicians and radiotherapists to improve the medical relevance of its research in radiobiology. Team's expertise is illustrated by its interactions with private companies such as Sanofi and Servier. ENRC members participate to steering committees and co-organise scientific meetings.

## 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 | 5 |
| Chargés de recherche et assimilés | 5 |
| Personnels d'appui à la recherche | 5 |
| **Sous-total personnels permanents en activité** | **15** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 1 |
| Post-doctorants | 0 |
| Doctorants | 6 |
| **Sous-total personnels non permanents en activité** | **7** |
| **Total personnels** | **22** |

# EVALUATION

## Overall assessment of the team

The team is at the forefront of its field. With 23 publications (12 as main authors), the scientific production of the team was very good to excellent given its composition. The visibility of the team is excellent. The former group leader is very well recognised in the field of radiobiology. The team obtained a very high level of funding at the national level (~3M€ over the period) and was very attractive, notably to PhD (12). Its socio-economic contribution is excellent to outstanding. In particular, it filed two patents and obtained various grants or contracts from EDF and biopharma companies.

## Strengths and possibilities linked to the context

This large team (~20 persons, including 10 researchers and 5 support staff) studies how radiation affects healthy brain tissue and brain tumours. They are particularly interested in how normal and cancer cells repair DNA. The research was divided into specific areas, each led by one of the two PIs.
1) Radiation-induced brain injury and neurogenesis
2) DNA damage and repair during brain development and neurodevelopmental diseases
3) Radiosensitisation of gliomas
4) Impact of lamin B1 on genome stability
5) Identification of new actors or modulators of cytosolic DNA production and IFN activation – to improve RT.

The team is attractive and promotes its members well. The PI of the team is the head of the UMR SGCSR since January 2019, and the head of Cellular and Molecular Institute (IRCM) since May 2022. He is also a member of various steering committees and research steering bodies. He has been nominated as a critical reviewer of United Nations Scientific Committee on the Effects of Atomic Radiation (Unscear) for the evaluation of nervous system effects from radiation exposure" and he is an editor for Cells. The team attracted twelve PhD students and it recruited two researchers during this contract (incl. one who then obtained an ATIP/Avenir to set up her own team). The team also obtained a very consistent level of funding at the national level (5 INCa, incl. 2 as coordinator; two ANR. as partner; several CEA programs and grants from French charities: AFM, ARC, Arsep, Ligue IdF...). The visibility of the team is attested by eighteen invitations as guest speakers to seminars or conferences (incl. 4 abroad), participation in the organisation of conferences (e.g., NHEJ 2023, SFRP 2020) and a good network of collaborations.

A total of 23 original scientific papers were published, including twelve as corresponding authors, some in very well-established journals (Sci Adv, Nucleic Acids Res, Cell Rep, Stem Cell Rep). Several of these publications contain highly original results that have led to further studies by other scientists and thus provide key results in the field of research. It also contributed to six reviews or editorials.

The socio-economic interactions of the team were very strong. Two patents were registered during the period. The team obtained a number of contracts with private companies and pharmas (EDF, BiovelocITA, Sanofi, Servier; ~1M€ over the period). The team was also active in public outreach ("Scientifique toi aussi", 25th Brain Week...).

## Weaknesses and risks linked to the context

The team does not recruit enough postdocs for its size.
The number of European and international grants remains low for a team of this size.
The production of some of its research staff could be improved.

## Analysis of the team's trajectory

The team leader will cease his functions in the unit at the end of 2025. One PI of the unit will replace him as head of the ENRC team with the creation of a distinct team led by another PI of the team, the ELRIC (Lamin, Radiation, Immunity and Cancer) team (corresponding to the actual CEA Lab, LREV). The new ENRC team will be composed of five CEA researchers (2 will be retiring during the contract), two engineers and one postdoc.
A better understanding of ionising radiation effects on the brain and brain cancers represents the team editorial signature.
The team scientific objectives and approaches will concern:

- Radiation-induced brain damage and adult neurogenesis
- Radiosensitisation of glioblastoma stem cells by deciphering the mechanisms of therapeutic resistance.

In relation with HIF-1a overexpression, JMY could represent a relevant target to improve radiotherapy efficiency for glioblastoma. The team trajectory will require complementary expertise in radiobiology, molecular biology, cellular engineering and immunology. In addition, the project overall scientific strategy seems rather risky, as it is highly ambitious given the number of researchers (5 from CEA) involved, and given the competitiveness of the field of radiation-induced brain lesions and radio-sensitisation of gliomas.

## RECOMMENDATIONS TO THE TEAM

For the team's trajectory, its researchers need to gain in independence and visibility. Also, the proposed team leader has to consolidate his leadership position, notably in terms of scientific production.
The team benefits from an excellent reputation in the field, but it should aim for more high-impact publications, and strengthen its international visibility.

**Team 4:** Differentiation of Germ Cells (EDG)

Name of the supervisor: Mr. Gabriel Livera

## THEMES OF THE TEAM

The team investigates the fundamental mechanisms regulating reproduction, with both basic and clinical implications. Their research focuses on the development of murine and human germ cell lineages from foetal life through adulthood, in both males and females. They aim to understand the key processes controlling stem cell self-renewal and the initiation and progression of prophase I in meiosis. From an applied perspective, they explore how chemical pollutants and radiation alter the germ cell lineage, potentially causing reproductive disorders such as infertility, aneuploidy, or testicular cancer.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report recommended using the impressive and unique number of experimental models of the team towards addressing more clinically oriented implications of disrupted germ cell differentiation, and focus on identification of differences and similarities between human and mouse germ cell differentiation, meiosis regulation and characterisation of SSC. It also suggested including clinicians in the design of experiments related to fertility preservation in prepubertal boys, to bridge knowledge obtained in their experimental models with epidemiological and clinical data. It suggested identifying one ambitious and high-risk 'flagship' project with the potential to be published in a high impact factor journal, and consider aligning their future project on 'preventing infertility with spermatogonial stem cells' with the ongoing competitive 'GrowSperm' project to avoid repeating experiments already conducted by others.

The team has made significant investments in identifying factors that characterise and influence SSCs, with promising novel findings derived from comparisons between human and mouse models. The involvement of clinicians has been strengthened, although no direct clinical implications have yet emerged, which may require more time. While a "flagship" project with the potential for publication in high-impact journals has not yet been clearly identified, the experimental system holds considerable potential and continues to open new avenues for discovery.

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

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 3 |
| Maîtres de conférences et assimilés | 1 |
| Directeurs de recherche et assimilés | 4 |
| Chargés de recherche et assimilés | 1 |
| Personnels d'appui à la recherche | 3 |
| **Sous-total personnels permanents en activité** | **12** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 3 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 0 |
| Doctorants | 3 |
| **Sous-total personnels non permanents en activité** | **6** |
| **Total personnels** | **18** |

# EVALUATION

## Overall assessment of the team

The team, consisting of eighteen members, including three professors and two clinicians, achieved excellent scientific production with fifteen publications as main authors (+3 on bioRxiv), 24 collaborative papers, and seventeen reviews. They demonstrated excellent fundraising ability, securing approximately 2.9M€, and excelled in teaching activities. They also established strong links with clinicians, although no patents were filed or clinical outcomes have been yet realised. The team has a very good visibility, organised a national congress and has been invited to fifteen conferences (5 international), and showed very good outreach efforts.

## Strengths and possibilities linked to the context

The subject integrates fundamental research with clinical and environmental aspects, while maintaining a strong mechanistic focus. These fundamental studies, while significant in their own right, also address key health and societal issues, including fertility, cancer, and pollution. The team is an excellent combination of scientists (some of whom are involved in teaching) and clinicians, a balance that should be preserved. The team's substantial teaching activity, while time-consuming, provides valuable avenues for student recruitment and ensuring to remain at the forefront of emerging knowledge and methodologies. The team also benefits from a solid core of permanent scientists, technicians, and engineers, providing the stability needed to take innovative risks. The team demonstrates an excellent capacity to secure funding (~2.5M€ over the period, including 2 ANR, 1 INCa, 1 Plan Cancer, 1 ANSES and several other grants as coordinator). The visibility of the team is attested by its network of productive collaborations, integration in the COST network Andronet, organisation of the SALF 2019 conference and invitations to conferences (15, including 5 international). The team has been highly attractive to PhD (10 defended during the period, 3 ongoing).
The team was very productive, with eighteen research articles as main authors (including EMBO J, Env. Pollutant, HMG, Stem Cell Reports, and 3 BioRxiv) and ~20 in collaboration (e.g., Nature, Nature Genet, Nature Comm, PNAS, JCI Insight). They also contributed to thirteen reviews. The PI does not exclusively sign as the last author, allowing senior scientists to acknowledge their contribution and cultivate their potential.
The socio-economic interactions of the team are strong. It has established tight links with clinicians and obtained some important contracts related to clinical research (Agence Française de Biomedecine, ANSES). The team is engaged in outreach activities (public conferences, press interviews, online videos...). Its research is aligned with current social interests and the team is involved in different scientific instances (ABM, CSS, INCa...).

## Weaknesses and risks linked to the context

While the team benefits from a strong core of permanent staff, it attracted few post-doctoral researchers or international scientists, who are crucial for bringing fresh perspective and fostering a healthy dynamic of renewal. Over the long term, this could hinder the pursuit of high research standard projects".
The research subject is highly compelling and is well articulated in the report, including the broad implications of the discoveries. Given these factors -along with the size of the team and its substantial funding - the team own studies rarely hit broad audience scientific journals. Notably, there has been no patenting in a field with enormous potential. Furthermore, despite strong international collaborations, the team has had relatively limited invitations to international conferences and seminars, and no international funding has been secured, even though national funding is more than excellent. In summary, while the team's activities are of excellent quality at the national level, they lack significant international impact.

## Analysis of the team's trajectory

The team's trajectory is robust and coherent, seamlessly integrating past expertise with future plans. The focus on the mechanisms of meiosis connects the fields of DNA repair and stem cell biology, addressing fundamental questions that govern these processes, with significant implications for male and female fertility and cancer. The use of both mouse and human models provides a complementary approach.
The work has notably centred on the mode of action of a previously identified factor specific to meiosis (MEIOB), through its interactions with SPATA22 and RPA and its role in human primary ovarian insufficiency. The team also uncovered, in collaboration, the impact of vitamin C in impairing DNA demethylation, a critical step in meiotic entry, and identified transcriptional downregulation that coincides with mRNA stabilisation when germ cells enter meiosis. These findings have broader implications for understanding the potential role of pollutants in processes that regulate human germ cells.

The team also focused on the regulation of male spermatogonial stem cells (SSCs), identifying markers that define their stemness and a primitive state of these cells. They investigated factors influencing SSC behaviour, such as oxygen concentration and cell migration cues, particularly Netrin-1.
The team's future plans are firmly grounded in this solid foundation. They aim to use SSCs to address certain cases of male infertility, focusing on profiling these cells and identifying SSC subpopulations with higher regenerative potential. High-content screening will be employed to identify factors, including repurposed compound libraries, that could expand human SSCs for potential stem cell therapies. A major challenge nowadays is the expansion of human SSCs, and it remains unclear why current efforts do not fully consider the fact that Sertoli cells, which are essential for SSC expansion, are not included in existing paradigms (e.g., co-cultures, or analysis of factors secreted by Sertoli cells).
Future plans also include further investigation into the mechanisms underlying the previously discovered interplay between reduced transcription and increased mRNA stabilisation. The team will conduct in-depth studies of meiotic recombination and explore the potential for gene transfer (as tested in mice) to restore meiosis and spermatogenesis. The use of organ-on-chip models to reconstruct testicular microarchitecture is planned,
The team will also examine the role of DNA damage in both male and female stem cells.
In summary, the team is confidently building upon the solid foundation it has established, expanding its focus to identify novel regulatory factors for the expansion of male stem cells and the maintenance of genome stability in both male and female stem cells. These efforts hold the potential for interventions in cases of infertility and cancer prevention.

## RECOMMENDATIONS TO THE TEAM

The team should more effectively capitalise on the potential of their paradigm, which links the mechanisms of germ cell meiosis and genome stability to male and female infertility and cancer, and embrace greater involvement in more direct clinical applications.

They are encouraged to continue developing more complex and cohesive human models, with a focus on advancing multicellular models alongside single-cell type maintenance and differentiation in synthetic or heterogeneous human tissue (such as testicular) microenvironments.

The team is also encouraged to take more risks, include larger international presence in the lab, and expand its international visibility.

**Team 5:** Genetic Instability (ERIG)

Name of the supervisor: Mr. J. Pablo Radicella

## THEMES OF THE TEAM

The team's main focus is on the molecular mechanisms involved in the repair of oxidative DNA base damage through the base excision repair pathway in the nucleus and in mitochondria. The second focus concerns the mechanisms of genome stability and horizontal gene transfer of the human bacterial pathogen Helicobacter pylori.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations from the previous report were:
1-increase the numbers of high-impact publications.
It has been a success with the arrival of a second PI and the merging of teams.

2- Increase outreach activities with non-academics, and improve the impact of research in relation to society, economy or health.
Thus, it was not really addressed.

3-Numbers of PhD students could be improved.
It has been addressed, with seven PhDs over the period.

4- Some consideration should be given as to whether the H. pylori project should continue to be a line of research, given the lack of high-quality research output and grant funding support.
The work on H. pylori has produced, among others, two of the most remarkable publications of the team and has prepared the ground for future studies. This subject will be continued in the team by the actual leader, whereas research on oxidative stress will be pursued in the independent team by the leader of team 7.

## 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 | 4 |
| Chargés de recherche et assimilés | 2 |
| Personnels d'appui à la recherche | 5 |
| **Sous-total personnels permanents en activité** | **11** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 1 |
| Post-doctorants | 0 |
| Doctorants | 2 |
| **Sous-total personnels non permanents en activité** | **3** |
| **Total personnels** | **14** |

# EVALUATION

## Overall assessment of the team

The team is the result of a recent merge between two teams (2021) and has an excellent scientific production with a total of 26 accepted publications (23 research articles including 11 main ones, e.g., DNA repair 2023, NAR 2020, 2023, J C Science, 2018, Nat Comm, 2019 and 2022). The visibility is excellent with three new permanent staff (1 CR, 2 engineers), seven PhD students and three postdocs recruited as well as a regular capacity to attract funds with over 1.5 M€ (including 4 ANR grants). The non-academic activity is very good with outreach dedication (Médiathèque Fontenay-aux-Roses, TV documentary).

### Strengths and possibilities linked to the context

The team is the result of a recent merge between two teams (2021) and has an excellent scientific production with a total of 26 accepted publications (23 research articles including 11 main ones, e.g., Oncogene 2021, DNA repair 2023, NAR 2020/23, J. Cell Science 2018, Nat Comm 2019/22). The visibility is excellent with three new permanent staff (1 CR, 2 engineers), seven PhD students and three postdocs recruited as well as a regular capacity to attract funds with over 1.5 M€ (including 4 ANR grants). The recognition is also reflected in the invitations at international conferences and to give seminars (32 total including 13 international) in various national and foreign institutions. The two PIs are members of 3R meeting and international meetings (Griffith's legacy, 2024). PR was member of the scientific Committees for the Fondation ARC (CN2) and the Ligue contre le Cancer (Comité Scientifique Inter Régional Grand Ouest). He chaired several years an evaluation panel for the Scientia Fellows programme funded by the EU Horizon 2020 under the Maria Sklodowska-Curie scheme Cofund.

The non-academic activity is very good with outreach dedication (Médiathèque Fontenay-aux-Roses, TV documentary).

### Weaknesses and risks linked to the context

The team has no major weakness, but two main funding have been closed in 2023, leaving the team with some uncertainty for the numerous projects ongoing. Even if the number of projects has been reduced, it remains a certain dispersion and a risk for the PI.

The team has experienced a lot of in and out movement over the past years. It is hoped that the new configuration, with one PI continuing the H. pylori research with a smaller team, and another PI expanding her activity on oxidative stress with an independent team, will be as well balanced as it seems on paper. The PI will probably be at his last mandate, although the institutional rules allow him to stay even longer, provided he has funds and provides scientific production.

The outreach activities remain quite limited for the size of the teams and the participation of the other members of the team is not clear.

### Analysis of the team's trajectory

The team is now split with the actual leader continuing and focusing his work on H. pylori, and the leader of the future team 7 independently on oxidative stress, which was a common project before. The trajectory of the PI of team 7 is discussed separately, on the section of her own team.

The long-term aim of the project of the future team is to decipher the molecular mechanisms underlying the natural transformation (NT) process, from the capture of the TDNA up to its integration into the bacterial genome. The project will address various aspects of each of the NT steps, by using H. pylori and other pathogens with the help of key collaborations (a PI of the CBI in Toulouse, and a researcher at the University of Bloomington, Indiana, USA).

The trajectory seems rational but the question of the group structuration and funding can be raised.

# RECOMMENDATIONS TO THE TEAM

The team members should certainly continue the excellent science that they produce. They should also try to accommodate more with valorisation of their research (protecting some methodologies) but the most

important recommendation would be to secure that the restructured team will maintain its capacity to develop research now focused on H. pylori natural transformation, a subject on his long-term field of expertise, with the scientific project in agreement with funding.

**Team 6:** Lamin, Radiation, Immunity and Cancer (ELRIC)

Name of the supervisor: Mrs. Pascale Bertrand

# THEMES OF THE TEAM

This new team (creation proposed for 2026), a spinoff from Team 3, is interested in the mechanisms of genome stability in relation to nuclear envelope integrity and immunity.

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

For previous recommendations, see the report of Team 3.

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

NA: new team

# EVALUATION

## Overall assessment of the team

This new team will start in 2026. It is a spinoff of the current Team 3. The team is interested in understanding the mechanisms of genome stability, including DNA repair, replication stress management and telomere stability, all in the context of nuclear envelope integrity and immunity in response to irradiation.

## Strengths and possibilities linked to the context

NA: new team

## Weaknesses and risks linked to the context

NA: new team

## Analysis of the team's trajectory

The future team leader was previously the leader of an independent CEA group (LREV), which fused with another CEA group (LRP) to create Team 3 in 2019. With the future departure of the present group leader of Team 3, LREV will again be independent in 2026. This new Elric team will be composed of five researchers (CEA), one engineer and two technicians (all CEA), and four current PhD students. Additional recruitment is planned.

In the 2018-2023 period, the team leader led her group within Team 3, and published two papers as senior author on lamin B1 (NAR 2021, Sci Adv 2021) and four reviews (Gene x3, Med Sci). The team leader obtained a grant from Servier Pharmaceuticals to conduct a collaborative project (210K €, 2021-2025) and an INCa PLBIO grant (250K €, 2023-2027), both as coordinator, as well as a number of grants (local, national, charity, EDF, CEA) as coordinator or partner (>900 K€ in total).

The team is interested in the mechanisms of genome stability, including DNA repair, replication stress management and telomere stability, all in the context of nuclear envelope integrity and immunity in response to irradiation. It aims to propose new biomarkers and therapeutic strategies. The team will study:
1) the impact of lamin B1 on genome stability (6 sub-aims)
2) the link between genome stability, IFN modulators and innate immunity to improve radiotherapy (4 sub-aims)

The project has two aims that are loosely linked. The lamin B1 aim is the central strength of the team and the project is already financed. This part should yield interesting relevant results and solid publications. The immunity aim should get expertise from a researcher who joined the team in 2024; this part should also be funded at least at the beginning.

The mechanisms and players involved in the production of cytosolic DNA remain very poorly documented, particularly after exposure to ionising radiation. Thanks to an approach developed by the team, new molecular

players involved in the production of cytosolic DNAs have been identified. Despite a strong international competition, this is a highly interesting area of research that should lead to major advances in the production of cytosolic DNA and IFNs.

## RECOMMENDATIONS TO THE TEAM

With so many sub-aims, the team may need to prioritise its topics, and concentrate its resources on the core lamin B1 part of the project. The team is encouraged to increase its scientific production for the next period.

**Team 7:** Oxidative DNA Damage and Disease (EOX3D)

Name of the supervisor: Mrs. Anna Campalans

# THEMES OF THE TEAM

This new team (proposed for 2026) will investigate the mechanism of base excision repair (BER) that resolves oxidative stress-induced DNA damage, in the nuclear and the mitochondrial genome, and possible development of anticancer therapies.

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

NA: new team

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

NA: new team

# EVALUATION

## Overall assessment of the team

The group- currently part of team 5/ERIG is composed of eight persons, five permanent researchers, an engineer, and two technicians, all CEA staff, a PhD student at his third year, and a second student that should have been hired in 2024 (funded by the ANR project OXIREPTRA). All the permanent staff has worked together in the past, and with the PI, when they belonged to the Team 5. They are therefore in full operating mode from the beginning. The possibility to lead a team with a solid staff of eight permanent persons is a rare privilege to new (and established) PIs, granted by a few institutions nationally and internationally. This should encourage the team leader to make the most of this situation and continue pursuing and develop exciting new projects.

## Strengths and possibilities linked to the context

An ongoing, well-funded project with a strong core of permanent staff who have been working together for years provides an exceptional foundation for developing the new team. The project's originality lies in its integration of nuclear and mitochondrial responses to oxidative stress-induced DNA damage, and more recently, its exploration of the emerging role of BER factors in the activation of specific gene transcription.
The group was productive during the past contract (25 publications, including 2 Nucleic Acids Res, 1 J Cell Sciences and 1 DNA Repair as main authors) and it was successful in obtaining grants (e.g., 2 ANR, 2 CEA, 1EDF...) or for attracting PhD students (5).

## Weaknesses and risks linked to the context

The project investigating whether and how the accumulation of oxidised bases in mitochondrial DNA (which is thought to alter mitochondrial transcription and mitochondrial DNA (MTDNA) replication) affects cellular metabolism is highly interesting. However, the approach for pursuing this investigation is not clearly explained. Additionally, the study does not address the cellular fate of damaged MTDNA, such as its dilution through mitochondrial fusion, elimination by mitophagy, or other processes, which may significantly alter the readout. It also does not consider whether oxidative stress impacts the BER proteins themselves, and thereby their function. One of the major damaging effects of oxidative stress is not at the DNA level but also at the protein level. The consideration of these processes may have strong implication also for the development of anticancer therapies based on targeting BER factors, which is one of the aims of the project.
Furthermore, the role of oxidative stress in altering transcription and gene expression, an exciting and emerging field, is currently focused on investigating OGG1 (a BER protein)-dependent alterations. However, it is worth considering whether oxidative stress might affect gene expression independent of OGG1, potentially by altering transcription factor binding to promoters.

It is unclear whether postdocs are planned for the development of the project. While the project is not lacking in manpower, it could benefit from external contributions, particularly from individuals with international experience or diverse backgrounds and expertise.

### Analysis of the team's trajectory

The team shows a linear and solid trajectory, with the PI leading a group and a theme that were consolidated in the past condition. Within the team 5, in July 2021, the future PI took the leadership of the LCE laboratory (following the retirement of the former lab head). The LCE members were focused on cellular and molecular mechanisms developed by tumour cells at the origin of therapy resistance, thus an important restructuration of the laboratory has been carried on to combine some of the LCE historical projects together with the ones headed by the future PI of team 7. This operational period has facilitated the synergy between projects. However, the PI's primary expertise and interest in the mechanisms of oxidative stress in cell genomes will remain the key focus of the future team.

## RECOMMENDATIONS TO THE TEAM

Profit of the great momentum for the new team, based on a solid scientific theme, consolidated and numerous collaborators, and robust funding, to develop projects that not only extend the previous discoveries but also explore new aspects beyond the strict BER-linked mechanism in cell function. This may also have a relevant impact in anticancer therapies. If possible, hire postdocs with international experience.

**Team 8:** Skin regeneration and radiopathologies (ER2C)

Name of the supervisor: Mr. Nicolas Fortunel

# THEMES OF THE TEAM

The team will investigate the intrinsic properties and the regenerative capacity of skin stem cells, as well as the relationships taking place within their cutaneous environment. Exposure to ionising radiation will be studied as a model for exploring skin disturbances induced by the exposome.

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

NA: new team

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

NA: new team

# EVALUATION

## Overall assessment of the team

N.A.: this team is part of the IRCM, but does not belong yet to the SGCSR. It will join the unit for the next term.

## Strengths and possibilities linked to the context

In 2024 permanent team members include one DR CEA, three CR CEA, one CEA engineer, one CEA technician, and one Université Paris-Saclay/Évry research engineer.
The team has been productive, with 6 research articles in main authors, including one Nature Biomed Eng (2019), on the expansion of human keratinocyte precursors, and seven collaborative papers. The team benefits from very strong interactions with the industry (L'Oréal) and leads the PEPR Biotherapies and Bioproduction of Innovative Therapies. It is well positioned to develop clinically oriented projects for skin replacement strategies and regenerative therapies.

## Weaknesses and risks linked to the context

N/A

## Analysis of the team's trajectory

The team will join the unit in 2026. Team 8 will focus on three complementary and synergistic themes: 1) the deciphering of the molecular networks that define the "stem cell" character of the human epidermis; 2) the reconstruction of skin substitutes for regenerative medicine; 3) the skin disorders induced by ionising radiation as a model of the medical exposome.

1 – Molecular determinants of the 'stem cell' character or 'stemness'
This upstream research axis will focus on knowledge of the fundamental characteristics of the epithelial stem cells and progenitors present within the interfollicular epidermis and the hair follicle. Points of interest will include the search for phenotypic criteria associated with the 'stem cell' character, as well as the deciphering of the regulatory networks of the 'immaturity versus differentiation' balance. This research will integrate the conventional coding genome but also non-coding RNAs. The team will develop a more in-depth understanding of intrinsic regulators of human keratinocyte stem cells, integrating KLF4 and MXD4/MAD4 networks and functions provided by non-coding RNAs, in particular in relation with the regulatory role exerted by TGFB signalling.
2 – Reconstructed skin grafts for regenerative medicine
This translational axis will provide concepts and innovations for the benefit of the field of cutaneous cell and tissue therapies. A first line of study will concern the development of effectors promoting a pro-stemness action, thus allowing a more effective preservation of epidermal stem cells ex vivo, in the context of bioengineering architectures of skin substitutes. The approach will consist of vectorising molecules promoting a tolerogenic signal into skin cells, with the aim of generating grafts with attenuated immunogenicity.

3 – Cutaneous radio-pathologies as models of medical exposome
This axis will focus on the cutaneous consequences of genotoxic stresses induced by ionising radiation, in particular exposure of healthy skin in the context of medical applications. A first aspect will be the impact of medical exposome on the integrity and functions of epidermal stem cells and progenitors. One aspect of interest will concern dermal fibroblasts, studied for their status as primary effector cells in the development of radiation-induced skin fibrosis. Epidermal sheets reconstructed in association with healthy or fibrogenic dermal organoids will be characterised, in order to assess epidermal abnormalities resulting from dermal disturbances.
This pathophysiological modelling will provide a basis for exploring an approach aimed at counteracting fibrogenic involvement and preventing or correcting its deleterious impact on skin integrity.

The interaction network is already well identified and appears to be established and developed. On the other hand, these numerous collaborations in a variety of fields (immunology, regenerative therapies, biomaterials, organoid vascularisation) do not help to clearly identify the expertise of team members in the research areas concerned, and give the impression that many rely on external collaborations.
The trajectory did not bring a precise presentation of the major challenges. The scientific questions appeared very general. For instance, axis 3 will focus on the cutaneous consequences of genotoxic stress induced by ionising radiation (these fundamental aspects are not detailed enough). These points have to be precise. Fibrosis of the skin is indeed commonly observed after irradiation. Amongst patients' post-radiotherapy, at about 70% develop radiation fibrosis that significantly impairs quality of life post-treatment. The activation of myofibroblasts, leading to excess collagen deposition, and dysregulation of extracellular matrix remodelling are all hallmarks of radiation fibrosis. Precision is crucial as radiotherapy dosimetry constraints are the first means to prevent severe fibrosis.
Also, the international positioning of the team was not very clear and there was no mention of competing teams at national and international level. Notably, it was not specified whether the planned experiments aiming to pro-stemness effectors will take into account, or will overcome, outstanding results obtained internationally in the field, namely full-body skin grafting of Crispr-Cas9 corrected cells through powerful stem cell expansion, etc.).

As the three research axes are a continuation of the LGRK previous work, the links with the other teams in the UMR and the added value of being part of the UMR, are not obvious. Most members of the team will remain located in Evry. This may limit the integration of the team in the unit and its interactions with the other teams.

## RECOMMENDATIONS TO THE TEAM

The future axes of this project are in continuity; however, this field of research is very competitive. In this context, it would be useful to identify priorities, as there are not many members in the team.
The clinical application fields appear to be very wide. They would benefit from being refocused. The unit and the team should consider further measures to facilitate the practical and scientific integration of this new team in the unit.

**Team 9:** (ATIP-Avenir): DNA replication and genome stability

Name of the supervisor: Mrs. Annabel Quinet

## THEMES OF THE TEAM

The topic of the team is to study DNA replication and genome stability.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

NA: new team

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

NA: new team

## EVALUATION

### Overall assessment of the team

NA: new team

### Strengths and possibilities linked to the context

NA: new team

### Weaknesses and risks linked to the context

NA: new team

### Analysis of the team's trajectory

Team 9 was selected as a new group leader following an international call in 2021. The PI first joined the team 3 thanks to a starting package from the CEA and was appointed as permanent researcher (Inserm). In 2022, the PI obtained an ATIP-Avenir grant and the team created in January 2023. The group is now composed of a PhD student (CEA fellowship) and a postdoctoral fellow (ARC foundation).
The main objective is to understand the responses to replication stress in human cells, and their impact on (epi)genome stability as well as on sensitivity to environmental insults and cancer treatments.
The project has three aims. First, further defining the molecular bases of the repriming mechanism and then, aiming at studying how these gaps are formed and filled in the context of the chromatin by using approaches to study chromatin restoration during gap filling at single-cell and single molecule levels.
Finally, exploring how repriming and gap filling affect genome and epigenome integrities, as well as cancer cell's sensitivity to chemo and radiotherapy.

## RECOMMENDATIONS TO THE TEAM

The research program in three aims looks sound and clear with strong collaborations. There is no specific recommendation except secure long-term international grants with such an excellent profile.
It will be important too to attract permanent scientists and support staff either through repositioning of current SGCSR members or through external recruitment.
The mentoring scheme deployed by the unit is expected to facilitate the success of this new team (scientific strategy, grant acquisition, recruitment...).

# CONDUCT OF THE INTERVIEWS

## Date

**Start:** 29 November 2024 at 8 a.m.

**End:** 30 November 2024 at 6 p.m.

**Interview conducted: on-site**

## INTERVIEW SCHEDULE

Assessment of the Unit, Scientific Plenary session

8:00 - 8:30 Site access (badges)
8:30 - 8:45 Presentation of the EC to the staff members by SO

8:45 - 9:30 Presentation of the unit by F. Boussin, F. Pflumio and S. Marcand (for the unit trajectory)
(30 + 15 min discussion with the committee)
Attending: EC, SO, all the unit members

*Presentation of the teams*

9:30–10:00 Team 1: DNA Repair and Chromosome Stability (ERSC)–S. Marcand
(15 min presentation +10 min questions)
Attending: Team members, EC, SO, direction members
+5′ private discussion with the PI (S. Marcand); attending: EC+SO

10:00-10:30 Team 2: Niche, Cancer and Radiation in Haematopoiesis (ENCRH)–F. Pflumio
(15 min presentation +10 min questions)
Attending: Team members, EC, SO, direction members
+5′ private discussion with the PI (F. Pflumio); attending: EC+SO

10:30-10:55 Team 3: Neurogenesis, Repair and Cancer (ENRC)–L. Gauthier
(12 min presentation + 8 min questions)
Attending: Team members, EC, SO, direction members
+5′ private discussion with the PI (L. Gauthier); attending: EC+SO

10:55-11:25 Closed session Expert Committee (EC)–Scientific Officer (SO)

11:25-11:55 Team 4: Differentiation of Germ Cells (EDG)–G. Livera
(15 min presentation +10 min questions)
Attending: Team members, EC, SO, direction members
+5′ private discussion with the PI (G. Livera); attending: EC+SO

11:55–12:20 Team 5: Genetic Instability (ERIG)–J.-P. Radicella
(12 min presentation + 8 min questions)
Attending: Team members, EC, SO, direction members
+5′ private discussion with the PI (J.-P. Radicella); attending: EC+SO

12:20–13:20 Lunch Break

1:20 p.m.-1:45 p.m. Team 6: Lamin, Radiation, Immunity and Cancer (ELRIC)–P. Bertrand
(12 min presentation + 8 min questions)
Attending: Team members, EC, SO, direction members
+5′ private discussion with the PI (P. Bertrand); attending: EC+SO

1:45 p.m.-2:10 p.m. Team 7: Oxidative DNA Damage and Disease (EOX3D)–A. Campalans
(12 min presentation + 8 min questions)
Attending: Team members, EC, SO, direction members
+5′ private discussion with the PI (A. Campalans); attending: EC+SO

2:10 p.m.-2:30 p.m. Team 8: Skin regeneration and radiopathologies (ER2C)–N. Fortunel
(10 min presentation +5 min questions)
Attending: Team members, EC, SO, direction members
+5′ private discussion with the PI (N. Fortunel); attending: EC+SO

14:30–2:50 p.m. Team 9: DNA replication and genome stability (ATIP-Avenir) – A. Quinet
(10 min presentation +5 min questions)
Attending: Team members, EC, SO, direction members
+5′ private discussion with the PI (A. Quinet); attending: EC+SO

2:50 p.m.–15:00 Meeting of the Committee (closed hearing)

3 p.m.–3:30 p.m. Meeting with the representatives of Inserm and Universities
Attending: expert committee, representatives of Institutions, SO

3:30 p.m.-4 p.m. Technical and administrative personnel
Attending: Technicians, Engineers, Administrative staff, EC

PARALLEL MEETINGS
4 p.m.-4:30 p.m. Thesis students and postdocs EC1
Attending: PhD students and postdocs, EC

4 p.m.-4:30 p.m. Researchers and teacher-researchers EC2
Attending: Researchers and teacher-researchers except group leaders, EC

4:30 p.m.–17:00 Meeting of the Committee (closed hearing)

5 p.m.–5:30 p.m. Meeting of the Committee with the head of the unit
Attending: Unit Direction, expert committee, SO

5:30 p.m.–18:00 Meeting of the Committee (closed hearing)

## PARTICULAR POINT TO BE MENTIONED

N/A

# GENERAL OBSERVATIONS OF THE SUPERVISORS

Université Paris Cité

Le Président

**Paris, le 06 février 2025**

HCERES
2 rue Albert Einstein
75013 Paris

**Objet :** Retour de l'Université Paris Cité sur le rapport d'évaluation de l'unité **DER-PUR260024974 - SGCSR**

Madame, Monsieur,

L'Université Paris Cité (UPCité) a pris connaissance du rapport d'évaluation de l'Unité de Recherche SGCSR – Stabilité génétique, cellules souches et radiations.

Ce rapport a été lu avec attention par la vice-doyenne recherche et le doyen de la Faculté des Sciences d'UPCité, par notre vice-présidente recherche et par moi-même.

Je remercie le comité pour la qualité de son évaluation et vous indique ne pas avoir d'observation de portée générale à apporter.

Je vous prie d'agréer, Madame, Monsieur, l'expression de ma considération distinguée.

Édouard Kaminski

**Présidence**

**Référence**
Pr/DGDRIVE/2025

**Affaire suivie par**
Marine MADANI - DGDRIVE

**Adresse**
85 boulevard St-Germain
75006 - Paris

www.u-paris.fr

Sciences
Université Paris Cité

Référence
MC/NE/VD/2025-066

**Faculté des Sciences**
**Université Paris Cité**
5 rue Thomas Mann
75013 Paris

Objet : Dossier DER-PUR260024974 - Évaluation HCERES de l'UMR-E 008 SGCSR – Retour Tutelle Université Paris Cité

Chères et Chers Collègues,

Nous souhaitons par ce courrier remercier les membres du comité de visite pour le temps qu'ils ont consacré à l'évaluation de l'unité SGCSR, ainsi que pour leur écoute et le travail considérable qu'ils ont accompli.

La Faculté des Sciences est fière de compter le SGCSR parmi ses unités de recherche et rappelle la grande qualité de la recherche menée par tous les membres du laboratoire.

Après lecture du rapport provisoire d'évaluation de l'UMR-E 008 SGCSR, la Faculté des Sciences n'a pas de remarque de portée générale.

En vous priant, chères et chers collègues, d'accepter nos chaleureuses salutations.

Maximilien CAZAYOUS
Doyen
Faculté des Sciences
Université Paris Cité

Nathalie EISENBAUM
Vice-Doyenne recherche Faculté des Sciences
Université Paris Cité

La tutelle, Université Paris-Saclay, n’émet pas de réponse institutionnelle de type « Observations de portée générale ».

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

**Evaluation of Universities and Schools**
**Evaluation of research units**
**Evaluation of the academic formations**
**Evaluation of the national research organisms**
**Evaluation and International accreditation**

19 rue Poissonnière
75002 Paris, France
+33 1 89 97 44 00