Research evaluation

EVALUATION REPORT OF THE UNIT

Dig-Cancer - Dynamique de l'information génétique : bases fondamentales et cancer

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Institut Curie
Centre national de la recherche scientifique - CNRS
Sorbonne Université
Université PSL - Université Paris sciences et lettres

EVALUATION CAMPAIGN 2023-2024
GROUP D

Rapport publié le 12/03/2024

High Council for evaluation of research and hgher education

In the name of the expert committee :

Kerstin Bystricky, Chairwoman of the committee

For the Hcéres :

Stéphane Le Bouler, acting president

Pursuant to 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.
This version of the report is confidential under Decree No. 2021-1537 of November 29, 2021. The parts considered confidential and the responses to the points of attention of the supervising bodies will not appear in the public version of the report available on the Hcéres website.

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:	Ms Kerstin Bystricky, Université Toulouse 3 - Paul Sabatier - UPS
Experts:	Mr Jean-Christophe Andrau, Centre national de la recherche scientifique – CNRS, Montpellier Mr Fabrice Lalloue, université de Limoges (representative of CNU) Ms Stefania Millevoi, Inserm - Institut national de la santé et de la recherche médicale, Toulouse Ms Mylène Robert, CNRS, Grenoble (representative of research support personnel) Ms Ludivine Walter, Université Claude Bernard Lyon 1 - UCBL (representative of CoNRS)

HCÉRES REPRESENTATIVE

Ms Catherine Etchebest

REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Mr Christian Muchardt, INSB DAS5C
Ms Tatiana Malherbe, Centre de Recherche de l'Institut Curie
Mr Philippe Agard, Sorbonne Université.

CHARACTERISATION OF THE UNIT

- Name: Dynamics of genetic information: fundamental bases and cancer
- Acronym: Dig-Cancer
- Label and number: UMR 3244
- Composition of the executive team: Director: Mr. Antonin Morillon / Deputy Director: Mrs. Valerie Borde

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

UMR3244 research focuses on RNA, Genome Dynamics and Epigenetics.

The unit's main research themes are DNA replication, maintenance and expression with a particular focus on the role of DNA recombination, non-coding RNAs and cell cycle checkpoints in tumour progression.
The unit is part of the INCa certification of Integrated Cancer Research Sites (Siric) to characterise intrinsic cellular mechanisms of resistance to treatments using model organisms and the core expertise in DNA functions.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The UMR3244 is one of the thirteen mixed research units of the research centre of Institut Curie (IC), led by Alain Puisieux since 2019. This research centre brings together 1225 people organised in 86 teams distributed between the Paris, Orsay sites and Saint-Cloud sites mainly linked to CNRS and/or Inserm and universities. The research centre hosts also a translational research department connected to the hospital group, a training unit and nineteen technological platforms organised in a structure called CurieCoreTech. The research centre was organised in scientific domains to foster interactions between research units. UMR3244 was part of domain 2 – Development, Cancer, Genetics and Epigenetics – based on the Paris site which associated two other units of IC: Nuclear Dynamics (UMR3664) and Genome Plasticity and Genetics and Developmental Biology (UMR3215/U934. As part of the Research Centre reorganisation, the unit was part of the thematic area of Epigenetics, RNA and Genome Dynamics, focusing on a multidimensional exploration of the genome as an essential line of research. UMR3244 is located on two different floors of Trouillet-Rossignol Pavilion and the first floor of the hospital building. It is currently headed by Dr A. Morillon since 2019 with Dr V. Borde, as deputy director.

RESEARCH ENVIRONMENT OF THE UNIT

UMR3244 is one of nine units of the IC Research Centre in the centre of Paris. The other units share common research interests, in particular the Nuclear Dynamics [UMR3664] and Genome Plasticity and Genetics and Developmental Biology [UMR3215].

The unit is affiliated with Sorbonne University, hosting several faculties.
The IC provides outstanding support through personnel, technological core facilities (CurieCOreTech) and administrative offices. The connection with the Hospital and access to clinical studies and samples is exceptional.

IC is certified by Inca as one of the Integrated Cancer Research Sites (Siric) and the unit coordinates Program 1 characterising non-genetic cellular mechanisms.

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

During the period, some changes due to professional promotion or personal reason occur in the Unit: one MCU (T2) left for a full professor position at Paris-Saclay University, one PR and one MCU bound to leave the unit at the end of the current contract but one MCU (T3) will be hosted by the Unit for the next period, and training a significant number of graduate and undergraduate students on a regular basis.

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	5
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	13
Sous-total personnels permanents en activité	**24**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	8
Post-doctorants	3
Doctorants	15
Sous-total personnels non permanents en activité	**27**
Total personnels	**51**

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

Nom de l'employeur	EC	C	PAR
INST CURIE	0	0	15
CNRS	0	5	7
SORBONNE UNIVERSITÉ	4	0	0
Total personnels	**4**	**5**	**22**

GLOBAL ASSESSMENT

The unit's research in genome biology and function are at the forefront in its field and is recognised at an international level. The established strengths in determining fundamental mechanisms that regulate genome maintenance and expression, have successfully been brought to more translational activities in the field of cancer. The unit has pushed new technologies such as single cell omics, next generation sequencing and single cell imaging 'Bionano' methodologies. With more than 130 papers, the scientific production is excellent and achieves an international visibility (more than 3200 citations) with papers published in prestigious journals (e.g.Nature, PNAS, Nature Comm, Science Advances) and several invitations of the PIs in international conferences. This contributes to the outstanding attractiveness of the unit that has welcomed 27 PhD students, 26 postdoctoral fellows and five international visitors.
Research is extremely well funded with national (e.g.13 ANR, 2 ATIPE-Avenir project, 'Impulscience' – Bettencourt Foundation, Equipe FRM) and European grants (3 ERC grants at all level). Efforts to translate basic research output into the clinic or to create startups is outstanding. Notably, the Unit has deposited eight patents, established industrial partnerships (6) and signed more than twenty industrial contracts (e.g. EDF, Google, Home Biosciences), some of them granting PhD students (2 Cifre). The unit has founded three startups (Skiagenics for RNA biomarkers discovery, *One Biosciences* for the discovery of novel targets and biomarkers with single-cell data, with seven million euros seed funding, and *Meiogenix*, which offers an original

technological solution for regulating the frequency of homologous recombination in eukaryotic cells).
Remarkably, the unit also contributes to a clinical trial 'Hope' with the Institut Curie, Hôpital Henri Mondor and Institut Mutualiste Montsouris. It aims to characterise new circulating biomarkers, avoiding unnecessary biopsies in prostate cancers. It is based on a set of sequences significantly overexpressed and identified by the unit in these cancers.
The future projects are ambitious. The scientific project around single cell genomics in the context of genome stability, maintenance expression and relevance to cancer diagnosis and innovative therapy of the unit is very exciting. The project is at the heart of a larger project federating other units and/or teams within the IC into a 'Genome Biology' program.
The unit is well structured into coherent teams. Teams are led by very active and brilliant team leaders. The unit's modest size and limited number of permanent faculty and scientists may pose a threat to sustain the outstanding and internationally highly visible research activity.

The integration of the Unit forces into federative IC projects should respond to the need to increase the critical mass of the unit's research perimeter and to join forces for administrative and institutional mandatory tasks. It would also enable the direction to improve their role in staff promotions, career perspectives and recruitment, key to maintain the motivation of all staff.
The unit should accompany the new team hired to expand on spatial single cell genomics by clearly pushing the links to the clinic via the new axis on viral infection and making sure to stabilise the team. The project to attract another team should be discussed within the 'Genome Biology' perimeter, the IC and the supervising bodies (CNRS and University).

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Most recommendations of the previous report were taken into account mainly through the hiring of permanent scientific support staff (2 IR, 1 AI CNRS, 1 IR Curie) and two CRCN positions at CNRS (T5 and T6). Of note, the unit's contours changed with two new teams joining and one departing since the last evaluation. Nevertheless, the number of permanent research scientists remains very low (9 of which 4 A category).
The dynamic of the unit improved with regular meetings, involvement in courses and international collaborations. Of note, the number of first author PhD articles has improved for the teams to which this requirement was specified in the previous report.
Additional laboratory and office space was allocated to the unit in the Trouillet building first floor and the translational department of the Curie hospital.

However, staff scientists, MCU and IR in particular are still in need of recognition. They were not sufficiently involved in the scientific life of the unit and not in a position to lead projects (apply for grants, even small ones, corresponding author, etc.).

B – EVALUATION AREAS

Considering the references defined in the unit's evaluation guidelines, the committee ensures that a distinction is made on the outstanding elements for strengths or weaknesses. Each point is documented by observable facts including the elements from the portfolio. The committee assesses if the unit's results are consistent with its activity profile.

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

Assessment on the scientific objectives of the unit

The unit's research objectives in Genome biology and function are at the forefront in its field with the main aim to unlock tumour cell plasticity mechanisms. The established strengths in determining fundamental mechanisms associated to the regulation of genome instability and the role of non-coding RNAs have successfully been brought to more translational activities. With three startups companies created, the unit has pushed new technologies as biomarker transcriptomics (Skiagenics), single cell omics (One Biosciences) and genome editing (Meiogenix). The PIs are internationally visible and recognised.

Assessment on the unit's resources

The institutional unit's budget assignments were stable throughout the period (~230 kEUR) with significant funding from the Institut Curie (~150 kEUR). The main asset the institutions provide relies in HR (15 support personnel from IC, 7 from the CNRS).
External grant resources (ANR, INCA etc.) are outstanding for four of the teams present during the evaluation period and bound to continue to the next contract. International funding is outstanding with two ERC grants obtained over the period (ERC POC and ERC Stg). Total RP was thirteen million euros over the evaluation period.

Assessment on the functioning of the unit

The unit is well structured into coherent teams. Teams are led by very active and brilliant team leaders. Research is extremely well funded. Efforts to translate basic research output into the clinic or to create startups is outstanding. However, there appears to be a lack of cohesion among the unit's members overall, at least partially due to spreading of the teams at distant locations in the building. The interaction with neighbouring units of the IC also appears limited.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The unit's research activities in the field of Genome Biology are internationally highly visible. As a mark of visibility, almost all team leaders have been invited to prestigious conferences. The teams develop state-of-the-art technologies, in particular in single cell approaches and associated bioinformatics analyses, with particular emphasis on describing and understanding heterogeneity of cell dynamics and function. They explore macromolecular structures, epigenetics using microfluidic and high-throughput technologies. The teams successfully exploit yeast and mouse model organisms, and human cancer cell lines and samples. Research results are amenable to translational applications. The scientific objectives are outstanding.

Weaknesses and risks linked to the context

The projects are very ambitious. The unit's small size and limited number of permanent faculty and scientists (5 C/DR CNRS, four faculty at the end of the evaluation period with two A rank personnel leaving – T1/T2) may pose a risk to maintain the level of world-leading research the unit is known for.

2/ The unit has resources adapted to its activity profile and research environment, and makes use of them.

Strengths and possibilities linked to the context

Financial and human resources provided by the governing bodies – IC and CNRS – are excellent. 230 kE per annum to cover recurrent expenses, numerous personnel in particular from the IC support research and administration of research. The IC provides all financial and HR support which is streamlined thank to two permanent personnel within the unit who are in charge bridging the unit's personnel's needs with the relevant department of the IC and outside funding and managing bodies. IC provides access to nineteen technological platforms which are extremely well equipped and staffed. The IC provides access to patient samples. This is outstanding.
Funding of the research activities is outstanding: approximately EUR twelve million obtained from local (IC, PIA Paris region…), national (ANR, FRM…) and international (ERC…) obtained by the team leader over the evaluation period in addition to two million from private partnerships.

Weaknesses and risks linked to the context

Funding bodies will, of course, expect the coordinators to produce data, publications and patents in adequation to the level of funding. The diversity of grants has to be managed in a timely and efficient fashion. The administrative department seems to be under a lot of pressure. Numerous PhD students are clearly key to productivity but also need to be well trained and supervised. Numbers of PhD students are variable but appear to decline recently (10 at the time of the visit vs 20 as the report was done). Management qualities and a well-functioning environment are key. Permanent staff scientists (CR, MCU, IR) need to be recognised for this activity. The new team needs to be accompanied within this competitive environment.
The development of single cell genomics requires bioinformatic staff which is hard to find because the salaries offered are largely uncompetitive compared to non-academic offers. In addition, to contract personnel, even a recently hired CNRS permanent IR left the unit. The committee felt that a strategy needs to be put in place to share/hire bioinformatics personnel through companies rather than through the supervising bodies.

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

Strengths and possibilities linked to the context

The DU ensures that all regulations are in place. The DUA assists. Training sessions are in place.

Weaknesses and risks linked to the context

The small size of the unit implies that mandatory safety regulations have to be fulfilled by few people, the direction and dedicated technical personnel which puts strain on their time and availability for research.
During the Hcéres evaluation period, i.e. five years, and based on the elements provided for and during the visit, the committee has noted that there was only one promotion "de corps"(AI-IE Institut Curie) for 22 ITA personnel. This point was underlined by the personnel during the visit. The management is advised to better support and assist the advancement or promotions of ITA, CNRS or Institut Curie staff.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The unit has an outstanding scientific attractiveness, several PIs obtained prestigious awards and prizes.

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

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

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

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

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

The unit has an outstanding scientific attractiveness, several PI obtained prestigious awards and prizes. The Unit members received ERC POC award – Prostator in 2019 and Price Gallet et Breton, Académie Nationale de Médecine, 2018, the Impulscience award of the Fondation Bettencourt Schueller (2022) and one team was labelled ATIP-Avenir and ATIP-Avenir plus (2018–2023).

One member is holding an expert position on international grant panels, in particular at ERC, during the evaluation period. She has won multiple awards for her innovative research (Innovation Medal CNRS – 2022; Embo Young Investigator, Innovation Prize Région Île-de-France, Fondation Schlumberger Education & Recherche, Simone et Cino Del Duca Prize for Cancer Research -2021; Institut Necker/Fondation Tourre Prize for Cancer Research – 2019; Bronze Medal CNRS, 2018).
The unit organises international courses and workshops. Teams 4 and 5 have been involved in the organisation of Genome Instability & Human Disease course, Team 2 in the organisation of Cancerology course and Mouse Genetics course in collaboration with Institut Pasteur. T3 is organising the annual international course Non-Coding Genome in collaboration with Frankfort University, and T6 participates in the organisation of Epigenetics Course and Breast Cancer Course.
Team leaders are members of national funding bodies (ARC, ANR..) and evaluation committees (Hcéres, CNRS..).
The unit obtained funding for and trained 30 PhD students over the evaluation period, which given its size is outstanding. Postdoctoral students, including one via MSCF, key to research productivity.
Two CNRS permanent researchers were hired during the period.
Most team leaders were very successful in obtaining grants enabling them to hire highly skilled personnel:
~EUR 13 million including three ERC (2014 CSD and 2020 POC to Morillon, STG to Vallot in 2021) and thirteen ANR (of which 5 as coordinators).
IC is certified by INCA as one of the Integrated Cancer Research Sites (SIRIC) and the unit coordinates Program 1 characterising non-genetic cellular mechanisms.

Major state-of-the-art equipment is available through the CurieCoreTech facility. The unit has been instrumental in setting up and acquiring funding for the NGS (T1), Single Cell (T6) and BioNano (T4) facilities. Facilities are staffed with highly qualified personnel which is also partly taking part in the unit's research activities.

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

The limited size of the unit appears as a threat to the sustainability of the extremely high-profile research activities at all fronts (fundamental, translational, R&D). In light of the discussions held during the visit, the committee notes that the PIs are not easily able to delegate activities. Senior personnel are few and not sufficiently trusted to take part in leadership, expertise and training activities, and if they do, appear not to be sufficiently recognised for their activities. The number of postdoctoral students appears low with respect to funding. Difficulty to attract postdoctoral students was cited by several team leaders. The number of PhD students is high (2/team) but decreasing.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production is excellent. The published work is highly visible and source of attractiveness of the unit with articles in top visible journals such as Nature, Cell, PNAS, NAR and Nature Commun.

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

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

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

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

1/ The scientific production of the unit meets quality criteria.
The scientific production of the unit is excellent with seven original studies (unit members first or corresponding authors) and seven collaborative studies published in highly visible journals and in journals attractive in the respective fields of research of the teams as illustrated in the portfolio.

2/ Scientific production is proportionate to the research potential of the unit and shared out between its personnel. Based on the information provided, the unit produced 104 original articles and 23 reviews and perspectives over the evaluation period. This quantitative output is excellent. The production is proportionate to the size of the unit, although some differences exist between teams.

3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science. Scientific integrity is ensured at all levels through inventories, training or signing of lab books when aimed at patenting.

Quality and volume of scientific production are excellent both through deciphering new fundamental insights into mechanisms of single variability in genome stability and expression and opening avenues for diagnosis and treatment.

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

Although research themes are very close, surprisingly few collaborative studies are published, in particular with neighbour units of IC, i.e. UMR3664.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

Non-academic interactions of the unit are excellent with respect to bring research into the clinics, partnership with private companies and startup creation. The unit's involvement in outreach, teaching and general public communication is very good.

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

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

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

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

The Unit has considerably evolved these last years to promote non-academic interactions (with the hospitals through clinical trial Hope-T3, partnerships with companies – T1, T6 and T3), and to generate products for the socio-economic world (8 patents, software – 2 with copyright protection –, 3 startups (**(Skiagenics, One Biosciences, Meiogenix)** and one more in 2023). Affiliations with biotech companies allowed Cifre contracts (T6 with Google and One Biosciences), postdoctoral fundings (T1, Meiogenix) and engineers on the single cell initiative platform and within the unit (T6, One Biosciences). Six partnerships and supports by companies and donation grants were generated (by One Biosciences, Meiogenix, AFER, Humanis Malakoff, Home biosciences, BioNano – Teams 1, 3, 4 and 6) for a total of more than 1900 k€.
Outreach activities were done by a few PIs through round table discussions with patients and IC donators.

One can underline the outstanding socio-economic involvement of some teams. The patenting and licensing activity is remarkable given the mainly fundamental research orientation. Opportunities were clearly seized.
The unit assigned a technology transfer officer whose role is to make the link between researchers/engineers and the IC Development office (DVPI) smoother and more efficient. It also relays open calls for support in technology transfer and assists candidates in drafting their proposals. This activity is very valuable and seems to have produced the expected outcome.

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

The unit's activities are very close to the ones from neighbouring units within IC, similar technologies are used and developed, added value may be gained from collaborating and sharing resources toward developing socio-economic activities. The CNRS deploys 'IR valorisation' precisely toward identifying and accompanying tech transfer, IR valorisation are usually shared between institutes.

Some researchers, mainly PIs are involved in biannual IC courses. However, teaching at Sorbonne University was not clearly mentioned in the auto-evaluation nor during the visit except during the meeting with non-PI scientists and faculty. The unit could benefit from the link to teaching activities and students, making the heavy involvement of faculty more valuable.

ANALYSIS OF THE UNIT'S TRAJECTORY

The scientific project around single cell genomics in the context of genome stability, maintenance expression and relevance to cancer diagnosis and innovative therapy of the unit is very exciting. The project is at the heart of a larger project federating other units and/or teams from within the IC into a 'Genome Biology' program. The priorities to be developed for this project are (1) investigation of the genetic/non-genetic effects involved in tumour development, (2) the mechanisms of genomic integrity and (3) unlock the processes of tumour cell plasticity. The recent selection of the BOST team to join the unit at the IC is an excellent choice to expand on spatial single cell genomics with in addition a new axis on viral infection. The novel domain should be clearly identified as, on the one hand, reinforcing the single cell technological portfolio and, on the other hand, a new original approach to cancer in new specific contexts.
The 'Genome Biology' project should respond to the need to increase the critical mass of the unit's research perimeter, the need to join forces for administrative and institutional mandatory tasks in teams. It would also enable the direction to improve their view on staff promotion and recruitment.

RECOMMENDATIONS TO THE UNIT

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

The unit could seek more interactions with teams from neighbouring units in light of the creation of a 'Genome Biology' Centre as soon as possible to consolidate the area of outstanding research and international visibility.
The unit could search for solutions hiring competent bioinformatics personnel offering competitive salaries, hence not relying solely on the civil servant positions.

The unit should consider providing opportunities for scientists and senior research engineers to be recognised for the involvement in research projects and training, offering them opportunities to lead parts of projects from funding to publication,
The unit direction should install a venue to discuss staff promotion strategies at CNRS and IC together, plurennial rankings.
The proposal for advancement by management is currently only justified by exceptional work, although shared service functions increase each year and investment therein should be recognised.
The unit direction should envision to create multi-unit 'teams' of persons assuming responsibilities such as administration, health and safety, radioactivity, communication, training, etc. to share their experience and tasks.
The unit could take advantage of the opening of a Sorbonne university professorship. A dynamic colleague with an ambitious research project could join the unit and increase its visibility to students as a future group leader.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit is advised to remain focused on their areas of excellence and build on it. Since recruitment of new PhD students and postdoctoral students appears critical to maintain the level of excellence of the unit, it is recommended that PIs try to promote active advertisements to available positions through various social media and when talking at conferences. The unit's involvement in startups and development and clinical trials should pay in the future as many young people are motivated to work in a more applied environment. Cohesion of staff within the unit suffers a bit from social distance between the groups and could be improved by promoting more social events or specific locations for social contacts. It would be helpful that members of the future team(s) are well integrated from the beginning, in particular when coming from abroad.

Recommendations regarding Evaluation Area 3: Scientific Production

The scientific production has been excellent and the teams are encouraged to keep on aiming to this level of excellence. As a general matter, quality should prime over volume of production.

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

The POC project will reinforce the activities of the tech transfer ambassador to assist unit members in their projects. POC could also be shared with other unit, share within the 'Genome Biology Centre' with a better critical mass of potential projects.

Teaching should be seen as more valuable to the research activity. All four remaining PIs are extremely wide-spread and successful, one should not require them to further dilute their activities at the risk of decreasing performance. Hence, some of the outreach and evaluation activities can be delegated to various senior members or even PhD students in the unit.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Telomeres and Cancer

Name of the supervisor: Mr. Arturo Londono-Vallejo

THEMES OF THE TEAM

During the evaluation period, the team has studied Telomere biology, its historical major topic, genome stability and signalling, and the evolution of G-quadruplexes sequences with the input of a new emeritus member. More recently, PI of Team 1 initiated and developed a novel research axis on the physiopathology of lung fibrosis, which brought the team to move to a novel Curie department 'DNA Repair, Radiation and Innovative Therapeutics'. Team 1's PI took the lead of this department.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In the previous report, three main recommendations were made for (1) improving publication in high visibility journals, (2) enforcing the team cohesion and (3) strengthening cross-talks between topics. Concerns were expressed concerning the average level of publication of the PhD students and the lack of general public outreach. These recommendations were for the most taken in account. Two very good publications were published involving two PhD students as first authors. The integration of one person also appeared successful during the period. Finally, efforts were pushed to improve the general public outreach with the organisation of a public event on breast cancer, and participation to other public events organised by the Physics society.

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

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

EVALUATION

Overall assessment of the team

The team has initiated during this period a major thematic shift toward the study of lung fibrosis, DNA repair and therapy, which has brought the PI to change unit and start a new group in the Curie institute, most likely for strategic reasons. The performance of the group has been very good with several articles published in good/excellent journals and in general attracted good funding for the team. The output of the team during this period is considered to be very good to excellent.

Strengths and possibilities linked to the context

The new topic developed by the team and recently awarded by an excellent publication in Nat. Communication (submitted at the time of evaluation) has justified moving in a new environment in which synergy will be improved for the team. The team leader has chosen to develop himself, consistently with the technical expertise of the unit, single cell approaches. This transition represents a strong thematic reorganisation that might turn into an advantage in its new unit.

Weaknesses and risks linked to the context

Although the group has performed well during the period, the strength of the publication impact of the team could slightly improve. The recently accepted article describing atlas of pulmonary lesions in lung following irradiation using single cell approaches seems to give a proof of principle for the future.

Analysis of the team's trajectory

The team has already left the unit and this section is not relevant for this evaluation.

RECOMMENDATIONS TO THE TEAM

The team is no longer part of the unit but should progressively gain visibility by investing its new topic, taking advantage of its gained knowledge in single cell approaches while developing more links to clinics.

Team 2: Genetics of tumour suppression

Name of the supervisor: Mr. Franck Toledo

THEMES OF THE TEAM

The research theme of the team 2 is focused on the regulation and functions of the p53 pathway using mice models and is mainly articulated around two axes: i) Investigating the involvement of p53 in genomic maintenance and its implications to genetic disorders and ii) studying the biological functions of alternative spliced p53 isoforms.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In the previous evaluation, several recommendations were put forward: i) foster collaborations to integrate mice data with clinical data, ii) engage in a European network, iii) strengthen the team by increasing the number of HDR and attracting a full-time researcher and iv) focus the research toward gene regulation by p53 in the bone marrow failure syndrome. It is notable that an international collaboration led to one excellent publication corroborating clinical and mouse model data on the relevance of the role of p53 in telomere metabolism within the context of bone marrow disorders. Additionally, one of the permanent assistant professors within the team obtained its HDR in 2020. However, the team's ongoing projects maintain a broad scope. Further strengthening of the team's achievements could potentially be realised through a more focused research approach.

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

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

EVALUATION

Overall assessment of the team

During the evaluation period, Team 2 exhibited notable productivity in research and teaching activities. The team carries a heavy teaching load that should be considered when assessing the accomplishments. Overall, Team 2 conducts consistent research of very good to excellent quality and originality. The team has maintained collaborations at both the national and international levels. The team faces limitations in terms of funding sources which could potentially limit their research activities.

Strengths and possibilities linked to the context

During the evaluation period, the Team 2 has been active and successful in their research efforts in the field of p53 roles in bone marrow failures syndromes. The team has achieved a significant milestone with an excellent publication (*Science Adv. 2020*) co-signed by two PhD students and one supporting team member as first authors. This work integrates the role of p53 activity in telomere maintenance with clinical data through an international collaboration. Additionally, the Team 2 extended their research efforts by collaborating with DIG Team 3 to investigate the regulation of p53 at the full transcriptome level. They have identified a target of p53 as a putative male-specific prognostic factor in specific lymphomas. This suggests a broad impact of the research in cancer biology. The team consistently contributed to the field of p53 biology, maintaining a steady stream of review publications that underscore their expertise and standing in this competitive field (*e.g.Cancers, 2018*).
Team 2 has successfully trained two PhD students, both of them graduated with a co-first author publication. One of them obtained the Bettencourt Award for Young Scientists in 2019. Actually, they are mentoring two PhD students with one of them first author on the team's most recent publication (*Dis Model Mech, 2023*).
The three permanent teacher researchers of the team are deeply engaged in teaching responsibilities (two Master tracks at Sorbonne University) and duties (a total of 450 h/year for the team). Furthermore, one of them dedicates 880 hours/years on clinical studies.

Weaknesses and risks linked to the context

Although the Team 2 has generated significant output in the field of p53 biology during the evaluation period, there are weaknesses that constitute major risks. The scope of the research is very broad in relation to the size of the workforce dedicated to research. Furthermore, it is unclear how the main axes of research are distributed between the PI and the two assistant professors. It is unfortunate that there is no available information regarding the career paths of the PhD students. Understanding their post-graduation trajectories would provide valuable insights into the team's impact on their students' careers. It remains unclear how the Team 2 positions itself within the institute in terms of interactions, involvement in the institute's activities, and utilisation of available equipment. The team's research heavily relies on generating mouse cohorts, which is a time-consuming process. Unfortunately, this aspect of their work was significantly impacted by the Covid-19 lockdowns during the evaluation period. There were concerns about the funding level of the team, which seems barely sufficient given the costs associated with mouse studies.

Analysis of the team's trajectory

Team 2 is bound to leave DIG. Its trajectory is thus not relevant to the unit and not to be evaluated.

RECOMMENDATIONS TO THE TEAM

The team could put more effort to actively recruit postdoctoral researchers who could secure their own funding and can do research with more autonomy. This would likely enhance the team's research output and capacity. The team could secure funding by seeking collaborations to apply to networking grants at the European levels. Given limited resources, it's advisable to narrow the scope of research accordingly.

Team 3: Non-coding RNA, epigenetics and genomes fluidity

Name of the supervisor: Mr. Antonin Morillon

THEMES OF THE TEAM

The main research themes of team 3 are focused on eukaryotic long non-coding RNA, epigenetics and genome fluidity. The research activity is divided in four axes regarding the study of biogenesis, fate and activity of lNCRNAs within single cells and tumours and develop translational approaches for cancer therapeutical purpose. The team uses essentially yeasts and human as model organisms to perform both basic research and translational activities.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No major weakness identified on scientific outputs, reputation and appeal. The team is developing new themes that are well in line with Institut Curie's research themes. The organisation and the scientific strategy are excellent.
Given its implication in valorisation process with patent development on prostate cancer, its involvement in general public outreach was reduced. During this contract, visibility was greatly improved in social media and the team participated to general public events such as Grands Donateurs campaign in 2022-23 and Jonquilles to raise funds for Curie.
Previous recommendations mentioned that PhD students' publications could be improved. This has improved, for instance, the PI, who is also unit director, has cosigned excellent articles with PhD students in J Extracell Vesicles, Embo Reports. Moreover, two main project leaders have supervised PhD students and have or will pass their HDR (MW and MP), which will support team management. Finally, the previous report recommended developing collaborations with clinicians, which was essentially achieved as attested by recent publication using patient samples for lNCRNA analyses. A tight collaboration with clinicians was also required to enable the clinical trial (Hope) on Prostate cancer patient biofluids to isolate biomarkers. The main problematic point raised by the team, and that remains, is the chronic lack of permanent of bioinformatician. Overall, the team essentially responded to points raised previously.

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

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

EVALUATION

Overall assessment of the team

The team has an excellent scientific and translational output and its international visibility is also remarkable. While an emphasis of the priorities may have been given to translational research consistently with the local environment, this strategy has brought great achievements. This team has notably demonstrated a high capacity to raise regular funding while keeping a strong involvement in training activities. The difficulties to recruit a permanent bioinformatician may represent a risk. Despite this difficulty, the overall quality of the team remains exceptional in most fields.

Strengths and possibilities linked to the context

The team has an excellent scientific production and is able to develop efficient translational research from bench (yeast genetics and cancer cells) to bedside (patient tumours and liquid biopsy) which is remarkable. The quality of their research enables them to characterise new circulating biomarkers and thus to develop clinical trials in relation with their fundamental findings. The team's national and international visibility is also important and its ability to raise funds and attract regular funding (2 ERC, 1 ANR, 2 INCA, 1 ITMO, 1 SIRIC) is undeniable. More than 3 million euros over the last period.

Weaknesses and risks linked to the context

As with Team 6, one of the major risks remains the difficulty of recruiting bioinformaticians. The lack of permanent bioinformatic staff represents a weakness for the team.

Analysis of the team's trajectory

The scientific project is composed of three distinct objectives which are directly linked to the previous results from the team and concerns the great heterogeneity of INCRNAs and their rare phenotypically consequences regarding their high number. Based on these findings, three fundamental hypotheses have been formulated and a research plan is proposed to answer in four objectives. The first two objectives focus on INCRNA in yeast model, while the following ones are directly related to oncology. Taking advantage of its international recognition and research network, the team can rely on its various internal or external collaborations that are described in the scientific project. The first aim is focused on INCRNA decay, translation and evolutionary conservation and will require international collaboration in the field of IA. It will enable establishing robust procedures to systematically identify functional elements, using deep structural and machine learning approaches to predict functional potential for INCRNAs. The second aim is achieved in collaboration with Team six for INCRNAS reference-less profiling. Preliminary analyses of the team raise a new question about the antisense INCRNAs reciprocal impacts on their fate, translation, and cellular orientations. The third objective is to study the exact function of INCRNA in cells subjected to treatment-induced stress. Combined approaches will be implemented to analyse the role of several INCRNAs selected for their phenotypes in prostate cancer and TNBC resistant to treatments. This aim is particularly relevant and innovative and has already been allowed to set up an ERC-Syn project presently under evaluation. Finally, the last aim is to use the INCRNAs as diagnosis or prognosis biomarkers in prostate cancer. The team now has the opportunity to be involved in a clinical trial to profile and compare unreferenced RNA markers in urine and blood of prostate cancer patients. Its actual ambition is the development of a urinary test that could become extended to other cancer patients resistant or not to chemo- or immuno-therapies. The team is clearly engaged in translational research with medium-term implications for patients.
The project and perspectives are excellent and innovative and rely on various collaborations.

RECOMMENDATIONS TO THE TEAM

The major risk is the absence of a permanent bioinformatician within the Unit. The team will need to strengthen its position in this area in the near future due to developed topics. Given the immense scientific quality of the team and its visibility, the committee is confident that they should succeed in attracting a good bioinformatician in the future. While the team has performed extremely well in attracting funding and developing translational research, it should keep on its effort in publishing its scientific results in highly visible journals.

Team 4: Replication program and genome instability

Name of the supervisor: Mr. Chunlong Chen

THEMES OF THE TEAM

The team focuses on the regulation of replication, its interaction with the transcription, chromatin structure and the link to genome instability. The interdisciplinary project aims to study the extent of these regulations and the underlying molecular mechanisms, and to explore the consequences in physiological (neurogenesis) and pathological (cancer) contexts.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was not evaluated during the previous Hcéres, as it had just joined the unit under the ATIP program; however, a presentation from the team leader was included during the visit.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	**3**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	4
Sous-total personnels non permanents en activité	**6**
Total personnels	**9**

EVALUATION

Overall assessment of the team

The team's scientific productivity has been excellent to outstanding thanks to teamwork and several collaborations. Team 4 PI has leveraged the ATIP program to secure several prestigious national program funds. The team has excellent visibility and attractiveness, and is very dynamic in terms of teaching and training. The performance metrics are excellent overall, with some weaknesses to be addressed in order to bring the team up to the outstanding level.

Strengths and possibilities linked to the context

Scientific output is remarkable given the team's small size and its recent integration at Curie (2016), with 21 articles (11 of which the PI signed as last and/or corresponding author) in journals of excellent (Nat Comm) to outstanding visibility (Nature, Cell) and 2 AAP. This outstanding qualitative/quantitative productivity is the result of tackling fundamental unsolved questions about replication regulation linked to transcription/chromatin organisation linked to genome instability, using/developing cutting-edge genome wide technologies (to study

replication directionality and time, using single molecule/cell approaches) and bioinformatic tools (5, 2 with copyright protection, for the development of single-cell and single molecules), setting up international collaborations with leading groups in the field and building a dynamic team (PhDs, postdoctoral students, few permanent staff).

PI has an excellent visibility/attractiveness. The PI has been excellent at raising funds (6 coordinators, including ATIP avenir, 1 ANR, 1 INCA; 6 partners, including 3 ANRs) to cover running and salary costs (PhDs) as well as equipment (Bionano's Saphyr System) and been recently awarded by Impulscience from Bettencourt foundation (for the next period). National/international reputation is excellent, based on its ability to collaborate (leveraged by publications and grants, including ANRs), attract non-permanent staff from abroad (different nationalities, 3 postdoctoral researchers), and frequent requests to review articles for high-profile journals (Nature) and grants (including European – ERC), involvement in editor activity (guest editor and editorial board JCI), invitation to international/national meetings. The contribution to teaching/training is also excellent, based on the organisation of courses (albeit at local level), and student training with high quality publications.
Excellent implication in national committees.

It is important to note the PI's effort to build a balanced team M/W, nationalities, wet/dry labs, permanent/non-permanent, which reflects an excellent well-thought-out management strategy. The number of HDRs is not mentioned and may represent a limitation for the team.

Weaknesses and risks linked to the context

Although the PI has demonstrated a remarkable ability to federate, lead and animate the emerging team with national and international success indicators, it still has no permanent researchers, lacks strong interactions with DIG teams, and funding is restrained at the national/local level.

Analysis of the team's trajectory

The future project, funded by the Impulscience program of the Bettencourt Schueller Foundation (2023–2028), capitalises on the bioinformatics and technological tools already developed/used during the previous period to develop them further and thus answer more in-depth questions about replication and its link with genome instability at the population as well as at the single-cell level. This project will shed new light on the mechanisms of cell-to-cell variability in replication and related processes (transcription, chromatin organisation) in the physiological context (neurogenesis) and in the pathological context (tumourigenesis). With its innovative approaches, its interdisciplinary strategy, the scale and scope of the fundamental questions raised and the research models chosen, this project is likely to constitute a real breakthrough in our knowledge of replication, its mechanisms and its consequences on pathophysiology.

RECOMMENDATIONS TO THE TEAM

The team is doing an excellent to outstanding work and should consider reaching the next level e.g. by applying for ERC funding. Outreach activities, links with industry and clinicians, collaborations within the unit (only one publication with a DIG team) might be improved. The team's critical mass needs to be consolidated with the recruitment of permanent researchers.

Team 5: Chromosome dynamics and recombination

Name of the supervisor: Mrs. Valérie Borde

THEMES OF THE TEAM

The team is studying the mechanisms by which genetic information is faithfully transmitted to offspring during the reproductive process notably meiotic recombination in yeast. It is then seeking to transpose its mechanistic findings on homologous recombination to better understand the mechanisms that faithfully repair DNA double-strand breaks, and how they are deregulated in cancer.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recognition of the team and its international visibility are well established and undeniable as evidenced by the invitation of PI as an invited professor for one month in Japan and his sixteen invitations in international conferences. The PI was also currently the deputy director of the unit and was directly involved in the scientific strategy of the unit.
This observation confirms that the position of Deputy Director did not pose a threat to the scientific output. Similarly, for ensuring external funding for longer periods, several major grants (4 ANR and 1 FRM) have been secured to guarantee the stability and expansion of the team project.
As mentioned in the previous report, the number of permanent staff members holding an HDR is still extremely limited. In fact, the team leader is the only one occupying a position with an HDR. However, increasing the number of researchers with an HDR could contribute to an increase in the number of PhD students. Major changes occurred during the last year of this contract, which could partly explain the difficulties in increasing the number of HDR. Particularly, the departure of a permanent researcher who could likely have obtained an HDR. Despite these challenges and the low number of HDR positions, the scientific output has remained excellent, and the pursued strategy remains highly ambitious and promising.

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

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

EVALUATION

Overall assessment of the team

The great strengths of this team are undoubtedly its outstanding scientific output, its international visibility and dynamism. In addition, the team gains with high success regular funding in national calls and is highly involved in training of foreign students. The only sensitive point that can be perceived as a risk remains the lack of permanent researchers but the recent recruitment of a top researcher should remedy the situation.

Strengths and possibilities linked to the context

The team has an outstanding international visibility notably due to its excellent scientific output (Nature, Nature comm., PNAS, NAR). Indeed, the PI is regularly invited in international conferences (12 in the previous contract) and has also been invited professor in Japan (Osaka University) highlighting the recognition of team research in the international scale.
The capacity to raise funding in national call is also excellent with a total of five major grants (4 ANR and 1 FRM) between 2017 and 2022.
Finally, the involvement of PI in the co-organisation of the Curie international course Genome Instability and Human Disease has to be underlined and demonstrates that the team is a key player in his research field and that also participates actively in the knowledge spreading.
The team is also implicated in student training with the hosting of foreign postdoctoral fellow and many master and foreign students.
The excellent dynamic of the team pursues in cross-interaction with other units' team as evidenced by the recent procurement of a new collaborative grant (ANR funding) with another PI of the unit.

Weaknesses and risks linked to the context

The first risk is the lack of researchers in the permanent staff due to the departure of one member in 2021. Since the PI is alone to lead the team, this could potentially weaken the team and diminish its outstanding dynamic. However, the recent recruitment of a highly qualified researcher by CNRS in the scientific staff should reduce this risk and allows stabilising the team. The second risk was previously mentioned in the previous report, the PI is also deputy director of the unit that represents an additional heavy administrative charge as the team size even if it represents a personal exciting challenge. Finally, the team has no European grants for the instant. Given its high quality and international visibility, it is highly likely that they will obtain this type of grant in the future.

Analysis of the team's trajectory

The scientific project aims to pursue the study of crossover mechanisms and their links to chromosome structure. This ambitious and innovating project relying on original technological approaches and models with thigh collaboration is supported by recently obtained several funding and grants. In this context, the team intends to perform live imaging of the homology search in the nucleus. New sequencing and proteomic technologies to investigate DNA synthesis during DNA DSB repair by recombination are actively developed in order to use them first in our model organism, budding yeast, during recombination mechanism, then in human cells. The project is declined in four topics.
The first concerns the functional interactions between crossover proteins and chromosome structure. Based on their recent work and tight collaboration with one team at I2BC, the team intends to establish a link between the 'ZMM' proteins, the Mlh1-Mlh3 complex and the synaptonemal complex. This part will require various original technological development such as interaction point mutant or then the identification of the interactome of the synaptonemal complex by performing an inducible TurboID proximity ligation assay in order to evaluate the effect of mutants on meiotic recombination or on mismatch repair and to implement a thorough functional and evolutionary study.
The second goal regards the dynamics of the Rad51-Dmc1 recombinases filaments during meiotic recombination – live imaging, localisation and protein partners. This project step will rely on the collaboration with one Unit at IC, which permits to obtain a fully functional version of Rad51 tagged internally with GFP. The functional proteins will be used to determine the comprehensive interactome of Rad51 and Dmc1 during meiotic recombination, using an inducible proximity labelling assay and serve to identify new partners. This program is ambitious and very innovative.

RECOMMENDATIONS TO THE TEAM

Team 5 has a remarkable scientific output and excellent scientific recognition, but certain points need to be monitored in order to maintain and reinforce this excellent level. To tackle different axes of the team's future project, starting with omics approaches, then sorting and combining the data to focus on candidates answering the questions raised, the possible opening up to new human cancer cell models, it would be important to increase the team's critical mass beyond the researchers already recruited, in particular a bioinformatician and to further strengthen collaborations within the unit.

Team 6: Dynamics of epigenetic plasticity in cancer

Name of the supervisor: Mrs. Céline Vallot

THEMES OF THE TEAM

The main research themes of team 6 are focused on the heterogeneity of epigenetic mechanisms that may account for the adaptability of cancer cells to environmental, metabolic or therapy-related stresses. The contribution of chromatin structure to tumour evolution remains unknown.
The goal is to better understand the role and contribution of chromatin landscapes to breast tumour progression during tumourigenesis and in response to treatment. To achieve this, the team is mapping and modelling the heterogeneity of chromatin landscapes at single-cell scale. They are investigating their potential as drivers of tumour evolution with in vitro and in vivo models. Their works allow proposing new and original therapeutic strategies to prevent epigenetic processes and thus bypass resistance mechanisms.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Team 6 was not yet created in the previous evaluation 2017 campaign. The Unit was funded with two ATIP-Avenir starting grants. The current team leader was then the head team of an ATIP team. No recommendation was therefore made concerning this team in the previous report.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**4**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	1
Doctorants	5
Sous-total personnels non permanents en activité	**8**
Total personnels	**12**

EVALUATION

Overall assessment of the team

Team 6 demonstrates outstanding output and scientific activity, with significant national and international recognition. They have developed recognised knowledge and tools to enhance their research and are highly involved in valorisation and interactions within the socio-economic sphere. The project's perspectives are original and could conduce to improve therapeutic strategies to control resistance and enhance response to chemotherapy. However, to preserve its scientific quality and dynamism, it is required to ensure the attractiveness of young talents in the field of computational biology.

Strengths and possibilities linked to the context

The results of team 6 regarding drug response and tumour initiation open new therapeutic perspectives to improve response to treatment or for potential early interception of breast cancers.
Over the past five years, the team has taken advantage of major technological and computational challenges to fuel its scientific discoveries.
The capacity to characterise new tumour drivers is reinforced and ensured due to a large panel of breast cancer models (PDX, organoîds, mouse models). Thus, they succeeded in mapping epigenomes in tumours with single-cell resolution and developed a wide panel of computational pipelines and tools to mine large epigenomic single-cell datasets.
The outstanding quality of the work led by this team is reflected by the national recognition of Team 6 PI who was awarded the CNRS innovation medal for her work and the findings of her team in 2022. The team also has excellent national and international visibility. So, the team has a world-recognised expertise in single-cell epigenomics and more generally in cancer epigenetics with numerous international collaborations in Italy, South Korea and Canada.
The team is also involved in two large-scale European projects as participant and obtained substantial research funding.
The quality of its scientific output is also remarkable, with numerous publications in prestigious journals (Nature Genetics, Nature Communications, Genome Biology).
Strong potential of valorisation and interaction with socio-economic actors is illustrated by the founding of the startup One Biosciences in July 2020 or the filing of two patents.

Weaknesses and risks linked to the context

The permanent staff is relatively reduced since it is mainly composed of four members: two researchers (1 DR2 and 1 CR) and two BIATSS (1 IR and 1 IE).
At this stage it becomes critical for the team to keep talents and consolidate the know-how, especially for computational expertise. Nevertheless, attracting and retaining know-how and talents in the field of computational biology is a problem due to the competition from private companies in terms of salaries.
Similar difficulties are encountered to attract postdoctoral students and thus maintaining the team's attractiveness and the current growth.

Analysis of the team's trajectory

The project's perspectives are clear and divided in two parts regarding (i) breast tumourigenesis in mice and humans and (ii) non-genetic mechanisms of response and resistance to chemotherapy. The actual perspectives are ambitious but achievable given the team's scientific expertise and quality. Short-, medium- and long-term prospects are logically in line with the continuation of previous work. In particular, they are based on the team's ability to develop animal and organoïd models, as well as on the optimisation of technologies for single-cell epigenomic analysis on frozen tissue patients. While the project is very ambitious, its perspectives are important and this team and her leader have all the skills and abilities to bring it to success.
The long-term objective is of prime importance since it addresses the problem of the epigenetic evolution of triple-negative breast tumours under treatment and its contribution to chemoresistance. The team has established an original schedule in three parts, which could open therapeutic strategies to control resistance and enhance response to chemotherapy. This program is consistent with the first part but could be extended to a larger cohort of patients.

RECOMMENDATIONS TO THE TEAM

The team underlines the difficulties to attract and recruit young talents, more specifically in computational biology. This concern is shared with other teams, in particular with that of Team 3. More generally, and given this common need within the unit, pushing an effort to build a bioinformatics facility by combining resources, possibly external ones, might help this (and other) teams to secure bioinformatics/computational task force in the future.
From the conceptual point of view, although the question of the mechanism of clonal heterogeneity in cancer is considered as 'non-genetic' in some of the models used by the team, a formal demonstration of this point remains a difficult task but could receive more attention by this team in the future.

Team 7: Transcriptome dynamic and heterogeneity in the context of infectious diseases

Name of the supervisor: Mr. Pierre Bost

THEMES OF THE TEAM

The new team intends to study the question of the viral transcriptome heterogeneity by combining scRNA-seq analyses to multiplex imaging techniques. Information gathered may help understanding the origins of this heterogeneity beyond the cell size. The model systems proposed are HSV1, RSV and human Coronavirus.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Not relevant for this evaluation.

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

The team will join the unit for the next contract. So, this item is not yet relevant.

EVALUATION

Overall assessment of the team

The future team leader has an excellent record relating to its PhD and postdoctoral experience. He should reinforce the theme of single-cell approaches in the institute by bringing expertise in multiplex imaging of the cells and related computational approaches. This topic should bring an added value to the unit, while the team of Pierre Bost is building over the time. The committee emphasises that a special effort should be made for a full integration of the team into the unit relative to cancer biology and the opportunity to create bridges, beyond technological developments.

Strengths and possibilities linked to the context

The future team leader has an excellent track record and a good experience in multiplex imaging with good international connections that should help him develop in an excellent scientific environment. His strength is also his gained knowledge in multi-omics and computational biology. The team will benefit from a good starting package from the institute that should support its installation.

Weaknesses and risks linked to the context

The team will need to join a new environment in which it will be necessary to create links with topics distant from virology. Thus, an effort may be made to increase potential scientific interactions with the rest of the unit.

Analysis of the team's trajectory

Not relevant for this evaluation.

RECOMMENDATIONS TO THE TEAM

While the conditions for the team's setting up appear to be excellent, the team leader will need to recruit the right collaborators while developing his interactions with the rest of the unit. Thus, investing a topic that could overlap at least partially with one or several other teams of the institute could support the quality of his integration. Since the team leader will start his first team, he may benefit from mentorship within or in close proximity to the unit.

CONDUCT OF THE INTERVIEWS

Date

Start: 04 October 2023 at 9 a.m.

End: 04 October 2023 at 5:30 p.m.

Interview conducted: on-site or online

INTERVIEW SCHEDULE

8:00 – 8:15 Preliminary meeting of the expert committee (closed hearing)
8:15 – 8:30 Presentation of the HCÉRES evaluation to the unit (SVE3)
8:30 – 9:00 Presentation of the main outcomes of the Unit by the Director (15 mn presentation+ 15 mn questions)
9:00-9:30 Presentation Team Morillon
9:30-10:00 Presentation Team Borde
10:00-10:30 Presentation Team Chen
10:30-10:45 **Break/Short Debriefing**
10:45-11:15 Presentation Team Vallot
11:15-11:30 Presentation Team Toledo (bilan)
11:30-11:45 Presentation Teams Londono (bilan)
11:45-12:00 New team Bost (Trajectory)
12:00-12:30 Presentation of the Unit trajectory by the director (15 mn presentation+ 15 mn questions; all PIs present)
12:30-1 p.m. **Short Committee debriefing**
1 p.m.-2 p.m. **Lunch**

2 p.m.-2:30 p.m. Meeting with technical and administrative staff (in French**)**
2:30 p.m.-3 p.m. Meeting with thesis students and post-docs
3 p.m.-3:30 p.m. Meeting with researchers and professors
3:30 p.m.-4 p.m. Meeting committee and supervising bodies
4 p.m.-4:30 p.m. **Break/Short Debriefing**
4:30 p.m.-4:45 p.m. Meeting with the head of the unit/deputy director
4:45 p.m.-5:30 p.m. **Committee meeting/final debrief: overview of all teams, Unit Trajectory update of the reports etc..**

Teams: every 30′ (12′ presentation +10′ questions + 5′ PI only + 3′ for entry/exit…) including outcomes & trajectory

PARTICULAR POINT TO BE MENTIONED

N/A

GENERAL OBSERVATIONS OF THE SUPERVISORS

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