Research evaluation

EVALUATION REPORT OF THE UNIT

DN - Dynamique du noyau

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Institut Curie
Centre National de la Recherche Scientifique - CNRS
Sorbonne Université - SU
Université PSL – Université Paris Sciences et Lettres

EVALUATION CAMPAIGN 2023-2024
GROUP D

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High Council for evaluation of research and hihter education

In the name of the expert committee :

Claus Sorensen, Chairman 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.

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CHARACTERISATION OF THE UNIT

- Name: Nuclear Dynamics
- Acronym: DN
- Label and number: UMR3664
- Number of teams: 5
- Composition of the executive team: Mrs Angela Taddei, Unit Director, Mrs Nathalie Dostatni, Deputy Director

SCIENTIFIC PANELS OF THE UNIT

Panel 1
SVE3: Living Molecules, Integrative Biology (From Genes and Genomes to Systems), Cell and Development Biology for Animal Science

THEMES OF THE UNIT

Researchers at the Nuclear Dynamics Unit (DN) conduct fundamental research aimed at the mechanisms underlying the stability and the plasticity of genetic and epigenetic information in normal or pathological contexts such as cancer. The unit has an emphasis on nuclear organisation and its dynamics. They explore fundamental processes of chromosome biology such as DNA replication, repair, segregation, and regulation of gene expression during development, cell cycle, across evolution and in response to environmental stress. They use various biological models (Drosophila, Xenopus, mouse, yeast and bombyx Mori), cell lines (human, rodents, and insects) and samples derived from patients. For the evaluation period, the unit was composed of five independent teams including one team co-affiliated with the UMR 168 as a secondary affiliation.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The DN (UMR3664) was created in 2014, as a follow-up of the UMR218 'Nuclear Dynamics and Genome Plasticity', originally created in 2000, by Geneviève Almouzni. Angela Taddei became Deputy Director in 2013, and then director of the Unit in 2015. The Unit was renewed in 2019, with Angela Taddei as Director and Nathalie Dostatni as Deputy Director. DN has three supervising institutions: Institut Curie (associate member of PSL University), CNRS and Sorbonne University (SU). It is located at the Pavillon Pasteur, at the Institut Curie Research Center in Paris.

RESEARCH ENVIRONMENT OF THE UNIT

The DN is located at the Pavillon Pasteur, at the Institut Curie Research Center in Paris, which is a prestigious academic institution. Institut Curie employs 3,700 researchers, physicians, and health professionals across three sites (Paris, Orsay and Saint-Cloud). The Research Center aims to understand the complex mechanisms that make living organism function. The focus is on basic research with support for translational research mainly related to cancer. It brings together thirteen joint research units (86 teams) and provides nineteen state-of-the-art technology platforms. To ensure the implementation of the scientific program, the Research Center direction has two foci: a scientific and an administrative/technical. There are multiple support programs and entities in place which include: Gender Equality, Diversity and Inclusion Plan; Health and safety officers; a dedicated board and the appointment of a scientific integrity officer; Technology transfer office; Data Office to deal with all data aspects. Moreover, Institut Curie is part of numerous national and international consortia and alliances including the EU-Life alliance.

For the Unit per se, it has been composed of three senior and two junior teams. One team has a secondary affiliation with the UMR168, also Institut Curie. The Unit hosts one technological platform which is part of the Cell and Tissue Imaging Core Facility of Institut Curie (PICT-Ibisa). 60 people are at the unit. In collaboration with UMR 3215/U934, the unit has been awarded the Investissement d'avenir Laboratory of Excellence Development, Epigenesis, Epigenetics and lifetime Potential (labex DEEP: http://www.labex-Deep.fr/). The labex DEEP is a collaborative research program that combines genetics, cell biology, physics, bioinformatics and systems biology to reveal mechanisms involved in embryonic development, epigenetic processes and tissue homeostasis and their alterations in pathogenesis. It carries substantial funding and renewed in 2020, it will continue until 2024.

UNIT WORKFORCE: 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	4
Chargés de recherche et assimilés	5
Personnels d'appui à la recherche	17
Sous-total personnels permanents en activité	**29**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	7
Post-doctorants	11
Doctorants	10
Sous-total personnels non permanents en activité	**29**
Total personnels	**58**

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	12
CNRS	0	8	5
AUTRES	0	1	0
SORBONNE UNIVERSITÉ	3	0	0
Total personnels	**3**	**9**	**17**

GLOBAL ASSESSMENT

Profile, resources, and organisation
The DN is a flagship of fundamental research in nuclear organisation and its dynamics, which is a timely and relevant focus. Research at the unit is applying frontline experimental and theoretical approaches such as super-resolution microscopy, single-molecule tracking and mathematical modelling, and it is common to innovate going well beyond state-of-the art. The unit is part of Institut Curie with excellent academic environment and is part of labex 'Development, Epigenesis, Epigenetics and lifetime Potential', DEEP. Moreover, IC also provides high quality administrative and human resources support. The internal organisation is outstanding, and it has been transformed in a structured process based on a manifesto written by the entire unit with the support of external experts.

Attractiveness
The unit is highly attractive as evidenced by the capacity of individual researchers to obtain major international (16 EU funded, including two ERC, grants) and national (8 ANR projects as PI) grants, as well as by the recognition of several scientists receiving national awards (two bronze CNRS medals). The members of the unit are frequently invited to conferences (186 invitations in total; Gordon and EMBO Conferences) and they organise prestigious international meetings (EMBO, Keystone, Cold Spring Harbor…). The unit is attractive to international PhD and postdoctoral students, as well as to international PI for sabbaticals. Recently, a new excellent group leader (part-time, international PI) has joined the Unit. There is a clear desire and capacity within the unit to embrace new fields of research and to develop cutting-edge approaches (live imaging, biophysical and mathematical modelling, etc.). The unit is involved in several programs to ensure strategic funding, such as the labex, and

teams are also frequent coordinators or members of international consortia (within Horizon 2020 programs). Unit PIs and researchers are active in scientific institutions taking part in national and international review bodies, steering committees and scientific societies.

Scientific production
Considering the unit size (55 people), the scientific output is outstanding and all teams have made important scientific discoveries in the fields of nuclear organisation and its dynamics. An impressive number of excellent publications have been produced over the last five years (90 publications, including 80 peer-reviewed papers). Most have been published in well-established and prestigious journals (such as Science, Nat Commun, Nat Struct Mol Biol, EMBO Journal) with DN researchers as principal authors.

Contribution of research activities to society
The units' interactions with society are outstanding. DN has a strong record of innovative public outreach activities, which is remarkable given the modest size of the unit. Among the creative activities were the inclusion of musical engagement based on art as a mediation. DN conducts basic research, teaching and training, which all contribute to society. As a basic research science centre, training is particularly important; during the period, twelve PhD thesis were defended. In terms of translatable activities, the Unit has a partnership with several companies (ABCAM, Abbelight) and have filled four patents and a substantial European Innovation Council (EIC) grant.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Previous recommendations included improved guidance and mentoring of the junior teams to foster their scientific success and integration into the local scientific landscape. It also included concerns by the lack of information about the temporary move during the renovation and the layout infrastructure of the final renovated building. For both of these points, the unit leadership has acted. The junior PI teams are very well under way. Moreover, the relocation to the new building is still an issue that hasn't been accomplished due to process delays. It is apparent that the leaderships are aware of the need for structured planning and communication related to the relocation.

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 DN is a flagship of fundamental research in nuclear organisation and its dynamics. Objectives are of very high standards and ambitious. The unit is highly focused within this area, which creates an integrated research environment where teams have easily inter-relatable visions. Team research lines are somewhat varied which ensures necessary multidisciplinarity in systems and approaches.

Assessment on the unit's resources

Financial and human resources are excellent at the DN. The staff is highly qualified and flourish in a creative and ambitious environment. The research premise situation has remained challenging as the unit rebuilding situation remains a disturbing factor, and the expected construction/renovation period may negatively impact teams. However, teams were able to conduct cutting-edge research in the period of evaluation.

Assessment on the functioning of the unit

The unit is very well structured with visionary and creative leadership from its director. The management team conducted a manifesto process to shape the unit and identify areas of priority for development. This appears to have been highly successful with follow-up initiatives being launched to improve the unit. The unit complies with its institutional requirements in terms of health and safety, scientific procedures or data protection. The researchers and support staff are generally satisfied with the functioning of the unit.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The DN is a leading unit in the field of nuclear organisation and its dynamics. The overall scientific strategy of the unit is defined by the director in coordination with the team leaders as well as external input (see below). In this inspirational environment, each team has developed a unique research line. The unit has a dedicated focus

and a size that in combination result in a highly coherent entity with shared visions among teams. The objectives are ambitious and are experimentally explored in broad manner, in the sense that cover approaches and methodologies ranging from genetics to biochemistry, cell biology and diverse modelling aspects. The fundamental questions are relevant for general knowledge and could have a profound impact on human health with particular relevance for cancer. The unit also benefits from inputs of a scientific advisory board (SAB) composed of internationally renowned scientists who visited the DN in 2023. The SAB provided valuable advice concerning the unit organisation and future directions.

The unit also contributes to research-based student training and knowledge transmission. For training and education, the unit benefits from the presence of one professor, and now three assistant professors of Sorbonne University. DN also organises advanced courses, most notably the highly regarded International Course on Epigenetics. In addition, research valorisation was also a priority as evidenced by the filing of four patents, five prematuration/proof-of-concept fundings, and three partnerships with the industry.

Weaknesses and risks linked to the context

The DN unit is well managed and productive. Two senior team leaders are reaching retirement age, and the timely replacement with high quality team leaders are needed in the upcoming period. Given that the remaining teams within the unit are rather young, recruiting at least one outstanding senior team should be a priority.

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

The DN relies on several sources of funding, the main sources are project-oriented grants (often external and European) and core institutional funding from CNRS, Institut Curie, Inserm and Sorbonne University (including salaries for permanent contracts). The unit is highly attractive, and it has been able to maintain competitiveness in spite of declining funding from Institut Curie, with a 38% reduction between 2019 and 2022. This issue was addressed by increasing the contribution of each team to the common good. Moreover, the unit appears able to exploit its rather small size to create manoeuvrability that allows development of common, cost-efficient procedures such as sharing equipment, spaces and purchasing. A further issue with being a relatively small unit is a potential vulnerability if declining success rates in large funding schemes. Notably, this does not appear as a major issue, with a relatively new group attracting ERC grants.

The physical premises are up for renovation as they are outdated and not well structured for a cohesive unit (DN is spread over several floors). It appears that the unit has been able to develop an organisational setup to mitigate issues with the research premises.

Weaknesses and risks linked to the context

The dependency on external funding is marked, and this means that DN must recruit outstanding PIs with capacity to attract multiple external grants. The expected new calls are extremely important for the unit, and in an ideal scenario at least one of the applicants brings external grants in from start (ERC etc.).

DN is in an old building, which is up for rebuilding. This is expected to impact the unit during this period, but may in the long run offer a better environment for DN.

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 DN has very concrete policies and activities in place regarding human resources management. This is the case for all major relevant aspects including: Gender parity and non-discrimination, internal mobility and career development for its staff, working conditions, health and safety, the prevention of psychosocial risks, information storage, and environmental preservation among most important aspects. This is in part aided by the DN manifesto that outlines key areas and their goals. The unit clearly relies on being part of the greater Curie Institute

that provides necessary mass and competences within these important areas. However, DN has also established local officers (such as referent persons for psycho-social risk) that deal with specialised areas of human resources management. Managers are also clearly engaged, for example, in yearly appraisal interviews. The gender balance is somewhat skewed towards females in the management positions, however, given the small size of the unit each individual carries substantial weight.

Weaknesses and risks linked to the context

The unit is very well functioning with excellent policies in place. The premise renovation/relocation period may be challenging, and managers as well as officers need to have plans in place that support the smooth functioning of the unit. There is a need for extra and timely communication that outlines plans and actions in this regard.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the unit is outstanding as demonstrated by the recruitment of excellent staff members from various nationalities. The DN obtained two ERC grants during the evaluated period and DN teams have been remarkably successful in competitive calls. Senior staff are very well recognised internationally and hold prominent positions in academia. The network of international collaboration is impressive. The unit offers an outstanding research environment thanks to its innovative science, quality of expertise, and local concentration of talents.

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

1/ The unit has an attractive scientific reputation and contributes to the construction of the European research area.

The DN has an outstanding reputation which is demonstrated at multiple levels. This is for example by numerous participations as an organiser, chair or invited speaker at reputed conferences. The number of speaker invitations (186) even exceeds the capacity for the staff. Among conference organisations were established events such as the 'EMBL Chromatin & epigenetics' series of conferences every two years, several EMBO workshops on Histone variants, on Chromatin and evolution and Keystone meeting. The unit hosted five renowned Sabbatical professors, and it has a monthly seminar series with external profile speakers.

The unit is very active in European science and as example coordinated the LifeTime initiative, a preparatory action of EU commission Horizon 2020 with over 60 different groups to define a Strategic Research Agenda document defining a roadmap for interceptive medicine. One of the senior PIs is on the ERC council (2019) and has been chair of the EU-life network (2018–2019). Unit members serve in multiple advisory committees and policy advisory boards (CRG Barcelona, IEO Milan, Human Technopole Milan, Jeantet Foundation Geneva, IMB Mainz) and national committees (INCa, La Ligue contre le cancer, Inserm committee, college Hcéres and Hcéres Committees) often as chair of committees. DN faculty are engaged in several editorial committees including Cell and Current Opinion in Cell Biology. Finally, unit members have received several distinctions and awards such as the ERC awards and the bronze medals of the CNRS, the FSER prise, the Trophy XXI for Diversity in 2017 and Academic Palms in 2021.

2/ The unit is attractive for the quality of its staff hosting policy.
During this period, the unit has been attractive in hosting staff and it has improved conditions. The UMR3664 has endeavoured to improve the working conditions of its members and procedures are thoughtful and appropriate. A dedicated administrative assistant supports contracts and other administrative aspects of newcomers. Written material (including the manifesto) is delivered upon arrival, and a follow-up interview is conducted a month after arrival to ensure smoothness of integration. Two CNRS researcher positions were obtained during the period. Furthermore, a number of renowned international researchers came as sabbatical professors for extended visits at the unit (5, including Stanford and MIT professors) with support from the IC Mayent-Rothschild program and one Chaire Blaise Pascal award. This has been rewarding for the unit as one PI, following his sabbatical, responded to a group leader call and will join DN as 7th team leader.

3/ The unit is attractive because of the recognition gained through its success in competitive calls for projects.
DN scientists have been remarkably successful in competitive calls for projects, raising a total amount of 13.8 M€ based on 46 projects. There were sixteen EU funded projects for 4.9 M€ (incl. 2 ERC), and 29 National (including 8 ANR) Regional and internal projects for 5.4 M€. Finally, the labex DEEP (part of PIA, see below) supported with 3.5 M€. Postdoctoral student researchers' contracts were covered by grants obtained by individual teams, by postdoctoral students themselves (EMBO, Marie Curie fellowships, etc.) or with the funding from labex DEEP. Half of engineers' contracts were covered by grants, the other part by CNRS or Institut Curie. For the twenty PhD students, seven of them had their salaries covered by team grants (including 3 European ITNs), six were funded by the Institut Curie PhD program (labex DEEP contributes), seven PhDs obtained a Sorbonne Université/Université PSL PhD contract.
The labex DEEP covered mainly shared equipment, but was also used for other activities such as some postdoctoral student salaries. Equipment was mainly funded by the annual dotation of the Unit and by grants obtained by the five-team leaders or through collective applications. It is noted that Institut Curie is an associated member of the Université PSL whose Idex (Initiative d'Excellence) was confirmed in 2020, and DN is involved in different national investment programs (PIA: programme d'investissement d'avenir — funding from the French Ministry of Research).

4/ The unit is attractive for the quality of its major equipment and technological skills.
As part of the Institut Curie Research Center, all team members have access to the CurieCoreTech – the Research centre Core Facilities network which comprises nineteen state-of-the-art scientific platforms which include important facilities for the DN such as Bioinformatic, Next Generation Sequencing, Cell and Tissue Imaging, Mass-spectometry, and Single Cell facilities. Notably, the DN houses part of the Cell and Tissues imaging facilities of Institut Curie: PICT@Pasteur, that belongs to the PICT-Ibisa (Plateforme d'Imagerie cellulaire et Tissulaire). This is important as many projects rely on advanced microscopy, and it creates convenient opportunities to develop approaches that go beyond state-of-the-art in nuclear dynamics research. The facility is run by three members of staff and offers access to five advanced systems (2 Palm-Storm, one spinning disc, one confocal and one 4D microscope). Moreover, three team embedded microscopes are also available for shared use for DN users. Appropriate training, instruction, booking, and billing systems are in place to support the efficient running of the facility and equipment in general. Finally, three other microscopes are dedicated to the use of individual teams. Notably, 43% of the surface of the building is dedicated to shared equipment, which helps create a coherent research unit.

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

The DN is highly attractive and well recognised, the more recently recruited team leaders contribute very significantly. However, the anticipated retirement of one recognised team leader may impact the attractiveness of the unit, as she has been a major high-quality force in research at multiple levels. Thus, as a small unit, the DN is highly dependent on recruiting high-calibre team leaders. Such may not be available in France, hence, an early and dedicated international search process would be optimal. Moreover, the renovation of the premises can impact attractiveness at several levels, including the smooth running of the imaging platform as well as complicate general experimental work.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of the DN is outstanding considering its moderate size, both in terms of the number of publications but also in terms of quality. The teams have produced major contributions to scientific discoveries generally in the themes of nuclear structure and its functions. This is illustrated by an impressive number of excellent publications (90 publications, including 80 original research papers), importantly, most have been published in well-established and prestigious journals (such as Science and Nature series) with DN researchers as principal authors.

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

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

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

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

1/ The scientific production of the unit meets quality criteria.
The scientific production is outstanding despite the recent pandemic during the evaluation period. The unit has fostered 90 publications, including 80 original research papers (with 26 being last-authored). Most have been published in well-established and prestigious journals within the theme of nuclear dynamics and its functions with focus on development, DNA repair, epigenetics, and genome organisation. This level of production is important to contribute to research and maintain attractive as a small unit. The use of advanced methods and approaches is noted, which includes the use of super-resolution microscopy, single-molecule tracking and mathematical modelling. This helps shape an attractive and visible unit to the high level of DN.

2/ Scientific production is proportionate to the research potential of the unit and shared out between its personnel.
The DN scientific production is well balanced between the teams and reasonably proportionate to their size. The junior group leaders have contributed markedly to the scientific production with publications in excellent journals. PhD students generally publish well, seven of ten graduating students have first-author publications and others have second author papers and/or first author publications in preparation. Fourteen of eighteen postdoctoral students authored publications. Co-correspondence has been supported, and this supported the independence of two permanent members of the Unit.

3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science.
The DN has incorporated ethical and good practice aspects into its manifesto to ensure that this important area is prioritised and relevant actions are taken when needed. It promotes scientific good practices to prevent fraud, plagiarism and confidential scientific information leaks. The unit complies with the ethical, security and broader mandatory rules (animal experimentation, OGM etc.), in accordance with its governing bodies and the European regulations, which includes specialised training when needed. Regarding integrity, training sessions are organised with attendance of all unit members. Notebooks are required, though not all are electronic. To develop open science, all publications in peer-review journals are accessible on the open French archive HAL (Hyper Articles en Ligne). Researchers routinely post preprints of studies on bioRxiv, a commonly used open access preprint repository for biological sciences.

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

The overall production of the unit is outstanding. It is not clear if the DN has established and communicated guidelines on authorship for support staff working on platforms based on the auto-evaluation document.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The unit interactions with society are outstanding. The core activities are focused on basic research and its main contribution to society lies in high-level training and education. The DN also offers a research framework supporting economic transfers, and four patents were filed in the period. The unit prioritises outreach, and it has innovative activities toward the general public.

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

1/ The unit stands out by the quality of its non-academic interactions.
The DN is clearly dedicated to enhance scientific, technological, social, and cultural value. To reach it goals, the unit has multiple interactions with different non-academic sectors and institutions. The strong outreach activities entail many of these interactions (see 3. below). DN has several interactions towards the innovation and healthcare sectors, which include partnerships such as with ABCAM (in producing antibodies), and with Abbelight (a startup superresolution microscopy company) which led to joint funding from the EIC. The labex DEEP has initiated actions to promote innovation with pre-proof-of-concept funding which in turn enable to obtain Proof of concept funding. This is very important and covers an important, often overlooked, challenge for emerging inventors that seek spin-out support. The unit is also engaged in more clinically oriented interactions, which includes the 'Medico-Scientific Program on Epigenetics' to promote connections between researchers and clinicians from the Hospital group. Moreover, the unit is coordinating the PEPR program 'Cell-ID', to enhance French leadership in cellular medicine with a focus on paediatric brain tumours. The Unit Director is highly active in the LifeTime consortium working to improve healthcare by tracking and understanding human cells during disease.

2/ The unit develops products for the socio-economic world.
The unit has a structured approach with a dedicated project manager promoting tech transfer (funded by the labex DEEP). The manager scout projects, helps advance them and file patents. Four patents were filed in the period, which is outstanding considering the unit size and topical areas. With the strong focus on basic biological science, valorisation can be somewhat challenging.

3/ The unit shares its knowledge with the general public and takes part in debates in society.
The unit is extremely active in sharing knowledge with the public and they conduct innovative public outreach in several ways. The following mentions some of the activities as the list is impressive for a unit of this size. There are activities for high school students (both students at DN, and researchers at schools). They developed a kids' book collection 'Esprits Curieux' to educate children in science and research topics. The unit developed special public events to share science with the public based on art as a mediation, several concerts in the context of the Muse-IC project, exhibitions of research pictures. The unit participated in multiple coordinated public outreach events including the Institut Curie campaign 'Une jonquille contre le cancer' to raise awareness in the general public of the issues to fight cancer, and the 'Fête de la science', a national 2-weekscience fair event. There are extensive interactions with the press (written, tv, web/social media).

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

There are no major weaknesses.

ANALYSIS OF THE UNIT'S TRAJECTORY

The unit is a small but highly coherent and exceptionally well-run unit under the current management. Despite a pandemic and somewhat declining financial core support, the unit has maintained its outstanding performance at all parameters. The manifesto process and follow-up appear to have helped further shape the unit towards a common set of visions and procedures moving forward in a common process. Moreover, the SAB input contributes important strategic input to the management and team leaders. If the management and staff respect the manifesto and going forward processes, this should form a strong fundament at a time when the unit faces some uncertainty due to renovation of premises and the anticipated retirement of two team leaders.

The unit size means that it critically relies on high-quality and successful recruitment especially at the team leader level. This is further accentuated by the declining Institut Curie funding and termination of the labex in 2024. Importantly, the two junior PIs (hired in 2016 and 2017, both ERC grant holders) have been well integrated and are contributing to the excellence of the unit. One investigates the evolutionary dynamics of chromatin, and she was promoted to senior PI earlier in 2023 following an international recommendation. The other investigates the physical principles governing the 3D organisation and dynamics of chromosomes, which brings new active collaborations to the unit as well as direct support from CNRS. One team has also helped foster sabbaticals and indirectly the recruitment of one professor (MIT, USA). He has established a team in the Unit at a part-time commitment as he maintains a part-time MIT affiliation. He was recruited after an international call, he is a high-quality researcher with leading expertise in the physics of chromosomes. Moreover, DN has co-affiliated one PI (Cell Biology and Cancer, UMR144) to the unit in 2023 as secondary affiliation for Institut Curie, as a senior PI studying genetic and epigenetic mechanisms using live microscopy among major approaches. As such he is a good fit and an excellent scientist already collaborating with DN members. In general, the unit should be careful with such part-time and co-affiliation agreements as they can be demanding for all parties, especially during periods of adversity or if challenges arise. Moreover, such agreements tend to set a precedent that may be exploited by other PIs. Fully committed, high-quality team leaders should be the goal for the unit. Indeed, the unit will have the expected opportunity to recruit new group leaders in the upcoming period due to the anticipated retirement of two senior PIs.

An international search and call process is necessary to attract talents of exceptional quality. It would seem that areas such as chromatin biology and computational biology with genomic focus could be a relevant future addition. Finally, it is important for recruiting new teams but also to ensure the efficiency and well-being of the current staff, that the much-needed renovation of the DN premises and/or the relocation of the unit proceeds in a timely and ordered fashion, with minimal impact on ongoing projects.

RECOMMENDATIONS TO THE UNIT

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

The committee acknowledges the commitment of the direction and welcomes the different initiatives that were launched to develop the unit with the manifesto. Clearly, such a document is only one aspect of the process as reporting, evaluation, and corrective actions must be planned and involved in creating solutions that allow a smooth-running unit. Thus, it is important to continue to evaluate the unit relative to the ambitious visions in the manifesto, which include swift actions when issues are encountered.

Recommendations regarding the Evaluation Area 2: Attractiveness

The committee recommends that the DN maintains its outstanding level of attractiveness. It is important that the renovation period is tightly structured and that communication is well planned and involves all staff. For the recruitment of new teams, beyond the excellence of the candidates, the DN is a small unit and must look for strong applicants with 100% commitment at the unit. With declining Institut Curie funding, external grant competitiveness is crucial to maintain an outstanding unit with sufficient funding to continue the strong tradition of outstanding, visionary research.

Recommendations regarding Evaluation Area 3: Scientific Production

The committee encourages the unit to maintain its outstanding level of scientific production.

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

The committee encourages the unit to maintain its outstanding level of activities for society, including innovative outreach actions.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Chromatin Dynamics

Name of the supervisor: Mrs. Geneviève Almouzni

THEMES OF THE TEAM

This team investigates the functional dynamics of chromatin organisation, from fundamental components like histone variants and nucleosomes to higher-order chromosomal structures and nuclear architecture. They explore the assembly, maintenance, and modification of chromatin states throughout the cell cycle, with a particular emphasis on histone variants, their associated chaperones, and modifying enzymes. Their research also delves into how this dynamic network influences cell fate transitions in normal development, differentiation, and disease, including cancer. To study these processes, they employ a diverse range of biological models spanning from individual cells to tissues and whole organisms, employing a combination of biochemistry, imaging, and omics approaches.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Relocation of the building:

This aspect has not yet been resolved and does not depend on the unit's will.

Nurturing close nationally and international collaboration:

The recommendation to foster strong national and international collaborations to advance scientific progress has been acknowledged and embraced.

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	2
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**8**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	3
Post-doctorants	5
Doctorants	2
Sous-total personnels non permanents en activité	**10**
Total personnels	**18**

EVALUATION

Overall assessment of the team

The research performed by this group is outstanding in the field of epigenetics with important contributions on how histone chaperones and variants operate as a dynamic network for chromatin regulation in both normal and pathological contexts. Some of the discoveries led to collaborations with clinical and industrial partners.
The visibility of the team is outstanding as assessed by the publications, organisation of numerous international conferences, fundings and prises.
The contribution to society is outstanding due to the significant involvement in various initiatives that bridge science and society.

Strengths and possibilities linked to the context

The team is composed of eighteen persons including eight permanent members (2 DR CNRS, 1 CR CNRS, 1 CR Inserm, 1 assistant professor, 1 IE Curie, 1 IE CNRS, 1AAR Curie), five postdoctoral students and two PhD students. The team has an outstanding visibility and recognition and is attractive for students and postdoctoral students. Over the evaluated period, fourteen postdoctoral students were hired, seven PhD students and four of them defended their thesis with one publication as the first author for three of them (Nat Commun, Nat Struct Mol Biol); two of them had several other publications (3 articles and 1 review). The team obtained numerous grants including an ERC, ANR grants (1 as coordinator, 2 as partner) and several other highly competitive grants. The outstanding international visibility of the team is attested by numerous invitations to scientific meetings (>350). The team has organised several prestigious international conferences (EMBO, Keystone, Cold Spring Harbor…). The team leader has been honoured with several awards and is a member of the ERC Council and a member of the French Academy of Science. The team actively contributes to research activities that benefit society, including advocating for scientific integrity (workshops on Ethics in Science) and contributing to science policy at the European level. In addition, the PI had chaired a significant European initiative (the European initiative LifeTime) and she actively participates in advisory boards, committees, and administrative boards at both national and international levels, demonstrating her dedication to serving the scientific community.

The team identified a key role for Suv39h1 in marking chromatin (histone H3 modifications) to silence stem/memory genes during CD8+ T cells terminal differentiation. This discovery underlies a key role for histone H3 modifications in the epigenetic control of CD8+ T cell stemness. In addition, the team uncovered a significant role for histone H3 variants that creates a chromatin state permissive to the embryonic development program during Xenopus gastrulation. Using cutting-edge methods, the team characterised specific H3 variants dynamics in chromatin during transcription and replication. Using genome-wide mapping the team showed that the HIRA pathway maintains early replication zones by promoting the targeted replacement of H3.1 with new H3.3, thus contributing to a chromatin-based definition of early replication zones. Finally, the team characterised the role of the histone H3 variant CENP-A in cancer progression and its response to anti-cancer treatments. They translated these discoveries into clinical applications and forged industrial partnerships, including obtaining the Carnot label and filing three patents. Collectively the work led to nine publications as first/last co-authors, often published in leading journals (Genes & Dev, Science, Nat Commun, Nat Struct Mol Biol, Mol Cell). In addition, the team established collaborations within the unit or with international teams that resulted in top-range publications, including PLoS Genet, Nature, Cell Rep, Curr Biol, J Cell Biol.

The team inclusion in the society is outstanding marked by numerous initiatives bridging science and society. These include multiple media interviews, support for Art and Science activities, and efforts to promote women in the sciences.

Weaknesses and risks linked to the context

The team does not show any specific weakness.

Analysis of the team's trajectory

The project aims to delve into the dynamic regulation of chromatin by histone chaperones and variants in both normal and pathological contexts. They intend to explore the interconnectivity of genomic and epigenomic stability, considering histone variants and modifications throughout the cell cycle and in diverse states. Leveraging the cutting-edge tools developed, they will expand their investigations to include embryonic stem cells, 3D cultures, and organoids, to assess the impact of environmental factors.

Furthermore, they will use Xenopus and mouse models to examine the regulation of the histone H3 chaperone/variant network within the nuclei of various cell types at the level of a whole organism. Using 'omics' approaches at the single-cell level in combination with high-resolution imaging technologies, they intend to explore 3D chromatin organisation in relation to histone H3 variants, their chaperones, and modifiers, such as Suv39h1, in conjunction with chromosomal landmarks.
They will investigate how histone H3 variants and their chaperones collaborates with cellular metabolism to govern chromatin stability and plasticity and its impact on the epigenome during development and tumourigenesis.
Ongoing collaboration with medical teams and industrial partners will propel this research forward in the clinics. This project promises to deepen the understanding of the dynamic and adaptable organisation of chromatin.

In summary, this project is exceptionally promising, marked by innovation and feasibility, thanks to the team's expertise, state-of-the-art methods, robust national and international collaborations, and the potential of this dynamic research group.

RECOMMENDATIONS TO THE TEAM

The team should continue their excellent research on the functional dynamics of chromatin organisation. The team is encouraged to maintain their exemplary efforts in bridging science and society and in fostering clinical and industrial partnerships.

Team 2: Epigenetic Plasticity & Embryo Polarity

Name of the supervisor: Mrs. Nathalie Dostatni

THEMES OF THE TEAM

The team uses molecular genetics in Drosophila to interrogate chromatin dynamics and transcription factor gradient during larval developments and, more recently, gene regulatory networks controlling eye versus antennal cell identity. Live embryo imaging and mathematical modelling of quantitative data are used, in collaboration with physicists, to establish and test models of transcriptional dynamics.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (italics) have been addressed as follows:

a) to focus on a single project due to the small size of the group.
This has been addressed with the recruitment of an Assistant Professor and an ITA fully dedicated to the team's project. Nonetheless, the arrival of the Assistant Professor brings a new topic to the team.

b) to extend further the collaboration with theoreticians and biophysicists
This has been addressed with the team publishing several articles together with researchers from ENS Paris and McMaster University, Canada.

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

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

EVALUATION

Overall assessment of the team

The team develops cutting-edge interdisciplinary research projects deciphering transcriptional dynamics during drosophila development. Research projects are strengthened by collaborations with physicists. Visibility and scientific production are excellent and the trajectory involves technological developments in allowing the analysis of the very low number of cells that are present in imaginal discs. Non-academic and outreach activities remain limited.

Strengths and possibilities linked to the context

Visibility/Attractiveness
The team has an excellent visibility and recognition and attracts PhD students and postdoctoral students, with five PhD students during the contract and one postdoctoral student supervised by the two researchers. PhD students and postdoctoral students were authors of six publications. The head of the team has a strong capacity to lead research and acquire funding as a coordinator from national agencies (1 ANR), charity associations (2 ARC foundation grants plus 2 ARC 4th year PhD student funding), as well as Intramuros grants from the Curie Institute (EuReCA and IC-3i PhD programs, 2 labex DEEP) and PSL University. The head of the team was invited to several high-rated international conferences (EMBO, Q-Bio).

Scientific production
Given the size of the team, the heavy charges of teaching of the two permanent researchers, and the responsibilities exercised by the head of the team (Deputy director of the UMR3664 and of the Doctorate school 'Complexité du vivant'), the scientific production is considered excellent. The team published seven articles in leading journals during the period. These articles cover the different projects of the team including histone dynamics and histone chaperones (Genetics, Development), and Bicoid morphogen activity (PLoS Genetics, PLoS Computational Biology, eLife, Biophys J). Among these articles, four were signed as last and corresponding author by the team leader (Genetics, Development, PLoS Genetics, eLife). The team has also been invited to write three reviews/book chapters in Current Topics in Developmental Biology and Methods in Molecular Biology. In addition, the Assistant Professor recruited in 2018 published an article in 2019 In Developmental Cell which she signed as first and co-corresponding author with her former team leader (B.A. Hassan, Institut ICM, Paris). This article describes how transcription factors control alternative cell fates in the drosophila head during development. Her expertise in gene regulatory networks (GRNs) and fly development will foster the project she develops in the team.

Non-academic activities
The non-academic activies are considered very good. The team participated in the MUSE-IC initiative in which six composers were inspired by research discoveries. The piece Aiôn, composed for clarinet, marimba, harp and string quartet by Denis Ramos was inspired by a subject proposed by the team: From the cell to the embryo: these crucial hours that shape us. The six pieces were played at various places and this initiative promoted interactions between scientists, artists and the public.

Weaknesses and risks linked to the context

Visibility/Attractiveness
Although the team attracts PhD students and is successful in obtaining PhD funding, the only postdoctoral student present in the team is a former PhD student of the team leader.

Scientific production
While the team has increased its scientific production as well as its size during the last period, the development of a new research axis in relation to the recruitment of an assistant professor could put this small team at risk.

Non-academic activities
There is no interaction with industry. Interactions with the general public during the period are limited to the MUSE-IC initiative.

Analysis of the team's trajectory

The proposed trajectory builds on previous successful projects. The two main axes that will be pursued are 1) transcription regulation by Bicoid, and 2) role of gene regulatory networks in the control of the patterning of the eye-antennal disc. The team will use the MS2 system to decipher transcriptional regulation at endogenous Bicoid target loci and plans to run genome editing experiments to remove either the activation domain or the repression domain of Bicoid in parallel to expressing Bcd-domain-Gal4 fusion proteins and testing their activity on synthetic promoters. Thanks to the expertise of the team leader, and to the development of new tools to follow transcription factors at regulated loci in live embryos, it is expected that this project will generate novel inputs for the modelling of transcription dynamics. The second project, led by the recently recruited Assistant professor, is based on her expertise on drosophila imaginal discs and will interrogate how GRNs (including synthetic GRNs) affect patterning velocity. It will require the development of protocols for ultra-low cell single-cell RNA-seq. This challenging project is promising and will probably generate new insights on the networks involved in early patterning of the embryo, provided that the technological developments are successful.

RECOMMENDATIONS TO THE TEAM

The team should elaborate a strategy to attract postdoctoral students in order to increase manpower on the different research projects.

Thanks to its visibility, the team should diversify sources of funding.

Interaction with the society should be consolidated.

Team 3: Compartmentalisation & Dynamics of Nuclear Functions

Name of the supervisor: Mrs. Angela Taddei

THEMES OF THE TEAM

The team focuses on understanding how the genome is compartmentalised in yeast and recently in human cell lines through two main axes: the identification of the physical and molecular determinants in space and time of chromatin behaviour and the impact of nuclear organisation on cellular functions such as gene expression and DNA repair.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

a) Aim for some more senior author publications and ensure that PhD students leave with at least one first author publication.
This has been addressed with the team leader publishing five research papers (Cells, eLife, 2*Genome Research, EMBO Journal) and three reviews (Genes, Bioessays, Curr. Opin. Cell Biol.) as the last author.

b) Try to delegate more responsibility to staff scientists.
This was achieved by training new staff in microscopy, yeast genetics and molecular biology techniques by the team's highly experienced research engineer, by co-supervising some PhD students with a senior researcher of the team and by encouraging her to apply for funding as coordinator (PSL University).

c) Strengthen the team by the recruitment of experienced postdoctoral studentsand/or full-time scientists.
This has been addressed with the team succeeding to attract and recruit an assistant professor with a permanent position.

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	0
Post-doctorants	1
Doctorants	4
Sous-total personnels non permanents en activité	**5**
Total personnels	**8**

EVALUATION

Overall assessment of the team

The team performs original research, using cutting-edge interdisciplinary approaches, to study how chromosome dynamics and nuclear organisation regulate transcription and genome integrity. Both the scientific quality of the work and production are excellent to outstanding considering the small size of the team. The team's visibility is outstanding, as attested by its international recognition, the recruitment of PhD students and of an assistant professor, and the successful acquisition of regular funding. Non-academic contribution is also outstanding.

Strengths and possibilities linked to the context

(Visibility/Attractivness)

The team has an outstanding visibility and recognition, attested by the impressive number of invitations to communicate to both the team leader and the permanent researcher (20 invited conferences and 14 invited seminars), and by the participation in scientific evaluation committees (ANR, twice, 2). Three (3) PhD students were hired and (2) PhD defended during the last contract, which is excellent. The team succeeded to attract and recruit one assistant professor with a permanent position, strengthening the capacity to lead research projects with an additional model system (human cells) in a team of this size. The team has an excellent ability to raise resources from national agencies (2 ANR grants as partner, 1 CNRS-MITI 80 Prime, 1 PSL Qlife grant as a coordinator), international agency (ITN grant as work package coordinator) and three doctoral contracts (1 from Sorbonne University, 1 labex DEEP and 1 IC3I PhD program from Institut Curie). Moreover, one Blaise Pascal International Chairs of Excellence grant to host a renowned visiting scientist has been obtained by the team.

(Scientific production)

The team consistently produces excellent research, demonstrating high levels of both productivity and the quality of their work. As a highlight, major advances have been made to study homologous recombination in space and time; this was accomplished by creating a functional Rad51 allele that can be tracked using microscopy and by developing single molecule microscopy. The work is carried out through multidisciplinary approaches, based on yeast genetics, genome-wide chromatin analyses, quantitative microscopy approaches and on the frame of fruitful national and international collaborations, on more theoretical approaches such as computational modelling and biophysical analyses.
The team has an excellent to outstanding scientific production in terms of publications, with eight high-quality publications, five being signed in leading positions (Cells, eLife, 2*Genome Research, EMBO Journal) and three resulting from collaboration within the unit or with national teams. Moreover, seven review articles can be added to this list (including BioEssays, Curr. Opin. Cell Biol., Genes, …). In addition, the associate scientist published one article in 2017 in Mol. Biol. of the Cell which she signed as the first author with her former team leader (ENS, Paris). Publications involve all the team members.

(Non-academic activities)

The non-academic activity of the team is diverse and assessed as outstanding. The team organised Art and Science exhibitions, concerts, and wrote a scientific book for children. The team participates in science outreach programs in schools. The team filed a patent application relating to the development of a tagged Rad51 tool and its uses.

Weaknesses and risks linked to the context

The team leader is heavily involved in collective responsibilities as a director of the unit and as a regular member of evaluation committees. These functions are very positive, but can be compromising for the three PhD students whose mentoring relies solely on the team leader.
During the evaluation period, the associate scientist of the team has successfully launched its own research team. Her departure weakened the team in terms of both skills and management of yeast projects. Although the team has since successfully recruited a permanent assistant professor, given her teaching load and her project with human cells, the team still lacks an additional permanent researcher to strengthen the yeast part of the team.

Analysis of the team's trajectory

The suggested trajectory continues the path paved by previous successful projects, focusing on two main axes: (i) the identification of genome folding determinants and the functional consequences, (ii) the characterisation of homologous recombination in space and time. These two areas will be based on the use of a wide combination of leading-edge approaches (super-resolution microscopy, genetics, Hi-C and physical modelling), and on established collaborations with experts.
Firstly, the team will explore the factors influencing genome dynamics during transitions between quiescence and growth, with a specific focus on (i) the study of the impact of genome organisers and of their loop extrusion activity, (ii) the examination of mechanisms governing nuclear organisation and transcriptional activity, and (3) the investigation of the physical properties of silencing foci. Genotoxic stress will also be used as an environmental modification to determine the physical nature of repair foci. Secondly, based on their recent pioneering development of a new tool to study Rad51 filament dynamics using imaging, the team is in a unique position to characterise homologous recombination in space and time at the scale of the single cell. They will analyse (i) the mechanisms regulating the dynamics of Rad51 filaments in different contexts (replication stress, mitotic and meiotic DSB repair, and telomere maintenance) and (ii) how the dynamics of Rad51 filament guarantees the safety of repair by homologous recombination. Finally, thanks to the expertise of the newly recruited assistant professor in the team, they will explore the possibility of labelling human Rad51 using the same strategy as that developed in yeast, in order to expand their study in human cells.
In total, this project is both thrilling and feasible, given the extensive and longstanding expertise of the team.

RECOMMENDATIONS TO THE TEAM

In view of the fact that the PI is the only (1) HDR to supervise three PhD students, the PI should ensure that they receive appropriate support and publish on time.
The preparation of the HDR by the new lab member – assistant professor – should be considered as soon as possible to contribute to the supervision of PhD students.
The implementation of a new model (human cells) may be considered in line with available human resources and equipment.

Team 4: Evolution of Centromeres & Chromosome Segregation

Name of the supervisor: Mrs. Ines Drinnenberg

THEMES OF THE TEAM

The project of the team focuses on the evolutionary mechanisms that underlie centromere diversification and the plasticity of genome organisation. The main objectives are to characterise a new mode of centromere regulation in non-model organisms with a holocentromeric instead of monocentromeric organisation and to analyse the spatial organisation of holocentric chromosomes.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was considered as promising but it was obviously too early to assess the scientific output of this very recently established junior team.

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	1
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	**4**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	2
Sous-total personnels non permanents en activité	**4**
Total personnels	**8**

EVALUATION

Overall assessment of the team

The research performed by this young group is excellent to outstanding with important contributions in different lines of research. The team is internationally recognised for its work on the organisation of holocentric centromeres. The visibility of the team is outstanding as assessed by the publications, recruitment of PhD students and obtaining regular fundings and prises. Non-academic contribution is excellent.

Strengths and possibilities linked to the context

This is a young team composed of eight persons including 3.5 permanent members (1 DR CNRS, 1 CR CNRS, 1 IE Curie, 0,5 IE CNRS), two postdoctoral students and two PhD students. The team is working on different aspects of centromere organisation in order to explore the evolutionary mechanisms that underlie centromere diversification and the plasticity of genome organisation. The results obtained showed a robust correlation between the distribution of holocentromere formation and chromatin activity in Bombyx mori. These studies also unveiled that holocentromer formation, in a way recessive to chromatin dynamics is evolutionary conserved.

Altogether, these results revealed a new mode of regulation for centromere formation that depends on the chromatin landscape.
By analysing the composition of kinetochore in Lepidopteran, they identified multiple factors conserved in the formation of kinetochore in other eucaryotes. By studying the function of several of these components, they identified a key function of CENP-T in kinetochore assembly that allows microtubule capture. The developed system will allow the characterisation of kinetochore assembly in Lepidopteran.
Using HiC analyses, the team has also revealed in Lepidopteran chromosomes a new compartment (called X domains) in addition to the A and B compartments found in other eukaryotes. This indicates a new type of genome-wide compartment. These X-domains, present over the genome, are flanked by barriers and are spatially separated from A and B compartments.
Finally, using life-cell imaging, spindle morphologyand dynamics of holocentric cell division in B. mori show striking differences compared to other eukaryotes.
Considering the small size and the age of the team, the production is excellent to outstanding with two papers as PI in Current Biology, a primary journal in the field, one paper in preparation in BioRxiv and three papers including one in PLoS Genetics obtained through collaborations. The team has also produced six reviews and comments. Of note, the PhD students have published their work as first or second author (2 Current Biology and PLoS Genetics). Three PhD students have defended their thesis during the period. Two of them have a publication in Current Biology as the first author, the third as the second author in PLoS Genetics and a publication is in preparation.

The team has an outstanding visibility and attractiveness. The PI obtained an ERC Starting Grant in 2017, an EMBO YIP award in 2020, the médaille de bronze du CNRS in 2021, the Prix de de la Fondation Schlumberger in 2022 and was promoted DR CNRS in 2022. The team obtained a number of fundings for PhD (2) and postdoctoral students (2) fellowships (Doctoral programs, FRM). The PI has been invited as a speaker to fifteen international conferences (including 4 Gordon Conferences, ASCB and 3 EMBO conferences) and was selected to give talks in three international conferences. 24 seminars were given at international institutions during the period. The PI has been involved as a co-organiser in seven scientific conferences.
The team inclusion in the society is excellent with several initiatives towards the public (interview in the Journal Le Monde, Art and Science activity in the context of the labex, Mediation with the graphic arts school EPSAA).

Weaknesses and risks linked to the context

The team does not show any weakness.

Analysis of the team's trajectory

The project derives naturally from the results obtained by the team in the previous period. Concerning centromere formation, they wish to analyse the consequences of perturbing chromosome organisation by i) changing gene expression, ii) inserting ectopic DNA and analyse its ability to form centromers, iii) providing CENH3/CENP-A in B. mori. Through a collaboration, they want to reveal by Cryo-EM the structure of Lepidopteran kinetochore. Concerning the X domains, they want to assess the role of acculmulating chromatin loops blocked by genomic barriers flanking each domain. Finally, they want to analyse the spatial organisation of holocentric chromosomes during mitosis; by analysing the evolutionary conserved clustering of centromere along the surface of mitotic chromosomes, they want to understand how is achieved the faithful segregation of siste chromatids. Altogether, this is a very exciting, innovative and achievable project considering the expertise, the cutting-edge methods employed, the strong national and international collaborations and the potential of this young team.

RECOMMENDATIONS TO THE TEAM

The team is encouraged to pursue this very original and promising project and to remain focused on centromere organisation in different holocentromeric species.

Team 5: Genome Functions In Space and Time

Name of the supervisor: Mr Antoine Coulon

THEMES OF THE TEAM

This interdisciplinary team aims at deciphering i) the physical principles governing the 3D organisation and dynamics of chromosomes, and ii) the functional implications of this organisation for gene regulation. It relies on advanced imaging technologies and modelling.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Main recommendations from the previous report (italics) have been addressed as follows:

The team was just created at the end of the previous evaluation (2017), with already acquired secured funding (ERC starting grant and ATIP-Avenir), one permanent member of staff (1CR/Groupe leader), one PhD to come and one postdoctoral student. The main challenges were to establish and organise the team, as well as start publishing in top journals to get visibility in a very competitive field.

The team did an excellent work recruiting additional postdoctoral students (4) and PhDs (1) during the evaluation period, despite the pandemic. A permanent researcher CR was also recruited in 2022, stabilising the team. However, it seems that the two ITAs mentioned in the previous report are gone and not renewed.

The team successfully published in top journals (Science, 2022), which is an impressive tour de force in such a short period.

The team secured additional funding, including two ANRs and one local funding.

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	2
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**3**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	2
Post-doctorants	2
Doctorants	0
Sous-total personnels non permanents en activité	**5**
Total personnels	**8**

EVALUATION

Overall assessment of the team

With their highly original work, the team managed to quickly establish itself as a main actor in a very competitive field. Publishing a Science paper four years after establishing the team was a real tour de force. With this success, the team obtained a major international visibility, illustrated by many invitations to prestigious conferences, such as EMBO course, or Biophysical Society Meeting, and successful recruitment of permanent and non-permanent researchers. The level of secured funding is impressive. The non-academic activity is overall good. The link with the industry and applicability of the methodologies developed in the team to future medical applications should be reinforced.

Strengths and possibilities linked to the context

(Visibility/Attractivness)
The team has quickly gathered international visibility, resulting in several (11) invitations, including prestigious conferences (Biophysical Society Meeting, EMBO conference). Proof of its attractiveness is the frequent presence of Prof. Mirny (MIT), the leading polymer physicist and modeller of genome organisation and dynamics as well as the team's ability to attract students and postdoctoral students in the context of the pandemic. Indeed, six postdoctoral students were hired during the evaluation period, which is really high for such an emerging team. Two PhD students were trained (one defended and one is ongoing), and the PI defended HDR. One permanent researcher got recruited in 2022, a very critical achievement for the growth of the team. There is, however, no mention of supporting staff.
In addition to already secured prestigious funding (ERC starting grant and ATIP-Avenir), the team managed to secure addition funding through two ANR projects.
The PI got awarded by the CNRS bronze medal in 2023, highlighting the high scientific quality of his work.

(Scientific production)
The team has an outstanding scientific production for such a young and just established team. Their main achievement is their work on deciphering the cell nucleus viscosity, which they published in Science as main (first and last) authors (Keiser et al, Science, 2022). This work illustrates the strong interdisciplinarity of the team (biophysics, optics and modelling) and original methodological approach (microscopy, manipulation and labelling). The team also published three scientific articles in collaboration in prestigious journals (Nature Communication, Nature Structural & Molecular Biology, Molecular Cell), illustrating its capability to publish with international teams. This is also impressive dealing with the size and youth of the team. A few papers are obviously in preparation, maybe in collaboration with the local team, which will also be important for the future.

(Context)
The team benefits visibly from the integration into the unit and the scientific context at Curie (including a secondary affiliation to the Physico-chimie unit UMR168).

(Non-academic activities)
The non-academic activities of the team are good, more especially in teaching and scientific animation. However, it could be improved on translational applications (strength in Curie) and industrial collaborations.

Weaknesses and risks linked to the context

(Visibility/Attractiveness)

(Scientific production)
Improve the collaborative papers with the local environment (Inst. Curie). It is not clear if the team relies exclusively on its own instrumentations (microscopes) and/or using the imaging platform, as building and maintaining instruments is time and resource consuming.

(Non-academic activities)
Improve the translational activity and industrial partnership.

Analysis of the team's trajectory

The team masters and applies a surprisingly wide range of experimental techniques reaching from the mechanical manipulation of genomic sites over optical tracking method for FISH labelled DNA or RNA to

polymer modelling, which they plan to apply to a wide range of questions relevant to the function of the genome in space and time: the understanding formation of topologically associating domains (TADs) and their importance for gene regulation by enhancers, the unravelling of the interplay between the spatiotemporal organisation and the expression of the genome, and the probing the physical nature of interphase chromatin in various biological states and processes.

RECOMMENDATIONS TO THE TEAM

This is probably less a recommendation than a question: With their highly original work on the physical manipulation of chromosomes in live cells, the team disposes of a unique strength. Their ability to observe how a chromosome, inside a living cell, reacts to a direct mechanical perturbation offers an extremely valuable complement to the more standard visualisation techniques, which they use and extend as well. Might it not be worth focusing more on their unique 'selling point' to see, if they could not develop the live cell analogue of the extremely instructive mechanical single-molecule experiments of the 1990s?

CONDUCT OF THE INTERVIEWS

Date

Start: September 29, 2023 at 9 a.m.

End: September 29, 2023 at 6 p.m.

Interview conducted: on-site or online

INTERVIEW SCHEDULE

8:15 – 8:30 Closed session Expert Committee (EC) – Scientific Officer (SO)
Assessment of the Unit, Scientific Plenary session
8:30 – 8:45 Presentation of the EC to the staff members by SO
8:45 – 9:30 Presentation of the unit by Angela Taddei (30 + 15 min discussion with the committee)
Attending: EC, SO, all the unit members
Presentation of the teams
9:30 – 9:50 Team 1: Chromatin Dynamics (Geneviève ALMOUZNI)
(15 min presentation +5 min questions)
Attending: Team members, EC, SO, director of Unit
9:50-10:10 Team 2: Epigenetic Plasticity & Embryo Polarity (Nathalie DOSTATNI)
(15 min presentation +5 min questions)
Attending: Team members, EC, SO, director of Unit
10:10-10:30 Team 3: Compartmentalization & Dynamics of Nuclear Functions (Angela TADDEI)
(15 min presentation +5 min questions)
Attending: Team members, EC, SO, director of Unit
Break 15 min
10:45-11:05 Team 4: Evolution of Centromeres & Chromosome Segregation (Ines DRINNENBERG)
(15 min presentation +5 min questions)
Attending: Team members, EC, SO, director of Unit
11:05 – 11:25 Team 5: Genome Functions In Space and Time (Antoine COULON)
(15 min presentation +5 min questions)
Attending: Team members, EC, SO, director of Unit
11:25-11h45 Cellular and Tissue Imaging Platform – IBiSA (Patricia Le BACCON)
(15 min presentation +5 min questions)
Attending: Team members, EC, SO, director of Unit
11:45–12:30 Meeting of the Committee (closed hearing)
12:30–13:30 Lunch Break
1:30 p.m.–14:15 Technical and administrative personnel
Attending: Technicians, Engineers, Administrative staff, EC
2:15 p.m.–14:45 Thesis students and post-docs
Attending: PhD students and postdocs, EC
2:45 p.m.–15:15 Researchers and professors
Attending: Researchers and professors except group leaders, EC
15:15-15h30 Coffee break
3:30 p.m. – 4 p.m. Meeting of the Committee (closed hearing)
4 p.m. – 4:30 p.m. Meeting with the representatives of CNRS and University
Attending: expert committee, representatives of Institutions, SO
4:30 p.m.–17:00 Meeting of the Committee with the head of the unit
Attending: Unit Direction, expert committee, SO
5 p.m. – 6 p.m. Meeting of the Committee (closed hearing)

PARTICULAR POINT TO BE MENTIONED

None

GENERAL OBSERVATIONS OF THE SUPERVISORS

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Objet

Comments to HCERES Evaluation report of the Unit
Nuclear Dynamics / DN
DER- PUR250024478 - EV 0753172R
Evaluation campaign 2023-2024 / Group D

HCERES
For the attention of HCERES President,
Mr Stéphane Le Bouler
and the HCERES Expert Committee

Paris, 21st February 2024

Dear All,

We are very grateful for this careful and in-depth evaluation of our Unit and we thank the whole HCERES expert committee for their very positive appraisal and useful recommendations.

Regarding the question of the renovation of the premises currently occupied by DN, we would like to clarify that the Unit will not come back to the renovated Pasteur building. According to the current plan, the Unit will have to vacate the building during the renovation and be temporarily relocated to two different locations. The teams will be reunited in another building, the Trouillet one, several years later, in spaces that were renovated in the last few years or that will be renovated before the final move. The uncertainty of the organization for this period will certainly be a challenge for the cohesion and development of the Unit. Discussions with Institut Curie are still underway to minimize the consequences of these successive relocations.

Yours Sincerely,

Pr Alain PUISIEUX
Directeur du Centre de Recherche de l'Institut Curie

Dr. Angela TADDEI
Directrice de l'UMR 3664

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