

EVALUATION REPORT ON THE UNIT

iGReD - Génétique reproduction et
développement & Chelter - Role of intra-Clonal
HEterogeneity and Leukaemic environment in
ThErapy Resistance of chronic leukaemias

UNDER THE SUPERVISION OF INSTITUTIONS AND RESEARCH BODIES:

UCA — Université Clermont Auvergne, CNRS —
Centre national de la recherche scientifique,
Inserm — Institut national de la santé et de la
recherche médicale

EVALUATION CAMPAIGN 2025–2026
GROUP A



On behalf of the committee of experts:

Yacine Graba, Chairperson of the committee

For Hcéres:

Coralie Chevallier, President

In accordance with articles R. 114-15 and R. 114-10 8° of the Research Code, evaluation reports drawn up by the committees of experts are signed by the chairpersons of these committees and countersigned by the president of Hcéres.

To facilitate the reading of the document, the terms used in this report to designate functions, occupations or responsibilities (expert, researcher, teacher researcher, professor, lecturer, engineer, technician, director, doctoral student, etc.) are generic and gender neutral.

This report is the outcome of an evaluation by a committee of experts, the composition of which is specified below. The assessments it contains are an expression of the independent and collegial deliberation of the committee. The data within it are the certified accurate data extracted from the application forms submitted by the supervising bodies on behalf of the unit.

This version of the report is public under Article R. 114-23 of the Research Code. Sections of the report considered confidential, and responses to points of attention from supervisors are not included in it.

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Mrs Vanessa Prevot, Vice-présidente Recherche UCA — Université Clermont Auvergne

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Mr Eric Allemand, Inserm (CSS1) Chargé de Recherche (observer)

Mr Frédéric Jaisser, Inserm (CSS3) Directeur de Recherche (observer)

UNIT CHARACTERISATION

- Name: Institut Génétique Reproduction et Développement — Role of intra-Clonal HETerogeneity and Leukaemic environment in ThErapy Resistance of chronic leukaemias
- Acronym: IGRéD – ChelTer
- Label and number: UMR CNRS 6293, Inserm 1103, UCA – EA 7453
- Number of teams: 17
- Composition of the executive team: Director (current contract iGRéD): Mr. Krzysztof Jagla; Deputy Director (current contract iGRéD): Ms Anne Fogli; Director (current contract ChelTer): Mr Marc Berger; Deputy Director (current contract ChelTer): Mr Olivier Tournilhac; Director (next contract): Mr. Lucas Waltzer; Deputy Director (next contract): Mr. Silvére Baron

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement

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

THEMES OF THE UNIT

The Institute of Genetics, reproduction and development (iGRéD) is composed of 15 research teams aiming at investigating genetic and epigenetic regulation of developmental and pathological processes, taking advantage of a broad panel of model systems (mouse, chicken, Drosophila, plants, human and primary cell lines). This translates into three research axes: Integrative developmental biology, Genetic and epigenetic control and Reproduction physiopathology and cancer. The unit provides a rich technological environment with a full set of technological platforms essential for the team activities (animal and plant facilities, imaging, single cell/cell culture, bioinformatics and histo-pathology).

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

iGRéD was founded in 2008 by the fusion of a CNRS (Centre National de la Recherche Scientifique) and an Inserm (Institut National de la Santé et de la Recherche Médicale) research unit. It is affiliated to the CNRS, Inserm and Université Clermont Auvergne (UCA). Initially located on two different sites, the unit benefited in 2017 from a new building (5000 m²) located in the school of medicine university campus, allowing housing all teams together. Currently the unit hosts approximately 200 people.

UNIT RESEARCH ENVIRONMENT

The iGRéD unit with research interests spanning fundamental to clinical biology, has a broad network of local interactions. It appears to largely contribute to the structuration of science at the UCA, with iGRéD members vice heading the UCA and heading the Life Sciences, Environment and Health Institute (iSVSAE). Besides, iGRéD members are also part of several committees linked to the administration of the label Idex/I-site (I-site CAP20-25) awarded to the UCA through the Plan Investissement Avenir (PIA) or to the elaboration of the scientific policy of the UCA. Its translationally and clinically oriented research also fosters interactions with the medical school and the hospital and links several teams to the Cancéropôle Lyon-Rhône-Alpes-Auvergne (Clara).

UNIT WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	15
Maitres de conférences et assimilés	26
Directeurs de recherche et assimilés	13
Chargés de recherche et assimilés	13
Personnels d'appui à la recherche	39
Sous-total personnels permanents en activité	106

Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels non permanents d'appui à la recherche	2
Post-doctorants	13
Doctorants	40
Sous-total personnels non permanents en activité	56
Total personnels	162

BREAKDOWN OF THE UNIT'S PERMANENT STAFF BY EMPLOYER: IN PHYSICAL PEOPLE AS OF 31/12/2024. NON-SUPERVISING EMPLOYERS ARE GROUPED ON THE HEADING 'OTHERS'.

Nom de l'employeur	EC	C	PAR
Autres	0	1	0
CNRS	1	18	12
Inserm	0	7	9
UCA	40	0	18
Total personnels	41	26	39

GLOBAL ASSESSMENT

The Institute of Genetics, Reproduction and Development (iGReD) is one of the largest Life science units in the Clermont Ferrand area, hosting on average 200 people with an annual operating budget averaging 6.4M€. Founded in 2008, the unit occupies since 2017 a modern well-equipped building located in the School of medicine university campus. The unit benefits from a triple affiliation, CNRS, Inserm and UCA, and host 15 teams distributed in three research axes (Genetic and epigenetic control, Integrative developmental biology, Reproduction and Physiopathology and cancer), bridging plant/animal biology and fundamental/translational/clinical research.

The iGReD scientific objectives, organization and resources are excellent. The unit has clear scientific, technological, teaching and valorization objectives. Resources are commensurate to the objectives set, with a critical mass of researcher, teacher and technician/engineer, a very positive budget dynamic with a regular increase from 3,6 M€ to 7,5 M€ (>90% of which is grant money), and cutting-edge in house technological platforms, a strong asset for iGReD. Local facilities complement in house platforms collectively offering an attractive technological environment.

The institute has a good practice of decision taking, a well-balanced policy of budget use and allocation allowing for strategic actions. Scientific cohesion is good, and information flow is favoured by a communication team and plethora of scientific and social initiatives, resulting in a very positive atmosphere and general high level of satisfaction.

The principal threats to iGReD concern the future of the UCA hosted mouse animal facility, which uncertainties regarding its future (renovation/replacement) generate legitimate and important fears in the mouse community. This is a sensitive issue that requires special attention.

The scientific achievements of iGReD are overall excellent. The unit published overall 337 articles, of which 65% in leading positions, with regular publication in highly regarded journals (Nature communications, The Plant Cell, PLoS Biology, Science Advances, eLife, PLoS Genetics, PLoS Biology), and a widespread practice of open science publication. Scientific impact appears well balanced between the different thematic axes.

The visibility of iGReD appears excellent at the local (link with the hospital, university and local scientific boards) and national (contribution to public and charities scientific committees, learning societies and scientific networks) and success to national supports (27 ANRs, 3 ANR JCJC, 1CPJ, one label FRM équipe and one Ligue Contre le Cancer, AFM strategic network). This visibility translates in an excellent attractiveness with the hosting

of 60 PhD students, the recruiting of seven permanent researchers, including two new group leaders, and four hospital-affiliated scientists.

International visibility is more limited but has notably increased during the current contract, with an invitation to international renowned international meetings (Keystone symposia, Gordon Research conferences, EMBO meetings) and success to European grants (1 ERC starting, 1 ERC consolidator, 2 MSCA training networks. The high degree of international collaborations reached (30% of iGReD publications are co-signed with international collaborators) provides solid foundations to raise further international visibility.

The inclusion of the unit research to society is excellent. iGReD has strong interactions with hospital departments, benefits from multiple national (Messidor, PIA3-dignostic) and local (reference centre for rare neuromuscular disorders) translational grants, and contributes to multiple clinical trials. It also has interaction with economic partners through the R&D platform Evalsem 'business unit' in the field of human infertility, with the Biosyntex company to develop membrane based diagnostic tests, with the DSV (Deutsche Saatgut Veredelung) and Limagrain seed companies, and with the Greentech company for clinical biomarker development. Notably, the unit has strong ties with UCA and largely contributes to teaching and training, therefore actively preparing the next generation of scientists and develops actions for promoting science towards the general public.

Overall, the iGReD stands as a very complete, efficient and coherent research entity with strong ties with the university and hospital. Strategic decisions for the next contract have been taken (team and directorship changes). They are well thought will ensure a continued positive trajectory for iGReD, and, through the recruitment of the current Chelter unit/team, will reinforce the translational/clinical pole of iGReD. The committee wishes to congratulate the current direction in setting up a coherent and efficient research environment.

DETAILS OF THE EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

A few recommendations were formulated by the previous evaluation committee. Actions to take them into account have been undertaken for most/all of them.

1- Improve European funding

Significant efforts were deployed to apply to European funding. These resulted in the awarding of two ERC grants (1 starting and 1 consolidator), the coordination of two MSCA training networks and the participation in a third one. This constitutes a significant increase in European funding when compared to the previous evaluated contract.

2- Continue reinforcing the bioinformatic platform

The iGReD bioinformatic platform (BIM) provides support for both genomics and image analysis. Its activity relies on two engineers with permanent positions. The BIM platform was reinforced by the recruitment on a fixed-term contract of a third engineer, endowed with training missions. This position needs to be stabilized as training team members is essential to satisfy needs.

3- Recruit foreign group leaders and postdoctoral fellows to bring new ideas.

The iGReD launched two international calls for group leader positions during the current contract. These resulted in the recruitment of two new PIs, with high standard international postdoctoral experience, yet not foreign. The number of postdoctoral fellows has significantly increased when compared to the previously evaluated period (from 6 to 11), with roughly half of them being foreigners.

4- Increase publications in generalist journals

Publications (24) in generalist journals (Nature Comm, eLife, Science Advances, PNAS, PLoS Biology) during this contract seems commensurate to the size and research focus of the unit. Generalist publications are complemented by an equal number of publications in the best specialized journals (Genome Biology, Genome research, Development, Plant Cell, Molecular Cell, JCI...).

5- Sharing of the technical support to the teams

The iGReD seems to make every possible effort to recruit technical staff within a difficult general context. This resulted in the recruitment of two permanent technicians by the university, and one by the CNRS. Given the general sparsity of technical staff, the policy to priorities first platforms that provide services, and second-team support (in many instances part-time) is a good strategy.

6- Improve scientific life by increasing seminars and conferences given by invited foreign scientist.

This recommendation resulted in the launching after the Covid lockdown of the Friday Lunch Seminar Series, with the allocation of a dedicated budget. This allowed to invite external speakers, some coming from abroad, with a full-day agenda visit including discussions with students and postdoctoral fellows.

B – EVALUATION AREAS

EVALUATION AREA 1: THE UNIT'S SCIENTIFIC OBJECTIVES, ORGANIZATION AND RESOURCES

Assessment of the unit's scientific objectives, organization and resources

The unit's scientific objectives, organization and resources are assessed as excellent. The unit has set clear objectives, anchored in fundamental research at the interface with health and disease, with appropriate technological environments, notably a complete set of high standard technological platforms, a strong and positive dynamics of its financial resource, and a critical mass allowing for a wide diversity of scientific topics. Actions to maintain scientific cohesion are in place and decision taking obeys collegial rules, which conveys a positive spirit within the unit. A few aspects of the internal organization may be improved. The committee wishes to congratulate the current direction in setting up a coherent and efficient research environment.

Context-related strengths and opportunities for the four references above

Objectives

The unit has set clear objectives, anchored in fundamental research at the interface between health and disease.

The unit defined a set of five specific objectives, namely developing cutting-edge fundamental research at the interface of health and disease; developing new technologies and innovative tools; foster collaborations; establish clinical and private sector links; and structuring local research and teaching. Although broad and ambitious, the current institutional situation of iGReD, with joint supervision of CNRS, Inserm and UCA, the historical positioning of the institute and its members in key local decision-taking bodies, and 'services' dedicated to continuous education and international relationship, make these objectives fully realistic.

The institute is scientifically organized around three research axes: genetic and epigenetic control; reproduction physiopathology and cancer; and integrative developmental biology. This organization provides a good visibility to the diversity of iGReD research, without introducing cleavages that are sometimes associated with stronger structuration like departments.

Ressources

The institute has set up seven technological platforms, including plant and fly facilities, a histo-pathology core facility, an imaging platform, an R&D spermiology facility, a single cell and cell culture platform (including single cell omics) and a bioinformatics platform. Platforms are well driven, co-headed by a permanent researcher and an engineer, and generally seem well equipped, witnessing a consequent technological investment and allocation of human resources. They provide wide technical support suiting the different research demands at iGReD. Teams also benefit from shared technical services, covering glassware, media, waste management.

A number of local facilities, not directly hosted at iGReD, yet often involving iGReD members in their administration, complement the iGReD platforms. This notably includes two mice/rats animal facilities, platforms dedicated to metabolism exploration, genotyping and sequencing, proteomics, organoid, and bioinformatics. Collectively platforms and services available at iGReD offers an excellent and attractive technological environment favouring wide research directions.

The iGReD benefits from a critical mass of 200 researchers hosted in a recently renovated building of 5000 m² located in the school of medicine university campus, which accommodate all fifteen iGReD research teams. The nucleation of all teams within the same building has been a positive factor in the recent life of the institute. The balance of permanent/non-permanent staff appears well balanced.

The iGReD has benefited from an exceptionally positive dynamic in its budget during the current contract, with an increase from 3,6 to 7,5 M€ (110% increase). This is remarkable, especially within a highly-constraint period and with a very limited increase of institutional-recurrent support (0,59 M€ to 0,65 M€). It results from a substantial increase in the number (62 in 2019 to 99 in 2024) and size of grants obtained, and from a wide targeting of funding bodies: PIA, international, national, regional, charities and to a lesser extent industrial origin.

Organization

The institute has in general (see also weak points) a good practice of decision taking and communication, including a regular presentation of the iGReD director prior to seminars (10 min iGReD). Decisions are taken collegially, with a board of PIs meeting held on a monthly basis. Important and long-term strategic decisions are taken in consultation with a Scientific Advisory Board composed in the vast majority of foreign scientists. A laboratory council, including representatives of all research personnel, is held 3 times a year.

The iGReD has a clear and well-balanced policy of budget distribution. It guarantees minimal support for teams by redistributing 50% of institutional recurring support. The budget of the unit is complemented by a collection of 15% of research grant money, which together serves for regular general expenditure or strategic actions (equipment investments, support to specific teams).

Scientific cohesion seems good, and information flows are favoured by a communication team, an annual unit retreat organized outside the unit once every two years, weekly seminars including, internal and external seminars, and a set of thematic clubs.

The unit complies with health and safety measures, ethics and scientific integrity, and sustainable development plans enforced by institutional supervising bodies. This is relayed at the unit level by the iGReD health and safety service, which guarantees that all legal obligation (permission to used radioelements, animal handling, use of dangerous chemicals) is applied. Raising awareness to psychosocial risks is ensured by a mandatory course organized by iGReD for all newcomers. Waste disposal complies with environmentally responsible principles. Data management and protection are well handled, conforming to the Fair principle, and relies on solutions fitted to omics and image data sets, based on unit local (Omero, Mésocentre Clermont Auvergne) support.

Context-related weaknesses and risks for the four references above

Resources

The principal threat at iGReD is the future of the mice animal facility. Many teams at iGReD develop projects requiring a mouse facility, which at present is managed by the UCA and is hosted in a nearby building on the medical school campus. The project of closing this facility within the context of creating a more modern facility, or alternately of substantially renovating it to comply with the current legislation, has raised important concerns, both with regards to the exact content (housing, housing plus experimentation...) of the project, and with the prospective increase of costs. This is a poignant issue that is generating important worries for the scientific future of a significant number of teams at iGReD.

A strength of the iGReD lies in its high standard well-equipped technological platforms, which sustainability key to the dynamism of iGReD, will require maintaining engineers and technicians with relevant expertise, maintaining the correct budget for their functioning, and grasping equipment calls for acquiring and updating equipment. This certainly will be challenging in the context of a limited recurrent budget (0.6M€, considering support from its three institutional supervising bodies, CNRS, Inserm and UCA) and the general shortage of human resources allocation.

Organization

Although the process of decision taking is clearly defined, decisions relating to technological platforms could give more room to input from technicians/engineers. The committee noticed that such consultations happened on some occasions, yet it seems that they could be more frequent.

The lack of diffusion of written reports from team leader meetings, where decisions are taken, is to the iGReD staff a source of unequal access to information, depending on whether or not group leaders are proactive in spreading information, and generates frustrations.

The shortage of technicians/engineer resources, due in particular to retirement departures, results in multiple affectations, often spread between technological platforms and teams. While this appears difficult to avoid, it is sometimes a source of pressure that impairs an otherwise very satisfactory well-being at iGReD.

There is still a clear gender imbalance at the group leader level, with only five teams (out of 15) headed by women.

EVALUATION AREA 2: THE UNIT'S SCIENTIFIC RESULTS, IMPACT AND ATTRACTIVENESS

Assessment of the unit's scientific results, impact and attractiveness

Scientific production at iGReD was overall assessed as excellent, with a rather homogenous quality among research axes and teams, and a quantitative and qualitative positive dynamic during the current contract. iGReD benefits from an excellent local and national visibility, and has been successful in attracting permanent researchers including two new group leaders. These achievements together with an already large network of international collaboration will foster an increase in international visibility, which at present remains limited.

Context-related strengths and opportunities for the four references above

Scientific achievements

The unit published 337 articles, of which 65% in leading positions. Striking scientific achievements include:

—In the 'Genetic and epigenetic control' axis: the role of histones variants H2AW and H2AB variants, the identification of new functional partners of the PRC1 complex, the functional characterization of new components of the nucleoskeleton and the control of meiotic stabilization of allopolyploidy in plants.

—In the 'Integrative developmental biology' axis: the importance of early cell-cell communication between tendon and muscle precursors, the role of stochasticity in the molecular control of epiblast lineage specification, study of epiblast, the identification of neuromuscular progenitors within the anterior primitive streak epiblast, the cellular and molecular characterization of basement membrane cell exit.

—In the 'Reproduction and Physiopathology and cancer' axis: the role of undifferentiated germ cell homeostasis and its therapeutic potential for fertility disorders, a *Drosophila* model (accessory gland) to study the basal extrusion relevant to prostate cancer, the role of macrophages in the sexual dimorphism of adrenocortical carcinomas, the molecular control of sterile inflammation in late pregnancies.

The high quality of the research is attested by regular publication in highly regarded journals (Nature communications, The plant Cell, PLoS Biology, Science advances, eLife, PLoS Genetics, PLoS Biology) success to national (27 ANRs, 3 ANR JCJC) and European competitive research grants (1 ERC-Stg, 1 ERC-Cog, 2 MSCA training network, one World Wide Cancer Research) and to competitive charity grants (1 label FRM equipe and one Ligue Contre le Cancer, AFM strategic network).

The scientific impact appears overall excellent and well balanced between the different thematic axes, with in all cases publications in highly regarded journals.

iGReD teams have a widespread practice of open science publication.

Visibility and attractiveness

The visibility of iGReD is globally very good to excellent.

At the local level, iGReD has a strong link with the hospital (15 hosted hospital staff, 5 translational projects with the hospital, multiple clinical trials) as attested by the hosting of fifteen clinicians, five translational projects with the hospital, multiple clinical trials and a third of the publications co-signed with hospital departments.

iGReD members also have a strong link with the UCA, with half of its permanent staff with university positions. They are strongly involved in the functioning of the Faculty of Biology and Faculty of Medicine (UCA) with being part of the scientific board of I-SITE CAP 2025 program and UCA board of directors, Direction of the Life Science department, UCA vice presidency, scientific council of the doctoral school (Life Science, Health, Agronomy and Environment) and graduate and undergraduate programs. iGReD members bear teaching responsibilities (master of bioinformatics, master of genetics and physiology, international graduate track) and train numerous master (25–30/year) and PhD students (20–25/year).

At the national level, iGReD members extensively participate to public scientific committees (CoNRS, CSS Inserm and InraeE, CNU, Hcéres), charities' scientific committees (FRM, ARC, AFM), learning societies (President of the SFG and SFBD), they coordinate or are part of scientific networks (GDRs, Groupement de Recherche), and one newly recruited team obtained and Inserm junior professor chair (CPJ).

International visibility is more limited, but for some of the teams is attested by invitation to international meetings (including Keystone symposia, Gordon Research conferences, EMBO meetings), by the organization of international meetings, by teaching abroad, and by success to international grant applications (1 ERC starting and 1 ERC consolidator, and MSCA training networks). Most of the teams have international collaborations, resulting in 30% of iGReD publications co-authored with international collaborators.

The attractiveness ranks from very good to excellent. The unit hosted 60 PhD students, for 48 HDRs, with a very efficient mentoring, the vast majority (45) finishing with at least one first author paper. iGReD recruited seven permanent researchers, including two new group leaders, and four hospital-affiliated scientists.

Context-related weaknesses and risks for the four references above

Scientific achievements

Although multiple internal collaborations were apparent during the visit, there has been during the current contract limited internal collaborations (only 14 articles are co-authored by multiple iGReD teams).

Among the papers co-signed by iGReD teams, most of the interaction relies on teams from axis 1 'Genetic and epigenetic control' and axis 3 'Integrative developmental biology'. Teams from axis 2 'Reproduction, physiopathology and cancer' are only involved in one co-signed publication. While this reflects proximity in scientific topics for axis 1 and 3, there is room for more interaction with axis 2.

Visibility and attractivity

A large number of iGReD teams have a connection to medical research. This, however, only partially translates into support by charity grants.

The participation of iGReD members to European or international scientific committees appears limited.

Attractiveness for postdocs remains limited.

EVALUATION AREA 3: INCLUSION OF RESEARCH ACTIVITIES IN SOCIETY

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

The inclusion of iGReD research activities in society is assessed as excellent. The unit has strong connections with the hospital, contracted multiple links with economic partners including internationally, and largely contributed to the functioning and teaching at the UCA. The unit is also active in promoting science towards the public, including social, cultural and educational events, and interactions with patient associations. The valorization through patenting appears limited both in numbers and teams involved.

Context-related strengths and opportunities for the three references above

The unit's interaction with the clinic is excellent, as attested by a large set of interaction with hospital departments, which largely contribute to iGReD scientific production (30% of the publications), by multiple national (Messidor, PIA3-diagnostic) and local (Reference center for rare neuromuscular disorders) translational grants, and by participation in multiple clinical trials.

The interaction with economic partners is excellent. It notably involves the R&D platform Evalsem offering services focused on sperm quality and fertility. The platform labelled as a UCA 'Business unit' has multiple collaborations with national and international (Austria, USA) companies specialized in human infertility. Additional economic connections include participation in the scientific board for the Biosyntex company to develop membrane based diagnostic tests, collaborations with the DSV (Deutsche Saatgut Veredelung) and

Limagrain seed companies, and collaboration with the Greentech company for clinical biomarker development.

The unit has strong ties with the UCA and largely contributes to teaching and training, therefore actively preparing the next generation of scientists.

Research from two teams also resulted into four filed patents, focusing on cold plasma treatment in collaboration with the Greentech company, on resistance to BCL2 inhibition and on RT genomics in collaboration with the Broad Institute, and on controlled expression of a transgene in human T cells or NK cells for use in cellular immunotherapy.

The unit is active in promoting science towards the general public, with organization/participation to multiple social events (Fêtes de la science, Nuées ardentes, Journées portes ouvertes, Expo science, Declics), hosting college students, interactions with patient associations linked to rare diseases, AFM-telethon, Ligue contre le Cancer and ARDS, and a few media events in newspapers, radio and local TV programs.

Context-related weaknesses and risks for the three references above

Given the potential of plant biology and biomedical research, valorization through patenting appears somewhat limited, and only involves two teams.

ANALYSIS OF THE UNIT'S TRAJECTORY

During the current period of evaluation, the unit has had a positive trajectory with qualitative and quantitative increase of the scientific production, strong increase in financial resources, and efficacy in recruiting young scientists including two new group leaders. The iGReD has also reached an excellent level of internal organization, favouring an overall enthusiastic spirit and lively atmosphere and benefits from cutting-edge technological platforms that is a strong asset for attractiveness.

The next contract will largely be in continuity with the current ones.

The iGReD will maintain the same organizational chart and decision-making process, and keep current budget use and allocation, some of it mutualized, which allows for scientific strategic actions. A few positive initiatives will complement iGReD internal structuration, including mentoring actions to promote staff careers (researcher and technicians/engineers) and a stronger/more organized implication in sustainable research.

Scientific activity will remain anchored in fundamental research at the interface with health and disease, with the same three structuring axes: genetic and epigenetic control; reproduction physiopathology and cancer; and integrative developmental biology. The existing diversity in animal models (from human to plants) and in experimental approaches will remain. Three scientific priorities are identified:

(i) consolidate fundamental research. A critical point here is to maintain the technological platforms cutting-edge. Achieving this will require continuous funding and increase in human resources, targeting funding bodies (CNRS, Inserm, UCA), local (I-SITE) and CPER/FEDER initiatives, and whenever possible integrate national networks to offer additional possibilities. Maintaining the triple affiliations, CNRS, Inserm and UCA, which appears justified regarding the research topics and strong teaching and training contribution, will be key.

In addition, interactions with the local UCA Mesocentre for data storage and biocomputing power, for the ever-increasing needs of bioinformatics and AI for microscopy and omics data is also an asset.

(ii) consolidate the clinical link. The planned recruitment of the LYM-City team at the start of the next contract is one of the most visible actions. Further implication in the Clermont Ferrand clinical investigation center and the GCCA consortium (Groupe cancer Clermont Auvergne) will also contribute to achieving this goal.

(iii) consolidate the agro-industry link. The means here are not clear, and may require further elaboration.

Transversal to these priorities are actions to increase international visibility. iGReD can rely on existing international collaborations and its current European anchoring, with three MSCA training networks and the ARTEMIS consortium (UCA and 7 other European universities).

Several strategic decisions were taken in preparing the next contract.

A new direction with an already very involved director and deputy director endorsed by the SAB and approved by iGReD members is in place for the next contract. The new direction team, with a clear vision for the future, and a good knowledge of Inserm, CNRS and UCA institutions, appears suited for the next iGReD challenges.

An evolving iGReD team panel is proposed for the next contract. Considering the retirement or future retirement of two senior group leaders, calls for new teams were evaluated by the SAB and iGReD scientific council. This resulted in the sprouting of a new team. This is perceived positively by the committee from two angles: a promising research project, and the maintenance of a critical plant research mass at iGReD. In the second case, despite initiatives to maintain the internationally recognized expertise of one team in muscle biology, no satisfactory solution has emerged and permanent researchers from the team will join other teams at or outside iGReD. The committee regrets that conditions for keeping the muscle expertise at iGReD could not be found.

The integration of the LYM-City team is proposed. The team stems from the current Chelter unit. The scientific coherence of this integration is attested by previous publications and grant applications with iGReD teams, as well as broader prospects of collaborations in the future. The committee appreciates that this addition will reinforce clinical research at iGReD, contributing to equilibrating fundamental and clinical research. Care should be taken that interactions are not limited within axis 2, which aggregates clinical research, but also includes interactions with the two other fundamental research axes.

Co-heading of a few teams is proposed. The new co-team leaders proposed appears appropriate, attest a collegial spirit, and often reflects increased responsibilities taken by the initial team leader.

Postponing additional team recruitment is proposed. The iGReD has currently available space for hosting additional teams, which would provide opportunities for additional scientific impact and gain further international visibility (if recruiting internationally). The current and future direction decided to postpone the recruitment of new teams until 2029 to save resources and to better focus on supporting the recently recruited teams. This appears highly responsible and sends a very positive signal to the newly recruited teams. Although the next recruitment is delayed, a clear policy is in place, and strategic choices, favouring organoids and women recruitment to correct the gender imbalance, is foreseen.

Overall, the committee supports the strategic decisions already taken for the future of iGReD. These decisions are well thought, in line with the main objectives set for the future. They should ensure a continued positive trajectory for iGReD and enforce a stronger international visibility.

RECOMMENDATIONS TO THE UNIT

RECOMMENDATIONS REGARDING THE EVALUATION AREA 1: SCIENTIFIC OBJECTIVES, ORGANIZATION AND RESOURCES OF THE UNIT

The committee recommends to closely follow the future plans of the university for the mouse facility. The issue is a very sensitive one and generates important fears in the mice community. If not properly handled, this may create conflict in the future, and result in degrading the working conditions for several teams, ultimately affecting research quality. A user committee including iGReD members and the iGReD direction should be part of the discussion and decision process by UCA. The fact that iGReD teams are the main users of this facility legitimates their tight association to delineate the options to be taken and decision-making process. It is advisable that this committee is gathered rapidly to accompany the project from very early on.

The committee recommends maintaining the technological platforms at the high standard level they have reached. This is key for the continued research success at iGReD and for the attractiveness of the unit. This certainly will involve important/difficult decisions regarding budget and human resource allocation. Some of the platforms are prone for integration of national networks directly providing funds and favouring acquisition of grant money targeted for large equipment. Exploiting this possibility is a strategy that may release pressure on budget and human resources.

Important decisions at iGReD are taken collegially by the team leader assembly. Although the Director regularly informs iGReD members verbally within the '10 min iGReD', the committee suggests that written reports of the team leaders assembly meetings are made available to the whole iGReD community. This will ensure equal information access to all iGReD members. Also, decisions on the functioning and evolution of technological platforms should seek more frequently the view of Technician/Engineers bearing operating responsibilities of the platforms.

The multiple affectation policy, often between teams and platforms, imposed by the shortage of technicians/engineer resources is sometimes a source of pressure. The committee recommends identifying the critical cases and provide a personal accompaniment to individually identify actions that may improve well-being.

Although PhD students and postdoctoral fellows are generally highly enthusiastic regarding the working environment, making the offer for training courses more accessible and the setting of a career mentoring program would improve the current satisfaction.

The committee recommends working towards correcting the gender imbalance at the level of group leaders. Special attention should be given to that issue within the context of the future evolution of teams and new recruitment.

RECOMMENDATIONS REGARDING THE EVALUATION AREA 2: THE UNIT'S SCIENTIFIC RESULTS, IMPACT AND ATTRACTIVENESS

The team interviews during the visit highlighted numerous interactions between teams, above what is attested by the limited number of teams co-authored papers during the current contract. The committee felt that a positive interaction spirit has developed and will create rapidly more opportunities for finalizing through publications ongoing collaborations. The committee recommends pursuing in this direction.

It seems important to work towards strengthening ties of axis 2 with the other axes more deeply anchored in fundamental biology. The recruitment of the previous Chelter, now LYM-City team to iGReD for the next contract will reinforce axis 2, and provide novel internal collaborative opportunities to favour a better integration of axis 2 within iGReD global research. Incentive actions towards more inter axis collaborations may be favoured by supporting such initiative by the iGReD strategic funds.

iGReD has over the last contract increased its local and national network and has further grown as a very efficient scientific centre, in particular through internal structuration and high standard technological platforms. This endows iGReD with an excellent national visibility, and sets the stage for a broader international visibility and influence. The committee recommends iGReD to take any opportunity to 'internationalize' the Institute, including by recruiting foreign PhDs, Post-docs, researcher and team leaders, by joining European/international networks and scientific committees, and by organizing international and local events. The large set of international collaborations already in place at iGReD is a solid asset towards reaching this objective.

RECOMMENDATIONS REGARDING EVALUATION AREA 3: INCLUSION OF RESEARCH ACTIVITIES IN SOCIETY

The overall contribution of the unit to socio-economic activities appears excellent, with all teams whose scientific topic allows such initiative involved. Yet, the committee found that the large number of hospital-associated publications, the participation to multiple clinical trials, the conduct of multiple translational grants and links to companies offers more room for research valorization through patenting and recommends exploring whenever possible further patenting possibilities.

Evaluation of Research

TEAM-BY-TEAM ANALYSIS

Team 1:	Genomic Imprinting & Cell Lineage Commitment
Name of the supervisor	Mr. Philippe Arnaud

THEMES OF THE TEAM

The team focuses on epigenetic mechanisms regulating cell specification, in particular transcription factors, chromatin architecture and histone marks in neural specification. The objective is to understand how the imprinting control region (ICR) regulates gene expression during neural specification. As a model, they use an ESC-derived cortical in vitro system previously developed by collaborators. The team also collaborates with clinicians and is significantly engaged in pre-clinical research by investigating different pathological contexts (glioblastoma, Parkinson's disease) using approaches that fit with the fundamental research line of the team.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

While previous recommendations encouraged the continued development of the team's two model systems, there were concerns that the scientific output might be insufficient for long-term establishment and funding renewal.

During the contract, the team obtained multiple grants (ANR, FRM, I-Site), and has also recently recruited a researcher on a permanent position, indicating positive momentum.

The team fully addressed the previous recommendation to develop translational research by establishing collaborations with clinicians.

Through these collaborations, they gained access to patient samples and glioblastoma cell lines, enabling clinically relevant studies. A PUPH will also join in 2027 to lead a project focused on generating an in vitro model of Type 1 Myotonic Dystrophy using patient-derived iPS neuromuscular organoids.

Other recommendations were to increase both technical support and the use of genetic approaches, and to explore new research lines.

This was substantially addressed by recruiting a permanent engineer (25%) and two non-permanent engineer positions funded through national and local grants. They have expanded their expertise with CRISPR-Cas9 gene editing and organoid models. These advances have enabled the initiation of new research lines that form the foundation of upcoming projects.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	5
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	2
Post-doctorants	1
Doctorants	1
Sous-total personnels non permanents en activité	4
Total personnels	9

EVALUATION OF THE TEAM

Overall assessment of the team

The team basic research axes on the regulation of tissue specific imprinting and in disease are of major interest, with excellent visibility and a very good to excellent scientific production. The team's non-academic activity is very good. Outreach activities are limited.

Context-related strengths and opportunities

The scientific production of the team is very good to excellent with 6 research articles from the team in very good journals (Genome Research 2019; Mol. Oncology 2021; Mol. Cell Life Sci. 2021; Human Molecular Genetics 2022; Int. J. Mol. Sci. 2022; HGG Adv. 2024), and an additional two articles with team members as co-authors and one review. The CR of the team is well integrated with publications as 1st author and co-corresponding with the team leader. One MCF of the team is also co-author on a large clinical study. Most publications focus on imprinting, the main research topic of the team. The trajectory/projects are well thought and very interesting.

The workforce of the team is excellent. The team hosted ten people during the period. Five of them will leave during the next contract, including one PhD, one postdoc and two engineers, but the team will further gain personnel as it attracted a young researcher who is applying for a permanent position. Core to the team are four senior researchers, among which two are MCU or MCH. One PUPH will join the team in 2027 to develop novel translational aspects.

The team has a broad spectrum of expertise in basic research, bioinformatics, and translational science. The team engagement in local collective responsibilities is excellent, with strong implication at both the university and the institute. The team is also actively involved in many transversal activities in the institute, including the organization of an internal congress, the implementation of new communication tools, the creation of the novel unit's website, and the creation of videos to present the institute.

The PI has an excellent international and national visibility, as demonstrated by his participation in many scientific committees (HDR and PhD) and national and international conferences. The PI participates in several SABs (2 in

France during this period) and National (3) and international (1) committees. One PhD presented at an international meeting specialized in Genomic imprinting. The excellent international visibility of the team is attested by several invitations for talks in France, the UK and Portugal.

Training activities and teaching are excellent. Two members of the team are heavily involved in teaching, and two others contribute with a few hours every year. During the period, three PhDs were defended and one is ongoing. All the PhD students published at least one first author article illustrating the excellent supervision.

Funding is very good with many local and some larger national grants (1 ANR, and an FRN trans Snca as partner) and several smaller LNCC grants.

The valorization of the research outcomes is good with one ongoing patent application.

The diffusion to large audience activities is very good with the organization of open days at the institute and the participation in an online video on epigenetics (Unisciel project). The team is managing audiovisual students responsible for creating videos showcasing the iGReD teams: this is an original initiative.

Context-related weaknesses and risks

The team is diverging into many diverse topics. This does not seem to be a problem as all topics are currently funded, but may affect the future team's cohesion. For instance, starting with a new translational project (Mulchandani-Bhoj-Conlin syndrome – MBCS – and myotonic dystrophy type 1) might be at risk, although this choice aligns better with the basic research of the team than the previous translational project on neuroblastoma.

Publications are in quite specialized journals.

The team does not have many non-academic activities, and collective responsibilities remain very local.

The number of ongoing PhDs is low in comparison to the number of researchers holding the HDR. In particular, the MCFs are co-authors on some of the articles of the team, but they are lacking authorship in a leading position, likely due to a lack of involvement in PhD student supervision.

ANALYSIS OF THE TEAM'S TRAJECTORY

The project on nested genes in the H13/Mcts2 imprinted locus is very original. In the future, the team plans to continue to dissect the regulation of genomic imprinting during neural acquisition and to develop innovative tools. The shift toward an encompassing approach linking transcriptional regulation, gene isoform diversity, 3D chromatin organization, and disease relevance strengthens the team's core expertise in imprinting biology.

Ongoing projects indicate high-quality fundamental and translational research, including elucidation of insulator mechanisms and enhancer biology at imprinting control regions, functional analyses of complex loci such as H13/Mcts2 with direct implications for Mulchandani-Bhoj-Conlin syndrome, and translational modelling using patient-derived iPS neuromuscular organoids to study myotonic dystrophy type 1.

The team benefits from ongoing collaborations with clinical experts and international partners, enhancing both mechanistic insight and translational potential. Integration of cutting-edge genomic, epigenomic, and imaging technologies, alongside emerging CrisPR-based functional approaches, supports a comprehensive study of imprinting regulation and function.

Dedicated funding secured for each axis, including ANR, AFM-Téléthon, and institutional support, alongside plans for European and national grant applications, highlight a forward-looking strategy to consolidate and expand this niche. The recruitment and nurturing of promising early-career researchers is very positive and will further ensure continuity and growth.

RECOMMENDATIONS TO THE TEAM

The team should try to maintain a cohesive scientific focus.

The team should aim at publishing in more generic journals to increase visibility and attract more funding. One way could be by developing new cutting-edge approaches for epigenetic and gene expression study at single cells and/or spatial levels, in collaboration or within the team. For instance, while most of the studies conducted are on *in vitro* models, developing such recent technical approaches would help confirm their findings *in vivo* to reach broader audience journals. It would also help to apply to larger grants, in particular European grants. This could also help face competition that they identified themselves as a threat.

Team 2: Dynamics and epigenetic control of transposons
Name of the supervisor: Ms Emilie Brasset

THEMES OF THE TEAM

The team studies the mechanism underlying epigenetic regulation of transposable elements in somatic and germ cells, in particular. Recent work focused on how silencing is reestablished at each generation and maintained through cell divisions, and on the molecular understanding of the PIWI-interacting RNA (piRNA) pathway, essential for genome integrity and fertility, with distinct mechanisms operating in somatic and germline cells.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Previous recommendations were to continue producing high-quality science for which the team was successful. The team was previous to the last contract co-headed. The previous committee encouraged the 'next young PI' to apply to national/international funding and more specifically to young investigator programmes. During the period, the current team leader successfully obtained substantial national funds including an ANR JCJC and 3 ANR as partner. International grants were not successfully acquired.

They also recommended decreasing the teaching charge for the team leader, and to recruit more postdocs. The team leader successfully applied to an 'accueil en délégation', thus considerably decreasing the teaching charge, and allowing it to better focus on the team progresses, grants and articles writing. The team also attracted and hosted a young postdoc researcher with the aim of applying to permanent researcher position.

Finally, they recommended the team to increase its international visibility, for instance, by building international/European networks and by being more represented at international meetings. The team followed these recommendations and participated in several prestigious international conferences and publishing wide international audience research articles.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	5
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	0
Post-doctorants	1
Doctorants	1
Sous-total personnels non permanents en activité	2
Total personnels	7

EVALUATION OF THE TEAM

Overall assessment of the team

The team is ranked as excellent to outstanding. It has clearly established its own niche in a highly competitive field as demonstrated by the high quality of its scientific production with publications in top-ranked journals and strong national funding. It maintains a well-balanced and stable workforce, including senior researchers and emerging talent, and exhibits high visibility through international conferences and leadership in scientific committees. Training and public engagement efforts are excellent to outstanding. The team's innovative projects on transposable elements position it well to continue making significant contributions and to strengthen its scientific identity.

Context-related strengths and opportunities

The team is very-well balanced and solid, and the transition from co-PI to PI is successful. It comprises three permanent researchers (PR, MCF and CR), two permanent technical staff (engineers and technicians), one postdoc and two PhD students (one finished in 2024). They aim at recruiting the postdoc on a permanent researcher position in the near future.

The scientific production during the period is excellent to outstanding. Eleven articles were published during the period with five from the team in highly regarded journals (Nat Com, Cell Report, Nat. Struct. Mol. Biol.). There are also five reviews.

The team was very successful in acquiring national and local funds with one ANR JCJC as coordinator and four ANR PRC as partner, as well as several PhD grants from national charities (FRM) or local institutions (University).

The team has an outstanding visibility, demonstrated by invitations to give seminars and oral presentations at several prestigious national and international conferences, as well as a substantial number of poster presentations. The team has supervised four PhD theses. Additionally, the team is currently hosting a young postdoctoral researcher, who is postulating to a permanent research position. This will significantly strengthen the team's workforce and long-term stability. The team's strong national and international profile is further evidenced by the organization of two national meetings, one focused on transposable elements (TEs), and an online training session on epigenomes and epigenetic regulation. The team has been invited to deliver seminars abroad (e.g. in the UK and Austria) and has presented communications and posters at conferences and EMBO workshops in the UK, Germany, Switzerland, and Korea. Furthermore, team members serve on the scientific council for a GDR on TEs. Their excellent visibility is also evidenced by handfults and fruitful international and national collaborations. Editorial and peer-review activities are robust, with team members serving as reviewers for several journals, and participating in international evaluation panels for PhD fellowships and grant applications (including in Austria, Chile, and Australia).

The training activities are excellent to outstanding with all members of the team dispensing courses, some being co-responsible for a master's programme.

Public engagement and diffusion of science to large audiences are excellent to outstanding through original means (interactive workshops, films, and digital resources). Team members are actively involved in several events targeting a large population ("Nuées ardentes" festival; Fête de la Science; iGReD laboratory and university open days). The team is also involved in the Unisciel project i.e. an open access content to explain epigenetic to students and larger audience.

Context-related weaknesses and risks

There is an imbalance between the number of researchers in the team holding an HDR and the number of PhD students for whom they provide full supervision. For instance, there are three HDRs in the team but only one ongoing PhD.

In perspectives, the number of ongoing projects appears excessive, with five distinct projects being undertaken. Some of these are led by the same person (technical staff) with a Master 2 student, which may complicate research progress. This situation is further compounded by the continuation of previously initiated collaborative projects.

With the exception of one member (MCF) involved in activities at the university level, no collective responsibilities or leadership roles at the national level have been reported.

ANALYSIS OF THE TEAM'S TRAJECTORY

The proposed future projects are excellent. The team's trajectory encompasses five original projects in addition to the ongoing collaborative ones. Most of these projects are built directly on previous discoveries by the group, including the establishment and maintenance of transposable elements (TE) silencing, the functional role of TEs during *Drosophila* embryonic development, and the involvement of PRC2 in TE silencing within somatic cells. Two additional projects investigate the role of the *Env* gene in endogenous retrovirus infectivity and transmission, as well as the factors underlying Tirant instability in *D. melanogaster*.

All projects are well integrated and closely aligned with the team's thematic focus, drawing on solid preliminary data. They leverage cutting-edge methodologies, such as Nanopore sequencing and the generation of novel fly mutants via CrisPR/Cas9 technology.

The personnel assigned to each project is overall well balanced but somehow risky, typically comprising at least one student (PhD or Master's) and technical support staff (technician or engineer). Supervision is provided by the team's researchers, ensuring effective guidance and project continuity.

RECOMMENDATIONS TO THE TEAM

Overall, the primary recommendation is to continue conducting excellent science and to pursue their exploratory projects on transposable elements (TEs), their functions, and regulatory mechanisms. These projects are instrumental in helping the team establish a distinct scientific niche.

We encourage the team to actively seek funding from European grants and consortia, which could further enhance their research capacity and visibility. Additionally, attracting international postdoctoral researchers would strengthen the team's expertise and foster valuable collaborations.

To support future projects and ensure sustained productivity, the team should prioritize securing additional PhD students and postdoctoral researchers.

A noteworthy observation is that the high-impact publications from the team (e.g. in *Nature Communications*, *Cell Reports*, *Nature Structural & Molecular Biology*) list collaborators as co-corresponding authors, and often feature multiple PhD students as first authors. While this might be due to the collaborative nature of these works, the team should strengthen its distinct scientific identity by increasing publications where authorship positions more clearly reflect the team's leading role in the work. This approach will help to clearly distinguish the team's contributions and reinforce its standing in the field.

Team 3: Silencing and Transposons
Name of the supervisor: Mr. Olivier Mathieu

THEMES OF THE TEAM

The team investigates the molecular mechanisms of epigenetic regulation, using *Arabidopsis thaliana* as its primary model. The focus is on genome stability and the defence against transposable elements (TEs), with genetic and genomic approaches applied to study silencing mechanisms. More recently, the team has expanded its scope to wheat, liverworts and soon jellyfish, to explore both conserved and divergent epigenetic processes across evolution.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Recommendations focused on:

a) international visibility at conferences

In line with the previous recommendations, the team has maintained strong international visibility despite limited travel opportunities for the team leader between 2017 and 2024. This was achieved through online seminars and, notably, the co-organization of the Epiplant/Seb 'Plant Epigenetics' international meeting in 2024, which gathered more than 180 participants.

b) Postdoctoral recruitment and website visibility

The group has maintained a continuous presence on the institute's website. Regarding postdoctoral recruitment, the team deliberately supported a long-term position to strengthen the candidate's prospects to obtain a CNRS research scientist position, while also engaging with several international candidates. Among these, one submitted a Marie Curie fellowship proposal and plans to resubmit in 2025.

c) Collaboration with leading labs

The team has consolidated its collaborations by securing two national grants (ANR NeoDNAcontrol and ANR polyPMD) and two regional grants. It continues to work closely with world-leading laboratories, although opportunities for joint international funding have not yet materialized.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres 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 non permanents d'appui à la recherche	0
Post-doctorants	1
Doctorants	1
Sous-total personnels non permanents en activité	2
Total personnels	6

EVALUATION OF THE TEAM

Overall assessment of the team

The team scientific production is excellent, with original and influential work at the intersection of DNA replication, chromatin organization and TE control. Despite its small size, it delivers high-quality scientific output, with results published in top journals and supported by strong international collaborations. Its research combines mechanistic depth with translational perspectives in wheat. The main vulnerability is its limited critical mass and risk of dispersion, but its productivity and visibility make it a leading contributor in plant epigenetics.

Context-related strengths and opportunities

The team attractiveness and visibility are very good. The team enjoys strong national and international recognition in plant epigenetics and TE control. Its visibility is reinforced by collaborations with leading groups at UCLA, GMI Vienna, IPS2 and INRAE, as well as active participation in the GDR networks Epiplant and MobilET. The co-organization of the Epiplant/ebB 'Plant Epigenetics' symposium in 2024, which brought together over 180 participants, further highlights its role in the community. In total, the team has secured around 800k€ in funding from different sources. Editorial and reviewing responsibilities for top-tier journals and funding agencies also strengthen its reputation, while competitive funding from ANR and regional schemes confirms its attractiveness and momentum.

The team's scientific output is excellent, both original and influential, with clear mechanistic insights at the interface of genome replication, chromatin architecture and transcriptional silencing. Important advances include the demonstration of how replication stress destabilizes silencing through POL2A and RTEL1, and the refinement of H2A.W function – together with H1 and H2A.X—in shaping heterochromatin accessibility and DNA methylation. Work on Plant Mobile Domain proteins (Main/Mail1/Mail2) defined DNA motif modules (M1M/M2M) that counteract Polycomb-mediated repression, opening a new regulatory paradigm with evolutionary connections to DNA transposons. Translational studies in wheat identified and validated DDM1 orthologues and open a credible path toward epiRILs with agronomic potential. The team published nine research papers during the period from which five as the first and corresponding author. Publications in *Nature Communications*, *Genome Biology*, *Nucleic Acids Research* and other high-ranking journals, along with a preprint now accepted at *Nature Plants*, demonstrate the impact and visibility of the research.

The team non-academic activities are very good. The team shows a steady commitment to teaching, training and outreach. It contributes to Licence and Master programmes, supervises students from BTS through to PhD and postdoctoral levels, and presents its work at major international meetings. Engagement with the public through the Fête de la Science, institute open days and CNRS news features demonstrates effective science communication. The emerging translational direction in wheat, including the development of epiRILs, positions the team for potential fruitful collaborations with breeding stakeholders and external partners.

Context-related weaknesses and risks

With four tenured researchers, the team could further strengthen its profile by increasing involvement in student supervision and expanding contributions to teaching – particularly at the Master's level – to enhance training and improve prospects for funded PhD fellowships. Access to M2 and PhD candidates locally remains limited, complicating recruitment and succession planning. The recruitment of a UCA lecturer could help to attract students to the team.

While international collaborative funding has not yet been secured, an application is underway, and leveraging bilateral partnerships to join or coordinate consortia would be beneficial.

The current balance of permanent and non-permanent staff may limit resilience in the long term, underscoring the importance of strategic recruitment and fellowship-driven growth.

Sustaining the high quality of output will be supported by expanding staff and funding opportunities. Given the broad scope of the programme – spanning *Arabidopsis*, wheat, liverwort and *Turritopsis* – a phased approach, aligned with available resources, would help maintain focus and mitigate the risk of dispersion.

The funding environment for basic, non-medical plant research is challenging, with relatively few multi-year schemes dedicated to applied development. To maximize translational impact, strengthening and formalizing phenotyping and breeding collaborations would be valuable, and greater visibility in this area could facilitate stronger engagement with external stakeholders.

ANALYSIS OF THE TEAM'S TRAJECTORY

In the coming period, the team will deepen its mechanistic dissection of PMD proteins that antagonize Polycomb-mediated silencing. With support from ANR polyPMD, this work will define the Mail1/Mail2 interactome through biochemical approaches and in-silico interaction screening with AlphaFold-Multimer, in collaboration with GMI, Vienna. Genetic suppressor strategies will continue, including further analysis of *mail1* suppressors and a new screen in hypomorphic *Mail2* artificial microRNA lines. Because only 20–40% of M1M/M2M motifs are bound genome-wide, the team will investigate how local chromatin features, particularly DNA methylation, influence PMD targeting. The discovery of M2M motifs within terminal inverted repeats of Mule transposons suggests a role in their life-cycle. Since many transposases also carry PMD domains, the team will test whether PMDs and M2M motifs confer anti-silencing capacity against Polycomb repression.

A second axis will clarify the role of H3K27me3 in TE control. Building on findings that ~15% of *Arabidopsis* TEs are associated with H3K27me3, that PRC1 mutants show genome-wide gains, and that loss of H3K9me2 reduces H3K27me3 at some elements, the team will map dependencies between these marks. Tissue- and stage-specific depletion lines will help resolve context-dependent TE silencing. In collaboration with IJPB groups and with ANR NeoDNAcontrol support, the team will also study the active retrotransposon EVD to capture early chromatin events during new insertions and trace the initiation of silencing.

The translational branch developed with a group at INRAe targets wheat. By creating *DDM1* mutants, the team will identify active TEs in a genome more than 85% repetitive, and generate epiRILs with mosaic methylomes to reveal agronomic traits linked to epigenetic variation.

An evolutionary strand will extend previous work on *Marchantia polymorpha*, using *MET1* and demethylase mutants to test how CG loss reshapes non-CG methylation and H3K27me3 landscapes in TE-rich regions. Finally, a cross-kingdom project in the hydrozoan *Turritopsis dohrnii*, supported by the UCA I-SITE (epiMMortal) and a BBVA 'Fundamentos' proposal, will map DNA methylation and H3K27me3 dynamics during the life-cycle reversal, integrate these data with transcriptomics, and assess TE activity to build a regulatory framework for rejuvenation.

These projects are novel and ambitious, linking mechanism, evolution and translation. To maintain focus, the expansion into multiple models should be paced with resources and personnel, ensuring that each line of research is adequately supported to avoid the risk of dispersion.

RECOMMENDATIONS TO THE TEAM

The team is delivering excellent, field-leading research at the interface of replication, chromatin and TE control, with potential translational perspectives in crops. We recommend continuing along this trajectory while gradually strengthening capacity. Maintaining the PMD–Polycomb/*Arabidopsis* core as an anchor while scaling the work on wheat, liverworts and *Turritopsis* in line with resources will help preserve focus and avoid dispersion. Strategic recruitment—for example, a CNRS researcher or a UCA lecturer—together with active engagement in international consortia and fellowship schemes, would further consolidate momentum.

Team 4: Evolutionary Epigenomics and Genetic conflicts
Name of the supervisor: Mr. Antoine Molaro

THEMES OF THE TEAM

The team focuses on understanding how epigenetic information is inherited and evolves in mammals, particularly through studying rapidly diversifying chromatin processes in reproductive cells consequent to genetic conflicts. Their two main scientific goals are: (1) to identify functional domains in chromatin pathways that show signs of genetic conflict using natural selection and comparative genomics methods, and (2) to experimentally test how rapid evolutionary changes influence epigenome functions using mouse models and cell cultures. This approach aims to reveal how genetic conflicts drive epigenetic innovation and the functional consequences of this rapid evolution in mammalian reproduction.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

This is a new team, established at iGReD since 2020, after the previous HCERES evaluation.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

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

EVALUATION OF THE TEAM

Overall assessment of the team

This team stands out for its originality, strong external funding, and significant promise to advance the current understanding of epigenetic evolution in mammals. The high quality of recent and forthcoming research, the international visibility of the team leader, and credible future projects position the team for further success. To fully realize its potential, the team should prioritize the stabilization of its workforce, increase dissemination of current achievements, strengthen teaching involvement, and intensify student recruitment and outreach efforts.

Context-related strengths and opportunities

The team started in 2020 with the support of an FRM starting grant. The research topic is very original questioning evolution from a perspective clearly distinct from the classical ones.

The visibility of the team is excellent. The scientific production since 2020, mostly restricted to work of the team leader prior to its move to iGReD, is excellent with two articles as 1st author and one as co-last author in very good journals (Nature Comm, PLoS Biology). There are also two co-authors of articles and a bioRxive (for two years now not published). There are three review articles among which two features the team members as the last author. The team leader is also co-author on a US patent application. The team visibility will be further enhanced with the successful ERC. The team leader was invited to several seminars and conferences including workshop, organized a conference, and was awarded a prize for young investigators. All team members participated to either national or international conferences. The team leader also participated to the jury of three PhDs and two HDRs.

The team is largely funded. It started with an ANR JCJC and a FRM grant before obtaining the ERC.

The research of the team is excellent and yet to be published or in revision. They found that the short histone variant H2A undergoes rapid evolutionary diversification in placental mammals, likely due to a novel germline genetic conflict. In H2AB KO, chromatin is more accessible in post mitotic sperm. H2A.P KO rescue this phenotype, indicating that the 2 variants genetically interact in an antagonistic manner (in preparation for submission). In female, H2AB KO, chromatin is also less compact and more classical histone marks are increased or decreased. Finally, they are characterizing two new mouse models with 3XFLAG tagged endogenous loci. In collaboration, they also studied Schlafen genes evolutionary trajectories (under revision).

Training activities are good and restricted to hosting PhD and Master students in the lab.

Interaction with the general public is good (Fête de la Science, « Petit dej » de la délégation).

Context-related weaknesses and risks

The only permanent position of the team is held by the team leader. Other team members, including two PhDs and two technical non-permanent staff are funded by charities. By attracting and stabilizing young researchers for permanent positions, the team would be significantly strengthened.

The past work reports ongoing projects in the lab that are not yet published.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team trajectory is very well presented and credible. Future projects are funded by an ERC. The project is very original.

In the ERC project, the team aims to demonstrate, through phylogenetic analyses of rodent and primate genomes, positive selection signatures in testis-enriched TSPY histone chaperones and the H2A.Z exchange factor SRCAP in primates, as well as in the nucleosome remodellers Arid2 and CHD5 in muroids. Notably, rapid evolution localizes to previously mischaracterized functional domains and residues, underscoring how evolutionary studies can reveal novel biological roles and opening avenues to systematically explore genetic innovations shaping epigenome evolution.

RECOMMENDATIONS TO THE TEAM

The main recommendation is to promptly publish the pending BioRxiv articles, thus allowing the team to fully and effectively focus on the upcoming ERC-supported projects.

Finally, the team should broaden its participation in teaching to enhance its visibility and reputation. It is also encouraged to strengthen engagement with doctoral schools aligned with its research program to attract Master's and PhD students well suited to the team's scientific objectives. In parallel, the team should develop long-term strategies for recruiting permanent researchers and technical staff.

Team 5: Chromatin and 3D Nuclear Dynamics
 Name of the supervisor: Mss. Aline Probst/Mr Christophe Tatout

THEMES OF THE TEAM

The team investigates how chromatin organization regulates gene expression during plant development and adaptation, using *Arabidopsis thaliana* as its primary model system. Their work focuses on understanding how changes at the nucleosome and higher-order chromatin levels control transcriptional responses during key biological processes such as seed germination and environmental adaptation. The team combines molecular and genomic approaches with advanced quantitative bioimaging and deep learning methods to elucidate chromatin-based regulatory mechanisms.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Recommendations focused on:

(a) Recruit more postdoctoral fellows

A key recommendation from the previous Hcéres report concerned the need to recruit more postdoctoral fellows to strengthen the team's critical mass in a competitive research field. In response, the team has successfully recruited two post-docs and actively pursued additional fellowships (EMBO, MSCA). It has also increased technical support through ANR grants, thereby consolidating its capacity to sustain ambitious projects and enhance its international visibility.

(b) Concern about the work on nuclear periphery

The committee also expressed concerns regarding the research on the nuclear periphery, suggesting that the topic was too broad and technically risky. The team responded strategically by gradually reducing this line of research to concentrate on chromatin dynamics, while capitalizing on the expertise gained through European consortia. This sharper focus has reinforced the coherence and impact of the scientific programme.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maitres de conférences et assimilés	4
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	8
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	1
Post-doctorants	2
Doctorants	6
Sous-total personnels non permanents en activité	9
Total personnels	17

EVALUATION OF THE TEAM

Overall assessment of the team

The team has performed at an excellent level during the evaluation period. Its research has produced original and influential contributions in chromatin regulation, histone dynamics and nuclear organization, with a strong record of publications, training, and leadership in national and international collaborations. Its visibility is outstanding. The team has secured substantial funding, participates in European doctoral networks, and plays a central role in community building.

Context-related strengths and opportunities

The team is internationally recognized for leadership in epigenetics, chromatin dynamics and 3D nuclear organization. The team's attractiveness and visibility are outstanding. It has achieved strong national (five ANR grants) and international visibility through its leadership roles in major research networks such as the Cost Action Indepth and the GDR Epiplant network. It is a partner of the MSCA Doctoral Network EpiSeedLink, partner and future coordinator of MSCA DN Agile. The team maintains a balanced structure with permanent staff (1 DR HDR, 1 CR HDR, 1 Prof HDR, 1 IR HDR and 4 MCF) covering complementary expertise in genetics, genomics, imaging and bioinformatics, supporting its attractiveness for students and collaborators. Regular invitations to international meetings, a strong collaborative network, and a sustained capacity to attract external funding (a total of 2M€ for the evaluated period) testify to its solid reputation in the field.

The team's scientific output is excellent. Its work on histone variants, GH1-domain proteins and nuclear architecture has contributed significantly to understanding how chromatin organization influences gene expression during development and environmental adaptation. The team has contributed to seventeen research articles, including seven as corresponding authors, and ten review articles. It has been published in high-impact plant journals such as *The Plant Cell*, *The Plant Journal*, *New Phytologist* and *Plant Communications*. In addition to high-quality publications, the team has developed innovative imaging and deep learning tools, notably biom3D (preprint on bioRxiv), which position it at the interface of molecular biology and technological development. Its scientific production is both mechanistically deep and conceptually original, consolidating its position as a leading contributor in plant chromatin biology.

The team's non-academic activities are excellent and demonstrate strong engagement in training and outreach. It is heavily involved in teaching at Licence, Master and Doctoral levels. Its participation in national and international training schools and workshops reflects its commitment to knowledge dissemination. Outreach activities, including science festivals and local engagement initiatives, enhance its societal visibility. The team also collaborates with industrial partners in the seed sector, extending the potential translational impact of its research.

Context-related weaknesses and risks

As the team expands, there is a risk of thematic fragmentation and reduced cohesion between research axes. The diversity of research axes, while a strength, may also diffuse focus and slow progress in individual lines of research if not carefully managed. As competition in the chromatin and nuclear dynamic field is intense internationally, maintaining a clear synergistic core will be crucial.

The distribution of funding across axes is uneven (e.g. Axis 2), which may limit the development of certain lines of research.

Administrative tasks, especially linked to the coordination of multiple projects and infrastructure, can weigh heavily on key personnel, potentially limiting research time.

The scientific output is excellent, but its visibility could be further enhanced through a greater presence in high-impact, generalist journals.

The team is heavily involved in teaching and administrative responsibilities, which can constrain time available for research.

ANALYSIS OF THE TEAM'S TRAJECTORY

The trajectory of the team is coherent, ambitious and strategically defined to consolidate its leadership in chromatin biology and 3D nuclear organization. The research plans for the next period is structured around three complementary and integrated axes that connect mechanistic work on chromatin with advanced technological development and translational perspectives.

The first axis focuses on the role of histone variants and chaperones during the seed-to-seedling transition, a biological process characterized by massive transcriptomic and nuclear reorganization. By combining imaging, Hi-C, transcriptomics and single-cell analyses, the team aims to dissect histone eviction and deposition mechanisms and their impact on nuclear architecture and gene regulation. The use of rapeseed and seed priming strategies brings an applied dimension to this fundamental research.

The second axis addresses how GH1-domain proteins influence Polycomb activity and regulate developmental genes. Building on strong preliminary results, the team will integrate genetic, biochemical and single-molecule approaches to define the mechanisms underlying GH1 function and their impact on chromatin states. This work has the potential to reveal new principles of epigenetic regulation with broader relevance.

The third axis builds on the team's leadership in quantitative imaging. Developments in deep-learning image analysis (biom3D), Light sheet microscopy and Anchor technology will enable single-cell and single-molecule analyses of chromatin organization and gene positioning in real time. This axis provides strong technological leverage.

The trajectory is supported by substantial national and European funding, ensuring continuity and recruitment capacity (particularly in axes 1 and 3). The arrival of a new DR2 researcher in 2026 will further strengthen expertise in imaging. Overall, the strategy is well integrated, combining mechanistic depth, technical innovation and translational perspectives, positioning the team to maintain and enhance its international visibility.

RECOMMENDATIONS TO THE TEAM

The committee encourages the team to continue building on its excellent trajectory.

As the team grows, maintaining thematic synergy across axes will be key to preserving focus and ensuring the efficient use of resources. Efforts should be made to mitigate differences in funding levels between axes (e.g. Axis 2).

Increasing the number of publications in high-impact, generalist journals could further raise its international profile.

The team should continue leveraging its leadership in bioimaging and epigenetics to play a central role in international research networks.

The integration of the new DR2 member will offer opportunities for growth but also requires strategic planning to maintain coherence.

While the team engages effectively with industry and the general public, strengthening formal partnerships with external stakeholders could increase the translational impact of its work. These efforts could be particularly relevant as the team's rapeseed work and bioimaging expertise may open new application-oriented avenues.

Team 6: Epigenetic Regulation & Ontogenesis
Name of the supervisor: Mr. Lucas Waltzer & Ms Laurence Vandel

THEMES OF THE TEAM

The team uses *Drosophila melanogaster* as a model to analyse the mechanisms of epigenetic regulation. In the last years they have focused mainly on how the TET protein functions, finding that besides its classical enzymatic activity, it has non-enzymatic activities involved in muscle function aging and neural function.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Previous recommendations were:

a) to focus on their new project.

This has been addressed. The team has finished their previous projects and now focus on their new topics, on which they have already obtained two publications.

b) to obtain strong bioinformatic support.

This has been addressed with the team succeeding to make permanent the position of a bioinformatician who obtained a CNRS Research Engineer position in 2019. With the new position the bioinformatician will be able to dedicate 40% of his time to work for the team. PhD students in the laboratory are also encouraged to do bioinformatics training.

c) to prioritize research efforts with a relatively small team in order to acquire additional funding through competitive grants. Application for international funding will thus need to be considered.

The team obtained competitive national and international grants (ANR, CEPIFRA, ARC, Ligue contre le cancer) to support the research and additional grants to support PhDs. Larger European grants are missing.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
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 non permanents d'appui à la recherche	0
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	3
Total personnels	7

EVALUATION OF THE TEAM

Overall assessment of the team

The team has re-organized its areas of study finishing up their previous work and concentrating in a new chromatin regulation aspect focusing especially on the TET protein. Their scientific production has been excellent. The team has an excellent visibility with many national and international collaborations. The team of non-academic activity can be improved, although its basic focus does not allow much room. Outreach activities are excellent.

Context-related strengths and opportunities

The team structure is solid and attractive as it has two senior researchers and the support of a part-time bioinformatician and a part-time technician. During the evaluated period, there have been 5 PhD students (3 PhD students at present and 2 that have left after presenting their thesis). Students have published their work as first authors in very good or excellent journals. The team has a number of international collaborators. The visibility of the team is excellent and its capacity to raise funding is excellent. One team leader has been well funded leading nine national research projects (especially relevant is 1 ANR still active and 1 CEFIPRA) and several for PhD studentships. The other senior member obtained 1 grant from Inserm Cancer as a partner. The team leader organized one national conference, was invited to national talks and participated in 2 national and 2 international conferences. The team members participate in many Universities and Inserm boards and expert evaluation panels for national and European agencies (HCERES, MCSA, ERC, ARC).

The team has been in the process of reorganizing their focus. Both senior researchers have joined forces to analyse the function of the TET protein, both the classical enzymatic function, and a novel non-classical one. For that purpose, they have finished up their previous independent work. These resulted in the publication of a paper on the function of JAK-STAT signalling to control the differential behaviour of the *Drosophila* blood cells in the anterior vs. the posterior lymph nodes. They showed that while anterior lymph glands repress STAT and differentiate, the posterior lymph glands maintain JAK-STAT pathway activation allowing the preservation of progenitor cells (published in eLife as an international collaboration). They also studied the existence of adult haematopoietic lineages in the fly, finding the adult blood cells are mature differentiated cells. However, they discovered there is a persistent larval population that has capacity to proliferate in the adult (Frontiers in Cell and Dev. Biol.). On the more recent chromatin/TET project, the co-headed team has already published three excellent papers as senior authors (eLife, Science Advances, PLoS Genetics) indicating that the new line of research already has momentum. The scientific production during the period has been excellent with 10 publications, in 6 of which team members are corresponding authors. The team has also had numerous international and national collaborations.

The team does not report any non-academic activities, although there is clearly a good interaction with non-scientific and non-academic audiences with their participation in various events (Declics, Nuées Ardentes, iGReD Open Days, AFM telethon).

Context-related weaknesses and risks

The refocussing of the team into a new research topic may delay their international visibility.

During the evaluated period, the team included a number of postdocs, but currently none remain in the laboratory. The team is well aware of this problem and point as a threat the loss of some expertise after PhD and postdocs left the team after the teams' relocation from Toulouse to Clermont-Ferrand.

Their interaction with the public could be increased.

ANALYSIS OF THE TEAM'S TRAJECTORY

The trajectory is very well planned with co-PI increasing responsibility as team co-leader, as the team leader undertakes the leadership of the unit as the DU.

In the project, the team will study the unconventional function of TET enzymes (independent of the enzymatic catalytic activity) in muscle development and cancers, in particular by focusing on its gene regulation function. Each part of the project is very well presented and demonstrate strong credibility. The personnel involved are

well identified. The experimental approaches are well suited to the objectives and multidisciplinary (fly genetics, proteomics, scRNAseq). Long-term plans to study the epigenetic function of TET are also well presented and challenging.

After their arrival in the unit, the team has put great effort to develop the bioinformatics platform. This instrument is essential to both the team's future projects and will also benefit colleagues and the scientific community.

RECOMMENDATIONS TO THE TEAM

The committee support the co-leadership that should help make the team's work more efficient, especially while the PI is assuming the leadership of iGReD.

The committee encourage obtaining a solid preliminary data to support funding applications for the study of non-conventional function of TET in *Drosophila* and to increase the ambition of their research topic.

The team should aim at attracting postdocs and/or elaborate a strategy for recruiting young researchers on permanent positions.

The team should apply to European grants to increase their sources of funding.

Interaction with the society should be consolidated and broadened.

Team 7: Recombination and Maintenance of Genome Integrity
Name of the supervisor: Mr. Charles White

THEMES OF THE TEAM

The team's research focuses on understanding the molecular processes that maintain genome stability and ensure its proper transmission during development and reproduction. Central research topics include recombination, DNA repair, meiosis, and telomere biology, processes that are fundamental to both eukaryotic genome integrity and evolution. Using *Arabidopsis thaliana* and *Saccharomyces cerevisiae* as core models, and extending to human clinical collaborations, the work aims at elucidating the molecular basis of DNA break repair, meiotic recombination and telomere maintenance. These studies have broad implications ranging from fundamental biology to plant breeding and medicine.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous HCERES assessment was positive and did not include specific recommendations.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	9
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	0
Post-doctorants	1
Doctorants	2
Sous-total personnels non permanents en activité	3
Total personnels	12

EVALUATION OF THE TEAM

Overall assessment of the team

The team has been a leading force in the field of plant genome stability and meiotic recombination for over three decades. It has maintained an exceptional level of scientific output, contributed to the development of innovative molecular and genomic tools, and trained multiple generations of young scientists. Its leadership has had a lasting national and international impact. The restructuring under new leaders builds on this remarkable legacy.

Context-related strengths and opportunities

The team enjoys a very strong international recognition. Over its history, it has coordinated and participated in multiple European projects (EU-MSCA ITN, ERC), and co-founded the international EMBO workshop series on

Plant Genome Stability and Change, a key platform for the field. Its members have been repeatedly invited to international conferences and contributed to high-level collaborations worldwide. Its capacity to attract competitive funding, including ERC support through one PI, confirms its scientific reputation and visibility.

The team has made significant and lasting contributions to recombination and genome stability research. Over the period of evaluation, it has produced 21 peer-reviewed articles, with three more in preparation. Its research has led to advances in understanding RAD51/DMC1 regulation, CST complex function at telomeres, mechanisms of DNA break repair and evolutionary adaptation to allopolyploidy. The quality of its publications in top journals such as *PLoS Genetics*, *New Phytologist*, and *EMBO Reports* attests to its sustained excellence.

The team has been deeply involved in teaching, outreach, and societal engagement. It has trained numerous PhD students, post-docs, and interns, with many alumni now in permanent research or teaching positions. It has maintained active collaborations with industry (e.g. Meiogenix) and public research partners (INRAE), especially in the context of plant breeding. Its involvement in Exposcience and open days has enhanced its public visibility. Members have also contributed to national clinical research networks in telomere biology and cancer.

Context-related weaknesses and risks

None

ANALYSIS OF THE TEAM'S TRAJECTORY

The team has closed following the retirement of its group leader. The restructuring under two new PIs builds on the team's remarkable scientific legacy and has been well anticipated and prepared: an ERC starting grant, the existing collaborations and the critical mass of permanent staff provide a robust foundation. The strategic refocusing on meiotic recombination and polyploid adaptation will ensure both thematic coherence and international competitiveness.

The restructuring has been carefully designed to ensure thematic continuity while refocusing the scientific objectives on meiotic recombination mechanisms, integrating complementary expertise and leadership.

RECOMMENDATIONS TO THE TEAM

The team has played a foundational role in establishing Clermont-Ferrand as a recognized centre for research in recombination and genome integrity. Its scientific program has evolved over three decades to cover multiple aspects of DNA repair, meiotic recombination and telomere biology. Recent work has delivered mechanistic insights into meiotic DNA synthesis, RAD51/DMC1 regulation, and telomeric CST function, while maintaining strong activity in polyploidy and recombination control. The committee warmly acknowledges the outstanding contributions of the PI and his team to the field of genome stability and recombination.

Team 8: Meiosis, Recombination and adaptation
Name of the supervisor: Mr. Olivier Da Ines/Ms Heidi Serra

THEMES OF THE TEAM

This newly formed team emerged from the restructuring of the former team 'Recombination and Maintenance of Genome Stability'. It investigates the molecular mechanisms of meiotic recombination, a key process in sexual reproduction and genome evolution that ensures proper chromosome segregation and drives genetic diversity. Using diploid and polyploid *Arabidopsis*, the team explores how genetic and epigenetic contexts shape partner choice during meiosis. Combining molecular genetics, cytogenetics, epigenomics, and quantitative imaging, the research aims to reveal how recombination is regulated in diverse genomic settings, including allopolyploids, bridging fundamental and applied plant science.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

This is a newly established team, created in 2024, following the closure of one team after the retirement of the PI. No previous Hcéres recommendations apply.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	5
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	1
Post-doctorants	1
Doctorants	2
Sous-total personnels non permanents en activité	4
Total personnels	9

EVALUATION OF THE TEAM

Overall assessment of the team

The restructuring of the former team into this new team is well conceived. Building on strong foundations, the team has clear objectives and an ambitious research programme. The leaders bring complementary expertise in meiotic recombination, genome stability, and polyploidy. An ERC starting grant and international collaborations provide visibility and solid funding, positioning the team as a future leader in plant meiosis and recombination.

Context-related strengths

The creation of this new team represents an opportunity to consolidate expertise and increase international visibility. The award of the ERC starting grant to one PI provides significant prestige, autonomy and a stable funding base for the coming years. The team benefits from five permanent researchers (three HDR), ensuring a strong backbone for scientific and training activities. The group has already built international collaborations with key meiotic recombination laboratories (Cambridge, Vienna, INRAE), and enjoys high recognition through invited presentations and editorial activity. The combination of ERC funding and international partnerships makes the team highly attractive for postdoctoral researchers and students.

Although recently restructured, the team inherits an excellent publication record. Recent work has contributed major insights into RAD51/DMC1 regulation, meiotic stability in allopolyploids, and homoeologous recombination in wheat. Members have published in highly regarded journals such as *New Phytologist* and *PLoS Genetics*. The integration of an ERC-funded project and collaborations is expected to sustain a high level of scientific output. The team has already demonstrated its capacity to tackle both mechanistic and evolutionary questions with cutting-edge approaches.

The team has strong involvement in teaching and training. Three HDR holders contribute at Licence, Master and Doctoral levels, complemented by a lecturer with a significant teaching load. The team actively trains PhD students, postdocs and interns. The team engages in outreach through participation in Exposcience events, hosting school groups, and interacting with industry (e.g. Meiogenix, Inrae). Its work on polyploid crops has clear translational relevance for plant breeding.

Context-related weaknesses and risks

The team will have to ensure long-term funding balance beyond the ERC grant and maintain its high attractiveness once the initial boost from the grant fades. As a young team, consolidating its international visibility will be important.

The dual leadership structure, while synergistic, will require careful management to maintain a coherent strategic direction.

The team has inherited an excellent publication base, but its scientific identity as a newly established group still needs to be fully asserted.

Industrial collaborations are promising but still limited in scope.

ANALYSIS OF THE TEAM'S TRAJECTORY

The trajectory of the team is well defined, scientifically ambitious and strategically aligned with its core expertise. It is structured around three complementary axes.

The first focuses on the molecular mechanisms of strand invasion and partner choice during meiotic recombination, dissecting RAD51/DMC1 activities and chromatin context effects using molecular, biochemical and single-molecule approaches. The second explores how recombination is regulated in allopolyploid *Arabidopsis suecica*, aiming to elucidate the mechanisms that prevent homoeologous exchanges and enable rapid meiotic stabilization. The third axis extends this work to wheat, addressing the control of recombination under environmental constraints in a crop context.

This program is supported by a solid funding structure, with an ERC starting grant as its backbone, complemented by EMBO and I-SITE funding and several national and international collaborations. The team benefits from strong expertise, state-of-the-art infrastructure, and recognized international partnerships. The clear articulation between axes provides scientific coherence and strong potential for impact. Overall, the team's trajectory positions it to become a reference group in plant meiosis research.

RECOMMENDATIONS TO THE TEAM

The committee encourages the team to build on its strong start to rapidly assert its scientific identity as a new research entity. Continuing publication in highly regarded journals under the new team identity will strengthen visibility.

Efforts should focus on consolidating funding for all axes beyond the ERC and ensuring thematic coherence between axes. Ensuring focus and cohesion between mechanistic and polyploid axes will be essential to avoid thematic dispersion.

Expanding structured partnerships could help consolidate the non-academic impact and enhance funding diversity.

Team 9: Nuclear Receptors and Pathophysiology
 Name of the supervisor: Messrs Silvère Baron/Jean-Marc Lobaccaro

THEMES OF THE TEAM

The team investigates pathologies involving sterol metabolism and lipid-sensitive nuclear receptors in prostate and ovary diseases. The team is focusing on the mechanisms linking metabolism, endocrine responses and disease development, targeting liver X receptors (LXRs) alpha and beta as well as sterol-interacting proteins such as scavenger receptor B1 (Scarb1) and tetraspanins (TSPAN).

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

a) *Maintain its visibility by publishing its research in non-specialized journals with a broad audience.*
 The team has published articles in high-ranking journals (Nature Comm and PLoS Biology)

b) *Caution should be taken to use the Drosophila accessory gland as a model of prostate cancer, focussing on LXR as the main (only) regulator of cholesterol metabolism should be reconsidered.*
 The team's findings confirm that cholesterol metabolism and the ecdysone pathway play a crucial role in the development of cancer in Drosophila.

c) *Adapt the proposed projects to the size of the team and reconsider (reduce) the emphasis placed on new LXR ligands.*

A private partnership has been developed with a start-up company to support the team's activities in this area.

d) *Secure grant money beyond 2020.*

The team has received several grants that provide some security.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maitres de conférences et assimilés	4
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	10
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	0
Post-doctorants	1
Doctorants	4
Sous-total personnels non permanents en activité	5
Total personnels	15

EVALUATION OF THE TEAM

Overall assessment of the team

The team's research focuses are of great interest in a highly competitive environment. The team has a very good to excellent scientific production but needs to increase its international visibility by being more present at conferences and developing new and original models. The team's non-academic activities are excellent with a strong non-academic contribution: a joint venture has been set up and a patent has been filed. Outreach activities are also excellent, with a large number of conferences for lay people.

Context-related strengths and opportunities

The team has overall an excellent visibility and attractiveness.

The team is very visible and attractive to students and postdocs, including those from abroad: nine PhD students were supervised in the reporting period and four are expected to complete their doctorates beyond 12/2024, five were the first authors of publications and one postdoc was employed until 2026. The team consists of eleven full-time members, including professors, researchers and technical staff, and was expanded by two new members in 2021.

The team received grants from national authorities and charities, participating in European research networks and fostering university-industry partnerships (3 INCa PLBIO, one as coordinator) and from charities (8 La Ligue contre le Cancer, 6 as coordinator and 3 ARC). The team also participates in a European MSCA PhD network. Notable successes include the 'Innovation grant award' (100k€) and the 'Eliane and Gérard Pauthier Foundation prize' (30k€). The team has participated in six conferences/seminars and is involved in various national and international networks, e.g. the European Network for Oxysterol Research, Cancéropôle Lyon Auvergne Rhône-Alpes, Groupe Cancer Clermont Auvergne.

On an international level, the team collaborates with institutions in Belgium, Italy, the USA, Norway and in the UK. Two doctoral students have received awards for their work. The team members take on important tasks at local, national and international levels, e.g. leadership roles in clinical departments, higher education councils and scientific advisory boards. Remarkable is the strong involvement of one of its members in the Italian education system with high responsibilities.

The team has a very good to excellent scientific output with many years of expertise in deciphering the machinery involved in prostate and ovarian diseases, with a focus on sterol metabolism and lipid-sensitive nuclear receptors. In total, the work resulted in 39 publications, ten of which as first/last co-authors, the rest in collaboration. Of these ten, three have been published in excellent journals (Nat Comm, PLoS Biol., Oncogene). Collaboration with international teams is very active and has resulted in a high number of publications.

Each of the scientific axes has led to at least one publication: (i) Work on cholesterol sensing and PCa development has led to the conclusion that LXRs can alter the expression of factors in the EMT and control the expression of 'aggressive' factors; (ii) In collaboration with laboratories in Norway and the USA, they have identified dioxin as a chemical that increases the invasive potential of prostate tumor cells and is linked to the ACAT1 gene; (iii) They developed a *Drosophila melanogaster* model to study early epithelial carcinogenesis in the prostate equivalent and shed light on the role of MAPK/PI3K signalling pathways and cholesterol metabolism in tumorigenesis as well as the ecdysone signalling pathway as a molecular switch in carcinogenesis; (iv) In collaboration with physicists, the team is investigating the use of cold plasma as a potential treatment for prostate tumors and has achieved promising results in both cell cultures and preclinical models; (v) The LXR signalling pathway plays a crucial role in the ovarian response to hormones. LXR deficiency in animals shows similarities to PCOS in humans, including a high risk of overstimulation during fertility treatments; (vi) The team has used in-silico docking to identify flavonoids as potential LXR ligands and has developed and characterized several promising molecules, while also exploring natural extracts as a source of new ligands.

The team's non-academic activities are excellent. The team has partnered with the Greentech society for the 'XBioRepair' project to identify natural plant extracts that can modulate LXR activities, with Greentech focusing on tissue repair and the team exploring potential clinical applications. In addition, in collaboration with Institute Pascal, the INCa PLBio Pepith project has optimized the cold plasma treatment of prostate tumors and significantly improved its efficacy in killing tumor cells. This progress has led to a patent for the cold plasma treatment device, which represents an important step towards the clinical application. In addition, the team is strongly committed to science popularization and interaction with the local public (*The precision medicine:*

issues and controverses, seminars cycle for high school students UCA. 2024, Le "moléculaire" dans les nouvelles thérapies : enjeux et controverses, 2024, Le cancer : on en parle, shortcuts projection and round table November 2023, Plantes, fruits et décoctions...la sorcellerie au service de la santé, Fêtes de la Science 2023...).

Context-related weaknesses and risks

Since the team is mainly composed of members with important teaching or clinical activities, it is important that the co-PIs and members find a way to join forces for concrete, profitable and original projects avoiding too much dispersion of projects. This will result in more visibility.

Because of the important teaching activities, team members have limited time for meetings. It is however important that the team was present in key national or international meeting to present the work and strengthen the collaborations.

The team has increased the quality of its scientific work by publishing several articles in excellent journals (Nature Com., PLoS Biol., Oncogene). However, many articles were also published in journals with a lower impact.

The *Drosophila* accessory gland model is original and powerful as it enables high-throughput screens and precise mechanism identification. The partnership with the GreenTech society is a strong added value and should be pursued further.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team is restructured, with a new co-PI taking over the management, the previous PI stepping down to take on new tasks and the other co-PI taking on local tasks.

The scientific project will be narrowed down and focus mainly on the role of sterol metabolism and LXRs in particular. The project will be divided into two different axes: 1) investigation of sterol signalling metabolism in both prostate tumor and immune cells as a potential therapeutic option in advanced prostate cancer and 2) to investigate the role of LXR signalling and cholesterol homeostasis in the interplay between granulosa cells and immune infiltrate in polycystic ovary syndrome.

The first axis is divided into 4 tasks and the second axis into two. Each task is associated with several (2 to 4) team members. Technicians and non-permanent members are not mentioned, which makes the assessment of feasibility difficult. Some tasks are collaboration with foreign laboratories. The team mentions the heavy reliance on mouse models as a threat and the development of organoids and tumoroids as an opportunity. However, there is no explicit mention of the extent to which these, ex vivo approaches represent a real opportunity to simplify the approaches. There is also no mention of expanding and refining the use of the accessory gland of *Drosophila*. Similarly given the huge expansion of single cells and spatial approaches, it is recommended that the team adopt these approaches, master them, and use them to their advantage in their research, while also making them available to the community.

RECOMMENDATIONS TO THE TEAM

Due to the change in team leadership, care should be taken to ensure that this transition phase takes place under the best possible human and scientific conditions. Care should also be taken to ensure that the international collaboration, which is usually led by the previous PI, continues.

The team should elaborate on how to develop original and competitive research in a field that is itself highly competitive. In this respect, the development and validation of the *Drosophila* intermediate gland model, the possibility of developing organoids and tumoroids and the partnership with the private company to discover new and active compounds will be a strong added value.

As prostate cancer is a highly competitive field, the team should use its recent discoveries and model development to strengthen its international visibility.

The team should adopt and further develop omics approaches to better define their biological models and find putative new mechanisms.

The team should continue to raise its level of publication and avoid predatory journals or journals with a low-impact factor as much as possible. The team should find a balance between the number of publications and the quality of the journals. The use of MDPI 'predatory journals' such as 'Cancers' is also not recommended.

Research funding has been excellent but large grants have been mainly obtained with the INCa PLBIO. Based on their national and international collaborations and on their research projects, it could be advised to diversify the sources of funding to ANR and to European and international calls.

The partnership with the GreenTech Society represents great added value and should be continued.

Team 10: Translational Approach to Epithelial Injury and Repair
 Name of the supervisor: Messrs Loic Blanchon/Vincent Sapin

THEMES OF THE TEAM

The team studies the pathophysiology of frequent diseases (acute respiratory distress syndrome and premature rupture of foetal membranes) directly linked to injury of the epithelia barriers (lung and fetal membranes), with diagnosis, prognosis and therapeutic perspectives. New types of injury including volcanic emissions, anesthetic gases and pollutants are studied.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

1- The integration of the team in iGReD may be a fantastic opportunity for other iGReD teams that need access to patient material.

The team interacts with other teams working on human pathologies, and played an active role in preparing the integration of the clinical team.

2- The committee was slightly concerned about the quality of training the PhD students regarding fundamental research. The committee considers it unlikely that the hospital practitioners will find sufficient time for daily supervision of the students. There is one postdoctoral researcher in the team, and the committee considers that it is not sufficient.

This has been partly addressed, with the last PhD students having published articles, with co-supervision arrangements with scientists when necessary. Two post-docs have been recruited.

3- A senior MD-PhD, strongly involved in the team's past publications, has left the team. This is considered a significant loss.

The team has anticipated his departure to assure a continuity of the lung axis with a PI who obtained funding (ANR, Messidor, PHRC), supervised PhD students (3) and published articles. The team also recruited a new MCU-PH, a PH, a CNRS researcher and a technician shared at 50% and 30% respectively with the Laboratoire Magmas et Volcans.

4- It is strongly recommended that the team hires at least two, or more, fundamental scientists.

Two CNRS researcher at 50% and two postdoctoral researchers have been recruited.

5- Finally, the committee advises the team to increase the number of women among permanent staff.

The team has recruited 3 women reaching 45% of women.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	6
Maitres de conférences et assimilés	5
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	14
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	0
Post-doctorants	1
Doctorants	5
Sous-total personnels non permanents en activité	6
Total personnels	20

EVALUATION OF THE TEAM

Overall assessment of the team

The team research activities are very original and of major interest, with a very good to excellent (fundamental research) and excellent (clinical) scientific production, with national and international collaborations. The strong insertion in the clinic and the ability to lead clinical trials is a force. Insertion in the local and national framework and in education and training is also globally excellent. The link with the private companies may be improved to achieve the goals of the team to develop new tools for the clinics. The team attractiveness has been excellent and must be pursued to increase its international visibility and scientific production in fundamental research.

Context-related strengths and opportunities

The team visibility and attractiveness are excellent. The team is large with 26 persons, most of them with clinical duties. The team comprises six PU-PH, four MCU-PH, one senior lecturer (co-team leader), only one researcher CNRS at 50% (shared with Laboratoire Magmas et Volcans), one engineer, one technician at 30% (shared with Laboratoire Magmas et Volcans), one post-doc and nine PhD students. Another CNRS researcher at 50% has been recruited in 2024, which reflects an excellent attractiveness. The attractiveness for young researchers is globally excellent with 7 PhD thesis supervised (students of both medical and scientific background) and five that are ongoing, and good for post-doc with two post-docs hired during the period.

The team has a strong capacity to lead clinically oriented, translational and basic research projects, with 8 persons with HDR. The funding capacity of the team's project is excellent with local (Region, I-SITE), national (ANR DGOS, Messidore Inserm) and European (Horizon, Feder), foundations (FRM, Fondation du souffle) and clinical grants (PHRC) (total ~1.1 million euros per year). Funds are also obtained from private companies (Thea company).

The team also participate to international meetings organization (world foetal membranes). Communications and invited conferences are absent from the report.

Several team members have strong administrative responsibilities at the UCA (vice-dean, international relationship department, Carma platform), the hospital (vice-president of DRCI), are experts for the CNU (3), the Hcéres (2), the European medicine agency, the Inserm (Messidore), and international associations (IAVCEI, Francophonie federation of clinical biology).

The team has a very good to excellent (fundamental research) and excellent (clinical) scientific production, with 170 articles among which 46 research articles (25 as first/last/corresponding author, seventeen signed by the PhD students, four with international collaborators) with some in excellent and very good journals (Elife, J Translat Med, Respiriology, PLoS Biology, Sci Rep...), and 107 clinical articles (35 with the PhD students), with seventeen reviews/book chapters (14 as first/last/corresponding author, in Curr Opin, Clin Chem, J Clin Med, ...). All PhD students have been published in international journals.

The team has a long-time recognized expertise on the pathophysiology of lung and foetal membranes involving injury of the epithelia barriers, and their environmental causes (ash, gases, pollutants). The team has international collaborations on both the lung and the foetal membrane axes. The team has a very strong clinical anchorage and national and international collaborations and funding which contribute to its strong production with some high-level articles.

During the last period, the team has been strongly invested in the development of the volcano axis, a very original and dynamic interdisciplinary research project on the study of the effects of volcanic emissions on lung pathophysiology. The team develops it in collaboration with the magma and volcano laboratory LMV at UCA with which a CNRS researcher and a technician are shared, with several funding obtained (1 post-doc recruited during the period, with 2 new PhD students) and 5 articles published (Sci Rep, Nat Comm...). An original equipment (CelTox sampler) has been acquired to study the effects of ash, gases, pollutants on lung epithelial membranes at air-liquid interface. It constitutes an excellent opportunity to develop collaborations and attract researchers.

The research axis on the acute respiratory distress syndrome (ARDS) has had an excellent scientific production both at the basic (Sci Rep, J Vis Exp, Exp Cell Res, J Transl Med..., signed by the PhD students) and clinical side

(J Clin Med...) with international collaborations and clinical trials with CHU. One post-doc has been recruited and new *in vitro* and *in vivo* animal models (transgenic mice, piglets) have been developed to pursue the study of RAGE and sevoflurane in ARDS illustrating the excellent dynamic of this project.

The research axis on foetal membranes also had an excellent scientific production in the field of pregnancy and inflammatory response (Frontiers Immunol...), and on the negative influence of environmental pollutants (IJMS, Life, env exposure...). Besides to these works that involve both basic *in vitro* models and clinical studies during pregnancy, a very interesting work on the precise mapping of DNA methylome and transcriptome in human foetal membranes at terms of pregnancy (eLife 2022) opens avenues for future research. Clinical studies with international collaborators are also developed.

Educational involvement of the team is excellent with several members strongly involved at UCA in medical and scientific programs (with the responsibility of the Pass/Las at the medical school) and training (8 HDR, 12 PhD students during the period).

The team regularly participate to communication events to the general public, patients and society, and participate in the organization of Faculty open days.

Context-related weaknesses and risks

With the exception of two CNRS researchers at 50%, one lecturer and a few technical staff, all senior team members have important clinical duties, leaving little time for research.

The team mentions few interactions with private companies and no patent.

ANALYSIS OF THE TEAM'S TRAJECTORY

The scientific project proposed is in the continuity of the previous project is in line with the expertise of the team. It is focused on ARDS and premature rupture of foetal membranes (Prom) implementing the new knowledge and technologies acquired during the last contract. The project comprises three axes.

The first axis is on foetal membranes aggression by pollutants (phthalate, plasticizers) leading to Prom. The team plan to study the signalling pathways involved in response to pollutants in several cell types using fetomaternal organ on Chip (reproducing *in vitro* the complexity of this tissue in collaboration with a world expert in the field from USA). The study will be extended to clinical samples of the CHU, and collaborations with experts in bioinformatic (Lilles) and more originally with a laboratory « Activité, Connaissance, Transmission, éducation » (ACTé) will be developed to collect data from pregnancy women and develop prevention actions.

In the second axis, the team will pursue the study of epithelia pulmonary aggression by volcanic ash and gases, implementing the study of immune cells and signalling pathways modulated in the *in vitro* model developed.

The third axis on ARDS is also in the continuity of the previous work of the team, and will focus on the study of the interactions between alveolar epithelial cells and their microenvironment, particularly monocytes and macrophages, using 3D *in vitro* models and animal models (mouse, piglets). The team plan to pursue clinical studies on ARDS with national and international partners, and aim to develop ARDS biomarkers to create prognostic and predictive tools for a future European clinical trial.

The participation and role of senior members of the team to each project is not mentioned in the report, which made it difficult to assess how projects will be implemented.

RECOMMENDATIONS TO THE TEAM

As almost all of the seniors have clinical duties, except two CR CNRS at 50% and one lecturer, efforts must be pursued to attract post-docs and recruit full-tenured researchers/teachers to strengthen a high-level scientific production in basic and translational research, to sustain PhD supervision in the laboratory and develop interactions with other iGReD teams.

Collaboration with private companies may be strengthened to favour technological innovations and valorization for diagnosis and clinical applications.

Considering the originality of the research and the recent development of interdisciplinary projects and collaborations (volcanic emissions, 3D models), the impact of the publications and the international visibility of the team should be increased.

The team should integrate national and international consortiums on phthalates for better visibility and international collaborations.

Several projects involve the study of immune cells, which may require a strong immunology expertise in the team and/or collaborations with laboratories of immunology.

Team 11: Molecular Pathophysiology of Adrenal and Endocrine Tissues
 Name of the supervisor: Messrs Antoine Martinez/Pierre Val

THEMES OF THE TEAM

The team studies the molecular pathophysiology of adrenal and gonadal tissues, and uses preclinical models to study signalling pathways controlling differentiation, plasticity and carcinogenesis.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has taken into account the two main recommendations raised from the previous report.

The first one concerned the use of alternative models beyond mouse genetics (e.g., iPSC-derived organoids). The team has initiated a new collaboration with a team expert (iBV Nice) to differentiate ES cells and iPSC into functionally adrenal cells.

The second recommendation concerned the implementation of single-cell omics to analyse mouse models in greater detail. This has been successfully addressed in the past four years with the use of scRNA-sequencing and spatial transcriptomics to investigate adrenocortical carcinoma progression and treatment response. In addition, collaborations with leading experts in the field (Univ. of Geneva, Institut Cochin) have been developed.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

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

EVALUATION OF THE TEAM

Overall assessment of the team

The team basic and cancer translational research axes are of major interest and at the cutting-edge, with an excellent international visibility and an excellent scientific production. The team is well funded and its trajectory is in the perfect continuity of its current high-level research. The link with the society and private companies could be improved with regard to the potential of the team projects. The team needs to recruit to face the retirement of 3 seniors/PIs in order to maintain its excellent scientific activity and international visibility.

Context-related strengths and opportunities

The team visibility is excellent. The team has an excellent and internationally recognized expertise in pathophysiology of adrenal and gonadal tissue and adrenocortical tumorigenesis. The team has a strong clinical anchorage and insertion in research networks and an excellent capacity to collaborate. They use and develop original Gemms to model the pathophysiology and tumorigenesis, which contributes to its high-level production and national and international reputation. The excellent international recognition of the three senior members is as also attested by 23 invitations to national and international conferences among which eleven abroad. The funding capacity of the projects has been significantly increased since 2020 and is excellent, with funds from ARC, ANR (3), FRM, FdF, Groupama, Ligue contre le Cancer covering all the projects proposed for the next period at least until 2027.

The composition of the team is well equilibrated with fourteen persons including two DR CNRS, three PU/MCU, one PU-PH in endocrinology, one IR with HDR, two post-docs and two PhD students. The team has a strong capacity to lead research projects with six full-time tenured researchers possessing the HDR. The attractiveness for young researchers is excellent regarding the size of the team with a total of five post-docs and eight PhD students hired during the period.

The publication activity is original and excellent with 21 articles published since 2019, including nine in first/last/corresponding authors, often published in high-ranked leading journals (JCI, Nature Communications, J invest dermatology, Sci Advances), with eight including the PhD students among which six signed as first author. sixteen articles among the 21 are co-signed with international collaborators, highlighting the impressive international visibility and collaborative capacities of the team. The team has also published six reviews among which five as the first/last/corresponding author.

The team has a long-lasting expertise in deciphering the signalling pathways and molecular mechanisms regulating adrenal glands and gonadal homeostasis, endocrine pathologies and tumorigenesis. The two research axes of the team are productive in terms of scientific advances and publications. In the first axis on the mechanisms controlling adrenocortical zonation and maintenance of gonadal identify, the team has demonstrated the key role of SumOylation in maintaining adrenal cortex homeostasis and regulating hormonal adaptation to stress (Nat Commun 2022) and of the role of PKA and Wnt4 pathways in testis tumorigenesis (JCI 2022). In the second axis, using multi-omics analyses on original Gemms of adrenocortical carcinogenesis, the team has demonstrated that the sexually dimorphic activation (by testosterone) of innate antitumor immunity (macrophages) prevents adrenocortical carcinoma progression by acting on DNA repair mechanisms to clear antitumorigenic senescent cells and restore antitumoral immunity (Sci Adv 2022).

Context-related weaknesses and risks

Among the six senior researchers/teachers with the HDR, three will retire during the next contract, including the PU-PH in endocrinology. This will impact on the team capacity to recruit PhD students and to the link with the clinic for translational research.

Two of the three seniors signing the articles as last/corresponding authors will retire during the next contract. These two PI coordinate the two projects of the axis 1 for the next contract.

Multi-omics data analyses seem to rely on non-permanent staff members.

Despite the originality of the research and the excellent international visibility of the team in its research domain, there is no European funding, no patent, no clinical publication and no private contract with industry.

ANALYSIS OF THE TEAM'S TRAJECTORY

The scientific project proposed is perfectly coherent and in continuity with the projects of the current contract, fully aligned with the recognized expertise of the team. It comprises the same two axes, each with two research projects, each project being currently well funded with national and/or internationally established collaborations, and with sufficient manpower (including 1 PhD student or 1 post-doc in each) despite the risk linked to the retirement planned for the two PI heading axis 1 and the uncertain recruitment of the post-docs proposed for a future tenured position.

The first axis focuses on mechanisms of sexual dimorphism in adrenal cortex homeostasis (AR-Myc axis) with a project on androgen receptor signalling and myc in transgenic mice, and a second project on SumOylation modulation extended to other pathologies including polycystic ovary syndrome and primary ovarian and adrenal insufficiencies.

The second axis on adrenocortical tumor initiation and progression, contains one project on the antitumor action of testosterone and a second project on the improvement of the anti-tumor immune response, in the continuity of the recent publications of the team.

RECOMMENDATIONS TO THE TEAM

The team must develop strategies to attract and recruit full-tenured researchers/teachers to balance the three seniors' retirements during the next contract, including two main PI of axis 1 and the Professor-Hospital Practitioner head of the department of endocrinology to ensure the continuity of this translational research. Care should also be taken to maintain a good capacity to train PhD students, as the three seniors that will retire are holding HDRs. Notably, one lecturer has been recruited in 2023, which may help counterbalance the ongoing retirements.

The team leader should also encourage/support the young lecturer recruited to obtain the HDR to supervise PhD students, to apply to grants, to develop/fulfil collaborations and progressively reach a PI position.

The team should apply to European funding, and develop links with private companies for technological innovation, patent development and valorization.

Team 12: Environment, Metabolism, Spermatogenesis, Pathophysiology and Inheritance

Name of the supervisor: Mr. David Volle

THEMES OF THE TEAM

The team studies the Liver-Intestinal Microbiota-Testis (LIMiTe) axis and its role in male fertility and metabolism. They showed that bile acids, produced by the liver and converted by the gut microbiota, are key regulators of testicular homeostasis. They investigate how xenobiotics and metabolic changes disrupt endocrine function, germ cell development, fertility and how such disturbances may cause infertility, inherited defects, or testicular tumors. The project combines basic and clinical research to open new therapeutic perspectives.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Previous recommendations were:

1- 'The team should strengthen international collaborations. The PI should not dissipate his energies in side activities, but rather keep his mind on its research interests. He may benefit from mentoring by senior scientists from another axis or from outside the unit.'

2- 'The proposed project appears quite ambitious given the experience of the PI. The committee encourages the PI to concentrate on selected questions where competition is reasonable and for which he possesses the required expertise and tools, with aim to go as deep as possible in mechanistic analyses. Accordingly, the nematode model should be taken with caution given the huge differences existing with mouse/human germ cell physiology'.

The team reinforced its international visibility and sharpened its scientific focus. With the mentoring, the PI concentrated his efforts on research, leading to publications in high-level journals (Advanced Sciences, Environ. Int.), success to several highly competitive grants as coordinator (2 ANR, 1 ANR JCJC, plan cancer) and recruitment of a talented researcher and attractiveness for young researchers (postdoctoral researchers and PhD student). The team focused its strategy mainly on the original LIMiTe axis, shifting from broad exploratory approaches to in-depth mechanistic studies on bile acids and male fertility. More relevant cellular and translational models than the nematode have been implemented, such as spermatogonia cultures, transplantation assays, and iPS approaches. In parallel, the team has strengthened the project's visibility and collaborative dimension by organizing an international meeting and establishing clinical research networks to foster the translation of its findings into clinical practice.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maitres de conférences et assimilés	2
Praticiens hospitaliers	0
CCA	0
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	8
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	0
Post-doctorants	2
Doctorants	2
Sous-total personnels non permanents en activité	4
Total personnels	12

EVALUATION OF THE TEAM

Overall assessment of the team

The team has an excellent international recognition for its work on the LIMiTe axis, male fertility, and environmental impacts on spermatogenesis. The scientific production is very good to excellent with strong funding. Educational/outreach activities reflect excellent visibility and attractiveness. The team should continue to develop and strengthen international collaborations through joint publications and international project calls. Priorities include securing expertise for some proposed projects, and engaging with private partners to enhance translational impact.

Context-related strengths and opportunities

The team has an excellent visibility and national and international recognition in the fields of integrative physiology of male fertility, spermatogenesis and the study of their molecular and cellular mechanistic aspects with liver bile acids metabolism and exposure to environmental molecules (including anti-cancer drugs and metal-rich pollutants). The bile acids and xenobiotics receptors as well as spermatogonial stem cells are studied in testicular pathophysiology using in vitro and mouse models.

The team is composed of eight persons with permanent positions including a research director (the team leader), a full professor, an assistant professor, a researcher at 50%, two engineers (one at 50%), two technicians (at 50% and 25%), with postdoctoral researchers (2) and PhD students (2). The team has had an excellent attractiveness during the last period with (i) the training of six PhD students which is impressive for only two PI with the HDR (including the team leader and one professor), and (ii) the recruitment of an excellent young researcher with a tenured position (CNRS researcher) who got a competitive national grant (ANR JCJC) and currently co-supervise a PhD student with the two PI. A technician (at 25%) from UCA also joined the team recently. The team also recruited other post-docs (2) and attracted candidates for Inserm and CNRS researcher competition, which is an excellent proof of attractiveness and dynamism.

The team is very well funded with national grants as coordinator (3 ANR, plan Cancer), European funds (Feder, CPER) and locoregional grants (I-SITE UCA, canceropole) notably with charity associations (Ligue, ARC); eight are ongoing, which is excellent. The excellent international visibility of the team is attested by numerous (13) invitations to give conferences to international meetings including prestigious conferences (Gordon's conference) and by organization one of them (1st spermatogenesis fusion conference, 2023), the membership of three European research networks (Cost, Enor), expertise for international committees (including the IARC), several publications with international collaborators (Adv Sci 2022, Nature Comm 2022), European funds (Feder, CPER) and a recent grant with international collaborators (ANR JCJC) which is an excellent evolution and dynamic for the team. Several team members hold expert roles in international (IARC monographs), national (Hcéres, INRAE, CSS Inserm, ANR, INCa, PEPR), and regional (including ethics) scientific evaluation committees, as well as on editorial boards, serving as editors or guest editors for four high-quality journals, an accomplishment that is especially noteworthy.

The team scientific production is very good to excellent. The team published eighteen original scientific research articles among which twelve as first/last/corresponding author, some of them in high-level journals (Adv. Sci., Environ. Int.). Eight articles are co-authored by the PhD students among which five signed as the first author. Each PhD student over the last period has published articles as the first author. It should be noted that six of the seven articles co-authored with international collaborators were produced by the recently recruited young researcher. The team also published seven reviews and book chapters as first/last/corresponding author. No clinical articles are reported.

The team is strongly integrated into the University's educational programs, with two senior scientists leading teaching and pedagogical initiatives. The team excels in public engagement, including media outreach, science festival organization, activities for young audiences, and press releases.

Context-related weaknesses and risks

Despite strong involvement in international evaluation committees and scientific networks, the team has produced few publications co-authored with international collaborators, apart from one and those of the newly recruited permanent researcher.

There is a risk of reduced capacity to remain both cutting-edge and productive across all topics. Additional concerns relate to increasing difficulties in working with animal models, and the necessity to develop alternative approaches. Such alternative approaches (iPSC-derived germ cells, mouse-derived cultures, organoids) require advanced expertise that must be secured within the team.

There is an uncertainty about some of the projects as depending on getting the ERC starting grant.

The team currently holds no patents and has no contracts with private companies.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team's trajectory is focused and in direct continuity with its current projects and expertise. All projects are funded.

The Liver-Intestinal Microbiota-testis axis comprises 3 ambitious projects with the final expectations to develop novel disease biomarkers and targeted treatment strategies for metabolic diseases, fertility disorders and testicular germ cell tumors.

The first project is on germ cell analysis, in continuity with the past projects and with high-level international collaborators (USA) and newly established clinical collaborations with the hospitals of Grenoble and Clermont-Ferrand. The second project is on bile acids metabolism, a long-time expertise of the team, produced by the liver or intestinal microbiota in collaboration with EPFL Switzerland, Lilles and a Clermont-Ferrand laboratory expert in microbiota. The third project on the impacts of environmental pollutants, including perfluorinated compounds (with an ANR and an ARC grant and a 3-year post-doc wishing to apply for a tenured research position), and metallomic deregulation (by the recently recruited CNRS researcher with an ANR JCJC grant) on the liver-testis dialogue in collaboration with international (Peru, Spain), national (ToxAlim Toulouse) and local partners (another IGRéD team and the Magma Volcan laboratory). The projects include the use of Gemms to target cells of the liver, the intestine and the testis either in physiological conditions or in pathological conditions (atmospheric pollutants, endocrine disruptors, antibiotics to modulate the microbiota, anti-cancer drugs) to study the impact on bile acids homeostasis, spermatogonia stem cells and finally germ cell cancer, infertility and paternal inheritance. Complementary *in vitro* models to study spermatogonia stem cells (cell lines, mouse-derived or iPSC-derived) are developed.

RECOMMENDATIONS TO THE TEAM

The primary recommendation for the team is to continue conducting excellent science on their LIMiTe projects, pursuing new interdisciplinary, clinical, and translational ambitions.

These projects are instrumental in helping the team establish a distinct scientific niche. To support future projects and ensure sustained productivity, the team should prioritize securing additional PhD students. The team should clarify the leadership and manpower of each proposed project, the implication of the technical staff (engineers and technicians of the team) as well as its recruitment strategy of researchers.

Building on its strong current activity, the team should continue efforts to develop and strengthen international collaborations through joint publications, and to apply for international calls of projects.

There is an uncertainty about some of the projects if the recently recruited CNRS CR succeed in getting an ERC starting grant (to start his own team).

The team should maintain its excellent outreach and communication with civil society, while ensuring the involvement of all team members in these activities.

Given the originality and potential of the team's research, and the recent attempts to establish clinical collaborations, efforts to engage with private companies—through contracts and patents—should be continued.

Team 13: Lymphoid cancers and therapeutic immunity
Name of the supervisor: Messrs Romain Guïèze/Paul Rouzaire

THEMES OF THE TEAM

The LYM-City team (Lymphoid Cancers and Therapeutic Immunity) originates from the EA 7453 Chelter unit and is set to be integrated into the iGReD UMR as part of the upcoming contract. The team's research projects were previously focused on exploring genomic markers of therapeutic resistance in chronic leukemias (Chronic Lymphoid Leukemia–CLL and Chronic Myeloid Leukemia–CML). They are now oriented toward investigating the mechanisms underlying the transformation of CLL into Richter syndrome, as well as developing a more technical axis centred on immune cell engineering.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Previous recommendations were:

a) The team needs to further increase the quality and amount of the scientific outputs of the unit, primarily the scientific research publications in hematology journals with higher impact (Blood and Leukemia). They also need to keep publication record in top clinical journals.

Over the past five years (2019–2024), the team members have contributed to a very substantial number of publications (424 co-authored publications). The team has notably increased its presence in high-impact journals in the fields of hemato-oncology including Nature Med. 2023, Blood 2023, Cancer cell 2019 and 2023, Nature Com. 2023, Blood can. disc. 2023, J. of Clin. Invest. 2023. In addition, the team has produced a significant number of clinical studies published in leading journals.

b) They should benefit from an increase extramural competitive funding and an increase in extramural non-competitive funding from pharma companies and bio-techs. They need to maintain and expand productive collaboration with top scientist experts in the different projects of the unit.

The team has secured substantial funding from both pharmaceutical companies and national research grants (2800k€).

c) They need to maintain and expand productive collaboration with top scientist experts in the different projects of the unit

The team has maintained a collaboration with a distinguished group (Dana Farber Cancer Institute, Boston) and initiated a new partnership with Oslo University Hospital (Norway, post-doc fellowship).

d) The team needs to increase the critical mass of the group by attracting postdoctoral researchers and to incorporate new PhD students in critical areas (bio-informatics, NGS). An increase in local visibility is strongly recommended.

The team has recruited a postdoctoral researcher and two bioinformatics analysts.

e) The team needs to keep and consolidate scientific projects focused on specific and inter-related projects (CML/CLL; epigenetics/telomeres in CLL/CML), but they should also expand to near areas of potential interest and complementarity (i.e., age-related epigenetic changes in CML/CLL development, immunology/microenvironment, etc.). Based on the data generated by the unit from the analyses of clinical samples, they should define new biological hypotheses and objectives that need to be explored in relevant experimental models of disease (genetic manipulation of CLL/CML cell models, animal models, etc.) either performed in-house or through external collaborations. Beyond the studies performed on tumoral cells, the team should add characterization of the microenvironment (bone marrow, lymphoid territories) in the different projects, as well as the role of immune cells in the development of the disease.

Projects linking CLL and CML focused on epigenomics, telomere maintenance and aging have been developed, alongside new research on the immune microenvironment.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	6
Maitres de conférences et assimilés	2
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	11
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels hospitaliers	9
Post-doctorants	2
Doctorants	3
Sous-total personnels non permanents en activité	14
Total personnels	25

EVALUATION OF THE TEAM

Overall assessment of the team

The team has undergone a strategic and well-considered restructuring, building on the solid foundations of the previous Chelter unit. A more focused scientific direction is planned, based on the team members' high-level clinical expertise and integrating emerging complementary topics. The scientific output is excellent. The clinical research output is outstanding. The team has strong industrial collaborations, delivers patents and has robust connections with patients and the general public. Joining the iGReD will enable more consistent scientific oversight. The team now faces the challenge of integrating into an institute composed of groups with a strong fundamental research orientation.

Context-related strengths and opportunities

The team demonstrates a high level of national and international visibility in the field of chronic leukemias. Its long-standing involvement in these areas is reflected in its leadership roles within major national cooperative groups. Furthermore, the recent selection of the team to join the Institut Carnot Calym further confirms its scientific credibility and translational potential. Several members hold prominent positions in national scientific societies and registries.

The team also maintains long-standing collaborations with leading institutions (Dana-Farber Cancer Institute, the Broad Institute), and has trained several PhD students abroad (Cornell, Glasgow, Oxford). The upcoming visit of a student from Melbourne (6-month research stay) illustrates the team's capacity to attract international talent. Notably, team members are regularly invited to international conferences.

The team demonstrates a strong academic and clinical integration (8 hospital-university investigators actively involved in teaching hematology). Two members hold strategic roles in national (CNU 82) and local (coordination of internship programs in hematology) academic structures. The presence of eight HDRs confirms the team's capacity to supervise doctoral research. Over the past five years, the team has hosted six PhD students and seven Master 2 students, primarily hospital-based physicians and pharmacists preparing for academic careers. This profile highlights the team's role as a gateway to faculty positions.

The scientific output is excellent for fundamental research and outstanding for the clinical research. Over the past five years (2019–2024), the team has demonstrated a remarkable scientific productivity, co-authoring a total of 424 publications, including 33 significant selected articles. These publications span both translational research and clinical studies, and many appear in high-impact international journals (*Nature Med.*, *Cancer Cell*,

Blood, *Blood Cancer Disc.*, *J Clin Invest*, *Nature Com.*). Toward these publications, team members have demonstrated high-impact contributions in the field of CLL and CML, Richter syndrome, and therapeutic resistance, strong international collaborations, through a multidisciplinary scope (genomics, immunotherapy, cell engineering, and clinical trials). Of note, PhD students have contributed as first authors of several publications.

The team maintains strong interactions with the pharmaceutical industry (6 early-phase clinical trials, phase III randomized studies for drug approval in haematological malignancies, national phase II investigator-sponsored trials including ancillary basic research topics). The team has contributed to three patents, including one in collaboration with the Broad Institute and another related to the Nutrireg technology, with potential applications in cellular immunotherapy and Car-T development. Public engagement includes participation in the Groupe Cancer Clermont Auvergne and organization of events such as public oncology sessions.

Context-related weaknesses and risks

While the team demonstrates strong attractiveness, particularly for students from clinical backgrounds (e.g. hospital physicians and pharmacists), this focus may limit its appeal to students from more fundamental scientific tracks. As a result, there is a potential risk of insufficient diversity in student profiles, which could impact the balance between translational and basic research activities.

While the team demonstrates high productivity, maintaining a balanced output between basic science and clinical research publications remains essential.

ANALYSIS OF THE TEAM'S TRAJECTORY

The Lym-City team originates from the Chelter research unit (UR 7453). As part of the upcoming strategic plan, the entire unit will be integrated into the iGReD Unit. This is a positive perspective, that should be of reciprocal benefits, adding strength to the clinical research at iGReD, and setting a favourable context to increase further the fundamental impact of the team's research.

The team has previously developed translational research programs focused on chronic leukemias, alongside clinical studies. Over the past five years, the team has expanded with new members and established long-standing international collaborations, while maintaining a strong national network of haematologists.

Integration into the iGReD represents a strategic opportunity to benefit from the expertise of its members, access advanced technological platforms, and pursue Inserm labelling. Leadership will transition to two professors, succeeding the actual DU.

RECOMMENDATIONS TO THE TEAM

Given the team's strong clinical profile, it is essential to ensure sustained output in basic or translational research and maintain a significant share of non-clinical publications.

Integration into the iGReD institute should be fully leveraged to reinforce fundamental research axes and foster synergies with other groups. Integration is also expected to increase visibility within academic research networks and attracting candidates with stronger backgrounds in fundamental sciences. Proactive strategies may be needed to ensure a balanced recruitment pipeline and foster interdisciplinary training environments.

To strengthen the diversity of student profiles and attract candidates from fundamental scientific backgrounds, it may be advisable for team members to increase their involvement in teaching activities within research-oriented master's programs. Such participation would not only promote the team's scientific activities more broadly but also serve as a strategic lever to encourage students from academic tracks to consider internships and doctoral training within the laboratory. This approach could contribute to a more balanced recruitment pipeline and foster interdisciplinary dynamics between clinical and fundamental research.

Additionally, careful selection of publication venues is advised, avoiding predatory journals, even on very rare occasions. It could be detrimental to the career prospects of students, particularly those aiming for hospital-university positions.

Finally, the team should be supported in increasing the proportion of full-time academic researchers.

Team 14: Differentiation of cell lineage in the early mouse embryo
 Name of the supervisor: Ms Claire Chazaud

THEMES OF THE TEAM

The team is working on the specification between epiblast cells (Epi) and primitive endoderm cells (PrE) and on the further differentiation of PrE cells. The cells from which the foetus develops originate exclusively from the epi-lineage. Within this context, the team is investigating two important biological questions: (i) how epi-identity is acquired during pre-implantation development and maintained during a specific physiological state, diapause; (ii) how the embryo continues to develop at the time of implantation by producing new tissue and forming the antero-posterior axis.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

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

a) consider a wider range of international funding, including ERC and HFSP

Such international funding was not acquired.

b) increase the publication rate

The publication rate is still low, but the work is of excellent quality and highly visible. Although the team is small, it has gained a new member, an assistant professor, who will strengthen the team and improve its productivity.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

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

EVALUATION OF THE TEAM

Overall assessment of the team

The team's lines of research are fundamental and use precise and innovative approaches to understand the early stages of mammalian development. Scientific output is excellent, and the team has established a strong network of collaborations leading to publications in excellent to outstanding journals. The number of grants is substantial (including the prestigious FRM label). The team has recently recruited a young scientist who will significantly strengthen the team's production potential.

Context-related strengths and opportunities

The team enjoys excellent visibility and recognition in developmental biology, attracting students and researchers. It has supervised three PhD students: two completed their theses (with first-author papers in preparation), and one is ongoing. Two permanent CNRS engineers contribute significantly to scientific output, including a first-author publication in *Nature Communications* (2022). The team excels in securing funding (2 ANR grants, one Inserm IRP, one FRM label, and two grants from the Regional League Against Cancer).

Its international reputation is evidenced by four invitations to prestigious conferences (Great Lakes Developmental Biology, FSSCR, Visegrad Group Society for Developmental Biology) and the organization of two international conferences: 'From Cell to Organism' (Paris, 2024) and 'Stem Cell Development and Cancer' (Lyon, 2022). The team leader is an elected member of Inserm's CSS1 (since 2022), former FRM Scientific Council member (2016–2020), Vice-President and President of the French Society for Developmental Biology (SFDB) (2021–2026), and President of Aurastem (2019–2023). The team leader also directs the SC3 iGReD facility. The recently recruited staff scientist (PO) co-directs the iGReD Bioinformatics Platform and participates in the Organoid Platform, while an engineer manages the single-cell facility (SC3 iGReD).

The team scientific output is assessed as excellent considering the high quality of the research delivered, but the rate of publication of team led research appears somewhat low. With a strong expertise in early molecular mechanisms of lineage determination in mammalian embryos, the team work on the transcription factor *Nanog* led to publications in *Nature Communications* (2022) and *Cell Stem Cell* (2021), with a manuscript in preparation. Progress has also been made in understanding epiblast and primitive endoderm cell maturation. In total, the team produced thirteen original publications: six by the team (2 as first/last author) and 7 by the recruited scientist (PO) during their postdoc. Publications appear in top journals (*Cell Stem Cell*, *Nature Cell Biology*, *Developmental Cell*). Despite its small size, it collaborates actively at national and international levels, resulting in high-impact publications. It also contributed to two reviews (*Methods in Molecular Biology*, *International Journal of Developmental Biology*), and PO served as guest editor for a special issue on epiblast cells (2022).

The team hosted a PhD student from the University of Polynesia and is committed to science outreach, engaging with schools, public conferences, and producing a film to explain its research.

Context-related weaknesses and risks

During the reporting period, the team published only two original publications (Development 2019, Nature Com 2022).

Two doctoral students defended without a first author paper. This is probably due to the lengthy and laborious procedures required to obtain and analyze early wild-type or transgenic mouse embryos.

The Nature Com publication was very well received, but was not sufficient to increase the team's international visibility. It is expected that the arrival of the young scientific collaborator will bring new forces and new approaches to the team and that he will be able to recruit students due to his position at the University. Given these weaknesses, the team has not applied for or received any European or international funding and has not recruited any post-docs.

Due to the small size of the team and the biological approaches based on obtaining early mouse embryos, one might think that the number of axes or sub-axes are high and there is a risk of dispersion.

ANALYSIS OF THE TEAM'S TRAJECTORY

For the next contract, the team will continue to investigate the mechanisms of epiblast specification. The team will also continue to study the differentiation of the extraembryonic endoderm, but will also extend its analysis to the specification of the anterior visceral endoderm. It will also include a new biological question on the role of Netrin1 (Coll. F. Laval, Lyon) in the pluripotent state. The specification of the epiblast and Netrin1 projects are funded by the FRM Label. The extraembryonic endoderm project is supported by an ANR.

The team is at the forefront of these biological issues and is fully proficient in the different approaches. In addition, the various national and international collaborations, including mathematical modelling, which are not presented in this document, are clearly a great added value. The project is very well organized into axes and sub-axes, but many of the sub axes have only a small working group (sometimes a PhD student or an engineer), which could compromise the quality and diversity of the approaches.

The team also cites the administrative burden of the mice as a threat. The team has hired a young scientist who has dual expertise in manipulating embryos and embryonic or epiblast stem cells. To reduce the administrative burden on mice, some biological questions could be investigated using in vitro approaches instead of embryos.

RECOMMENDATIONS TO THE TEAM

Although the various axes have been productive recently, given the size of the team and the number of HDRs, the team should consider focusing on fewer axes or allocating more human resources to a single axis.

The recently recruited research assistant should obtain his HDR to increase the team's capacity to recruit PhD students.

In addition to the early mouse embryo, the team should consider developing alternative approaches, e.g. in vitro 2D or 3D approaches using pluripotent stem cells or epiblast cell lines.

The team should apply for European funding to expand its funding sources and its manpower.

Team 15: Dynamic Regulation of body Axis Morphogenesis
Name of the supervisor: Ms Charlène Guillot

THEMES OF THE TEAM

The team investigates how the vertebrate body axis forms from axis stem cells, i.e. neuro-mesodermal progenitor cells (NMPs), during normal development and in pathological contexts, with a focus on environmental influences. To this end, the team uses multiscale approaches such as single-cell RNA transcriptomics, in vivo live imaging, perturbations of tissue mechanics and dynamics, and single-cell lineage tracing.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team was established in late 2021 following an international call for proposals by the Université Clermont Auvergne in collaboration with iGReD. It was not evaluated under the previous contract.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

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

EVALUATION OF THE TEAM

Overall assessment of the team

The team's research focus is fundamental and has applications in healthcare. It uses innovative approaches to understand how the vertebrate body axis forms. Together with a strong and international network of collaborations, this should lead to high quality scientific output resulting in publications in excellent to outstanding journals. Very well funded since 2021, the team should continue on this path, quickly finalize publications and solidify its reputation. The team should ensure that the number of scientific questions matches the team's size.

Context-related strengths and opportunities

The visibility and attractiveness of the team are overall excellent to outstanding.

In 2023, the Principal Investigator (PI) secured an Inserm-funded 'Junior Professor Chair.' The team has since received significant funding: €400,000 from the university/iGReD (2021–2024), €200,000 from Inserm for the Junior Professor Chair (2023–2027), €225,000 from the French Association against Myopathies (2022–2027), and a PhD scholarship (2024–2027).

The team leader has co-supervised two PhD students since 2021. The team aims to enhance its visibility, which is already strong due to its international origins.

The team has secured a full-time technician position and plans to hire an engineer for 2025–2026. Additionally, an assistant professor/hospital practitioner, focused on translational research and hospital collaborations, and a postdoctoral fellow (2024–2025) has joined the team.

Internationally, the team collaborates with physicists in San Diego (USA), bioengineers in Leuven (Belgium), and neural tube defect experts in London (UK). It is also involved in scientific networks such as AFM MyoNeurAlp (neuromuscular diseases), the French Society for Developmental Biology, GdR Stem Cells, and AURASem, which connects stem cell researchers in the Auvergne Rhône-Alpes region. The PI serves on the board of AURASem.

The team's outstanding international visibility, driven by the team leader, is reflected in 13 invitations to prestigious conferences. She co-edited a special issue of *Developmental Biology* (Avian) and played a key role in organizing scientific events, including the Virtual Gastrulation Zoom Talk Series and Monthly Avian Seminar Series; The French Society of Myology Days (Clermont-Ferrand, 2024); The 5th International Conference on Stem Cells, Development, and Cancer (Montreal, 2024); The 11th Avian Meeting (Portsmouth, UK, 2023).

The scientific production remains difficult to assess at this stage. The youth of the team (settling-in period, implementation of systems) has not yet enabled proper production. The team leader has published two papers as the first author (eLife, 2021 and BiorXiv, 2024, both from her postdoc lab – Harvard Med School, USA –). Two reviews are mentioned in which the team leader is co-author – Current Opinion in Cell Biology 2021; Annu Rev Cell Dev Biol. 2019 –.

The team leader serves on juries for Exposciences – 2023 – and Student/Researcher Interactions – 2024 –, engaging in public science discussions – *Promenes ta science* –. She volunteers at 'Rencontres Professionnelles Personnalisées', guiding high school students on career choices. The lab fundraises for myopathy research via MyoNeurAlp and participates in outreach – lectures, lab practicals, and interactive events for students.

Context-related weaknesses and risks

The team leader does not hold an HDR which limits training possibilities.

Visibility in the medical/biomedical fields remains limited.

Work from the team has not yet been published.

ANALYSIS OF THE TEAM'S TRAJECTORY

For the next contract, the team will develop four different projects. (i) Investigate further the molecular mechanisms of folate deficiency leading to developmental disorders. (ii) Study the role of telomere length and gene regulation in human congenital malformations. (iii) Study the role of mechanical forces in coordinating the growth of NMPs. – iv – Explore the role of NMPs and the specification of muscle segments. Although each of the four projects is clearly defined and linked to a grant application, this seems a little too ambitious given the size of the team. Furthermore, of the two ANR projects mentioned for the project – i – and – ii –, none has been funded so far, and for the project – iii – the HFSP is highly competitive. So, there is a risk of too much dispersion at a stage where the team is not yet stable and also a risk of underfunding of the team.

RECOMMENDATIONS TO THE TEAM

The team leader should continue to strengthen her visibility by pursuing active networking, being invited into international meetings and continue the excellent fundraising.

Based on the team trajectory, she should also extend her visibility to medical/biomedical fields to show the power of the avian model and become an undisputed leader in the field. Hiring an assistant professor/hospital practitioner with this regard is excellent, although it will obviously not lead to a significant increase in manpower due to the very heavy workload in hospitals and teaching.

The team leader should defend her HDR as soon as possible and continue hiring PhD students and post-docs.

The team should take advantage of its recent research activities to publish high-profile papers and consolidate its reputation. The team leader should also write their own review papers to publicize their biological questions and model.

The team should be careful with scientific dispersion at a time when it should be consolidating itself.

The team leader and team members should maintain their excellent level of non-academic activities.

Team 16: Diversification of muscle and heart cells in normal and pathological conditions

Name of the supervisor: Mr. Krzysztof Jagla

THEMES OF THE TEAM

The team studies in *Drosophila* the diversification of muscle and cardiac cells in normal and pathological contexts. The technical approach is varied, analysing single cell, TRAP biochemical approaches and in vivo imaging.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

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

a) National and international collaborations could be increased.

The team has become part of a strategic AFM-Telethon with 18 different teams that have already resulted in a joint publication.

At the international level, they have had fruitful collaboration with a Japanese and a Swiss group which resulted in the publication of three collaborative papers in the evaluated period.

b) The number of postdocs has been reduced recently.

This has been achieved. In this period, they have recruited seven postdocs five of which are currently in the team.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

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

EVALUATION OF THE TEAM

Overall assessment of the team

The team basic and applied research focused on muscle biology are of great interest, with an outstanding visibility and an excellent to outstanding scientific production. The team's non-academic activity is also excellent to outstanding, with interactions promoting human research in the *Drosophila* model. Outreach is excellent.

Context-related strengths and opportunities

The team has outstanding visibility and recognition. It is very well funded which allowed them to recruit senior postdoctoral researchers. During the analysed period, 8 PhD students published at least one first author paper in an excellent journal. The team is very strong with 5 tenured members, and three postdoctoral fellows at the moment. The team also has an engineer bioinformatician and a PhD student. The team leader is invited to international conferences as a keynote speaker: In the USA to a FASEB conference in New Orleans, and to the Gordon Conference (twice); and in Costa Rica to the Frontiers in Myogenesis conference. He has also organized an EMBO muscle workshop. Funding has been very successful with 2.5 million euros in a 5-year period with several members of the team being involved in obtaining those funds. The team leader has also been a member of the Scientific Council Telethon, a member of the Inserm's Scientific Commission and director of iGReD. The team gives the opportunity to the tenured members to grow their independence by publishing articles as senior authors, getting funding through grant applications or occupying positions as members of different panels.

The team has an excellent to outstanding scientific production, with eleven research papers (10 of them with team members as first or last authors) and eight reviews. These publications appeared in prestigious journals (eLife, Biol. Open, two papers in Development, Molecular Cell, PLoS Genetics, PLoS Biology or EMBO reports) some of which were published with international collaborators while others are the lab's own production. The eight reviews were published in Seminars in Cell and Dev Biol., Adv. Exp. Med Biol., Cell and Mol. Life Sci. and Exp Cell Research among others showing the teams' leadership in the topic.

The non-academic activities are excellent to outstanding with members of the team involved in clinically applied projects. In some cases, they are involved in generating *Drosophila* models to assess the pathogenicity of human muscular mutations.

Context-related weaknesses and risks

The team published many papers in prestigious journals but were not able to publish in more generalist journals, revealing their high specialization.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team is closing in 2026.

RECOMMENDATIONS TO THE TEAM

In preparation of the team closing, it would be important to support the permanent members of the team finding a satisfactory plan to accommodate them within the institute after the lab's closure or by promoting their move to competitive jobs in other units.

The committee thanks the team leader for his contributions to science and his service to the iGReD.

Team 17: Epithelial growth and morphogenesis
Name of the supervisor: Mr. Vincent Mirouse

THEMES OF THE TEAM

The team focuses on the *Drosophila melanogaster* ovary as a model to analyse mechanisms controlling size and shape. They are interested in how the growth of the germ cells and the somatic follicle cells contacting them is coordinated. More recently they are also analysing the coordination of growth among different egg chambers in the same ovariole. Their research has taken them to study how molecules like F-actin, Dystrofin or Dystroglican affect ovariole elongation. This approach spans from the tissue to the cellular and molecular levels.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

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

a) Increase publication number: This has been partially addressed. The team is still not very prolific, but has published excellent research in reputable specialized journals like Development 2020, BMC Dev Biol 2020, PLoS genetics 2024 and PLoS biology 2025.

b) Hire more lab members, especially those with HDR

Although not in the current contract, this has been addressed with the team succeeding to recruit one member as assistant professor for the following contract.

c) Diversify funding: The team has obtained an ANR PRC grant

d) Establish international collaborations: They have published two papers in collaboration with UK and USA teams.

e) Focus project: They have discontinued part of the previous projects.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	3
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	6
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	0
Post-doctorants	1
Doctorants	1
Sous-total personnels non permanents en activité	2
Total personnels	8

EVALUATION OF THE TEAM

Overall assessment of the team

The team performs excellent basic research with very interesting projects aiming at exploring mechanisms controlling size and shape. Despite their research output being of great quality, its total production is limited. Visibility and outreach activities are very good to excellent but remains limited with regard to their potential.

Context-related strengths and opportunities

The team visibility and attractiveness are very good to excellent. The team's work falls perfectly within iGReD research topics, making the team attractive to researchers in the field. During the evaluated period, there have been four PhD students who published at least one paper as the first author in very reputable journals (PLoS Biology, PLoS Genetics, Development, BMC Biology). The team also has international collaborations resulting in excellent papers (EMBO reports, Nature Communications). The team has had good funding. The team is invited to talks and presentations at international conferences (not specified where). The team has been able to attract an Associate Professor (MCU) with an HDR who will start in 2027 that will have a very positive impact on the team's production and capacity to direct PhD theses.

The team has an excellent scientific output. The research, focusing on mechanisms controlling size and shape spans the tissue, cell, and molecular level that are studied in a very well-defined model in which the team members are very knowledgeable. Their proposed research projects are original and very interesting. With few publications but of excellent quality either as main authors (Development 2020, BMC Dev Biol 2020, PLoS genetics 2024 and PLoS biology 2025) or in international collaborations that resulted in excellent papers (EMBO reports 2024, Nat. Communications 2020).

The non-academic activities are very good, with a proposed workshop on genetics and models for schools.

Context-related weaknesses and risks

Although in the evaluated period there have been four PhD students, currently there is only one PhD student and little option of increasing much the number as only one team member holds an HDR. The recruitment of a permanent researcher with a HDR may reinforce the team.

The team produces high quality publications but the number is relatively low with the Associated Professors not being very involved.

Non-academic activities are rare, and principally based on presentations and courses for students.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team is going to continue using the *Drosophila melanogaster* ovary model in which they are experts. They will follow the three main research lines.

First, develop *Drosophila* as a model for ovary homeostasis. In vertebrates, the mechanisms controlling ovary dormancy are not well understood, although it is known they are under the control of IGF/PI3K signalling pathway. This pathway is also involved in atresia (degeneration of the follicle cells). The team noticed that, although in *Drosophila* the ovary germ cells behave differently, they also require the IGF/PI3K pathway and ecdysone showing an unexpected parallelism to vertebrate oogenesis. They also found that blocking of egg laying in the fly induces dormancy of earlier younger egg follicles due to IGF/PI3K pathway inhibition. The laboratory has found evidence for the involvement of a negative signalling molecule induced by ecdysone and want to extend the findings to vertebrates in collaboration with two Inserm groups. The laboratory also has evidence of a second mechanical factor involved in the inhibition of the IGF/PI3K pathway. This work is risky but very interesting and original and worth pursuing.

Second, study tricellular junctions and their control by actin dynamics. The team wants to analyse how tricellular junctions are resolved during epithelial rearrangement, they have preliminary evidence suggesting the involvement of a dual mechanism, one responding to tissue mechanics (Controlled by the *sdg* gene), and the other to biochemical signals mediated by the planar cell polarity (*fat2*). This is a very interesting project for which funding has not yet been assured.

Third, a study of the Dystrophin associated protein complex (DAPC) at the myotendinous junctions. DAPC is considered an Integrin-independent cell-ECM adhesion complex. The team wants to study its function at the myotendinous junction, which may be one of DAPC's most important sites of action. In this project, they will be analysing the spatio-temporal localization of the proteins at the cellular level. They plan to generate mutations and knock-ins to label the DAPC proteins. They also plan to dissect functionally the enormous Dystrophin protein. The conservation of the complex will allow doing this work in collaboration with *C. elegans* and mouse laboratories. This work will help to understand the function of the human protein which is the longest known vertebrate gene and understand the cause of certain dystrophies. This project will be reinforced by the arrival of a new member in 2027.

Globally, the project aims are excellent.

RECOMMENDATIONS TO THE TEAM

The associated professors should become, if organization allows it, more involved in research.

The tenured researchers should obtain their HDR to increase the capacity of the team to hire PhD students.

CONDUCT OF THE INTERVIEWS

DATES

Beginning: 1 October 2025, 08:30

Ending: 2 October 2025, 14:30

Interview conducted: on-site

PROGRAMME OF THE INTERVIEWS

Tuesday, September 30th

20:00 Dinner – Only for Hcéres Committee

Wednesday, October 1st

8:00–8:10 Presentation of the Hcéres evaluation to the unit (SA) *Attending: expert committee, SO, representatives of institutions and all unit members*

8:10–9:10 Presentation of the research unit by the unit director (including 15' questions) *Attending: expert committee, SA, representatives of institutions and all unit members*

9:10–9:20 Room change

9:20–11:00 Scientific team presentations session 1: *Attending: Team Members, expert Committee, SA, Director of Unit, representatives of Institutions*

9:20–9:50 Team 17, Berger, Guèze & Rouzaire, Lymphoid cancers and therapeutic immunity

9:50–10:15 Team 8, Baron & Lobaccaro, Nuclear Receptors and Pathophysiology

10:15–10:40 Team 9, Val & Martinez, Molecular Pathophysiology of Adrenal and Endocrine Tissues

10:40–11:00 Team 16, Serra & da Ines, Meiosis, Recombination and adaptation

11:00–11:15 Break

11:15–13:20 Scientific team presentations session 2: *Attending: Team members, expert committee, SA, director of Unit, representatives of Institutions*

11:15–11:40 Team 3, Mathieu, Silencing and Transposons

11:40–12:05 Team 1, Arnaud, Genomic Imprinting & Cell Lineage Commitment

12:05–12:30 Team 6, Waltzer & Vandel, Epigenetic Regulation & Ontogenesis

12:30–12:55 Team 10, Sapin & Blanchon, Translational Approach to Epithelial Injury and Repair

12:55–13:20 Team 13, Guillot, Dynamic Regulation of body Axis Morphogenesis

13:20–14:10 Lunch

14:10–14:50 Meeting with iGrED personnel: 3 parallel meetings

—Meeting with **technical and administrative personnel** (in French) (closed hearing) *Attending: Technicians, Engineers, Administrative staff, sub-committee 1 of expert Committee: A FREISMUTH, Y GRABA, M VARRET*

—Meeting with **thesis students and post-docs** (closed hearing) *Attending: PhD students and postdocs, sub-committee 2 of expert committee: J HOMBRIA, P JULIEN, C BRET*

—Meeting with **researchers and professors** (closed hearing) *Attending: Researchers except group leaders, sub-committee 3 of expert committee: T JAFFREDO, F MARMIGERE, C VARON*

14:50–16:55 Scientific team presentations session 3: *Attending: Team Members, expert Committee, SA, Director of Unit, representatives of Institutions*

14:50–15:15 Team 5, Probst & Tatout, Chromatin and 3D Nuclear Dynamics

15:15–15:40 Team 2, Brasset: Dynamics and epigenetic control of transposons

15:40–16:05 Team 4, Molaro, Evolutionary Epigenomics and Genetic conflicts

16:05–16:30 Team 11, Volle, Environment, Metabolism, Spermatogenesis, Pathophysiology and Inheritance

16:30–16:55 Team 14, Mirouse, Epithelial growth and morphogenesis

16:55–17:10 Break

17:10–17:35 Scientific presentation session 4 (visio): *Attending: Team Members, expert Committee, SA, Director of Unit, representatives of Institutions*

Team 12, Chazaud, Differentiation of cell lineage in early mouse embryo

17:35–19:00 Committee debrief (closed hearing) *Attending: Expert Committee, SA*

20:00 Dinner – Only for Hcéres Committee

Thursday, Oct 02

8:30–9:30 Committee debrief (closed hearing) *Attending: Expert Committee, SA*

9:30–10:00 Meeting with the representatives of Inserm, CNRS and University (in camera hearing) *Attending: Expert Committee, SA, representatives of Institutions*

10:00–10:15 Visit CLIC platform/passage through the lab *Unit Director, Expert Committee, SA*

10:15–11:00 Meeting with the head of the unit (closed hearing) *Attending: Unit director, expert committee, SA*

11:00–11:15 Break

11:15–13:00 Final committee deliberations (closed hearing) *Attending: expert Committee, Scientific Officer*

13:00–14:00 Lunch

GENERAL OBSERVATIONS OF THE SUPERVISORS

Clermont-Ferrand 12/01/2026

iGReD directors and team leaders observations in relation to the HCERES evaluation and comments:

We are grateful to the visiting HCERES committee for its insightful and encouraging comments and scientific inputs. We are pleased to read that the research achievements, scientific objectives, organization and resources of the iGReD are excellent. We provide below our observations concerning specific points for the unit and some of teams.

Observations related to the iGReD evaluation report:

- We would like to provide precision concerning iGReD participation in MSCA networks. We are involved in 3 MSCA networks. In one of them as coordinators and in two others as participants.
- We suggest to modify the sentence « The iGReD benefits from critical mass of 200 researchers... » to : « The iGReD benefits from critical mass of 200 persons including researchers, research support personnel and trainees »

Observations related to the team's evaluation reports:

- **Team 1: Genomic Imprinting and the epigenetic control of cell fate determination** Team leader: **Philippe ARNAUD**

We are grateful to the HCERES committee for their positive and encouraging assessment of our team, as well as for their valuable recommendations. We would also like to take this opportunity to provide the following clarifications:

- The report notes that the MCFs “are lacking authorship in a leading position, likely due to a lack of involvement in PhD student supervision.” We wish to clarify that this does not fully reflect our team’s activity during the evaluated period. C. Barrière independently leads a research project alongside her teaching duties, supervised two Master 2 students (who were unfortunately unsuccessful in securing doctoral school funding to pursue a PhD), secured three grants, and published a last-author article in *Human Molecular Genetics* based on a previous doctoral project. She is currently preparing another last-author article. Anne Fogli, while less directly involved in research due to her collective responsibilities, co-supervised a PhD thesis and was co-last author on a *Molecular Oncology* article. Her collective responsibilities, though described as “very local” in the report, have national impact: she serves as 1st Vice-President of UCA and Deputy Director of the unit.
- **Team 2: Dynamics and Epigenetic Control of Transposons** Team leader: **Emilie Brasset**

We sincerely thank the committee for the thorough evaluation and the "excellent to outstanding" ranking. We appreciate your recognition of the quality of our work, as reflected in our publications, national funding, international visibility, and outreach activities. In this short response, we would like to clarify one point that we feel is important for accuracy.

- Regarding the « context-related risk » highlighted in the report, the current snapshot (1 PhD student, 3 HDR researchers) largely reflects timing: one PhD was defended in October 2024, shortly before the evaluation. In addition, this snapshot does not reflect that the team had **two HDR holders for most of the evaluation period**, since I. Vaillant (Maître de conférences) joined only in 2023. Over 2019–2024, we supervised four PhD theses, i.e. **approximately two PhDs per HDR** over the period given the team composition. Contrary to what this snapshot may suggest, securing PhD positions is already part of our

established track record, and is therefore already in line with the recommendations mentioned later in the report.

- Team 12: **Environment, Metabolism, Spermatogenesis, Pathophysiology and Inheritance** Team leader: **David Volle**

We would like to express our sincere appreciation to the HCERES evaluation committee for its positive assessment of our team.

We would like to take this opportunity to clarify few points related to RECOMMENDATIONS TO THE TEAM:

1/ As mentioned in our report, Dr Sauzéat, who is an IRD researcher (and not a CNRS researcher as stated), will be completing her HDR (*Habilitation à Diriger des Recherches*, or accreditation to supervise doctoral research). This will strengthen the capacity of the team to recruit and supervise new PhD students; and subsequently help us to sustain our efforts and mitigate the risk of a decline in our ability to remain at the forefront of research and thus maintain our productivity in all areas; as recommended by the HCERES evaluation committee. Furthermore, the potential recruitment of CNRS and/or INSERM (e.g., Won-Ki PANG) would also increase the team workforce, thereby further enhancing our ability to attract and recruit PhD students across the various research topics covered by the team.

2/ Our team is engaged in further developing alternative approaches to animal models. As these developments require advanced expertise, we have already established international collaborations with leading research groups. This strategy will ensure that such expertise is embedded within the team through collective investment of research support staff, post-doctoral fellows and PhD students.

3/ One of our team's strengths is scientific projects co-construction. Guided by a strong commitment to the active participation of all members, our projects are structured to promote collective engagement. We take into account the HCERES committee's recommendation that leadership, staffing, the involvement of technical staff (engineers and technicians), and the recruitment strategy for researchers must be clearly specified for each project. While clear project leaders and core contributors (researchers and students) can be readily identified, we intentionally adopt a collegial governance model. This approach is designed to maximize expertise (physiology, biochemistry, geochemistry, etc.) and to ensure flexibility cross-fertilization of skills, and efficient resource allocation across projects.

In this regard, we would like to clarify the committee's concern regarding the potential award of the ERC Starting Grant to Dr Sauzéat: "There is an uncertainty about some of the projects if the recently recruited CNRS CR succeeds in getting an ERC starting grant (to start his own team)."; We would like to emphasize that this will not result in the creation of a new team; rather, it will strengthen our existing research group by enhancing research on the effects of environmental contamination on health.

Current iGReD Director :

Krzysztof JAGLA

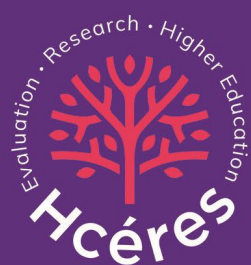


Next contract iGReD Director :

Lucas WALTZER



Evaluation of universities and schools
Evaluation of research units
Evaluation of the academic formations
Evaluation of the national research organisms
Evaluation and International accreditation



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