

## EVALUATION REPORT OF THE UNIT

Cirb - Centre interdisciplinaire de recherche en biologie

UNDER THE SUPERVISION OF THE  
FOLLOWING ESTABLISHMENTS AND  
ORGANISMS:

Collège de France,

CNRS - Centre national de la recherche  
scientifique,

Inserm - Institut national de la santé et de la  
recherche médicale,

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**EVALUATION CAMPAIGN 2023-2024**  
GROUP D

Rapport publié le 25/04/2024



In the name of the expert committee :

Manuel Mendoza, Chairman of the committee

For the Hcéres :

Stéphane Le Bouler, acting president

Pursuant to Articles R. 114-15 and R. 114-10 of the Research Code, the evaluation reports drawn up by the expert committees are signed by the chairmen of these committees and countersigned by the President of Hcéres.

To make the document easier to read, the names used in this report to designate functions, professions or responsibilities (expert, researcher, teacher-researcher, professor, lecturer, engineer, technician, director, doctoral student, etc.) are used in a generic sense and have a neutral value.

This report is the result of the unit's evaluation by the expert committee, the composition of which is specified below. The appreciations it contains are the expression of the independent and collegial deliberation of this committee. The numbers in this report are the certified exact data extracted from the deposited files by the supervising body on behalf of the unit.

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

## MEMBERS OF THE EXPERT COMMITTEE

### Chairperson:

Mr Manuel Mendoza, Institut national de la santé et de la recherche médicale - Inserm, Inserm, Illkirch

### Vice-chairperson:

Ms Sophie Pantalacci, Centre national de la recherche scientifique – CNRS, Lyon

### Experts:

Ms Sandrine Bertrand, CNRS, Bordeaux

Mr Laurent Duret, CNRS, Villeurbanne

Mr Pierre-Olivier Fernagut, CNRS, Poitiers (representative of CSS Inserm)

Ms Simonetta Gribaldo, Institut Pasteur Paris

Mr Matthew Holt, University of Porto, Portugal

Mr Philippe Huber, Commissariat à l'énergie atomique et aux énergies alternatives – CEA, Grenoble

Mr. Guillaume Junion, Inserm, Clermont-Ferrand (representative of CSS Inserm)

Mr Christophe Le Clainche, CNRS, Gif-sur-Yvette

Mr Mickael Marin, Inserm, Paris (representative of research support personnel)

Mr Nicolas Minc, CNRS, Paris (representative of CoNRS)

Ms Homaira Nawabi, Inserm, La Tronche

Ms Agnes Petit-Paitel, CNRS, Valbonne (representative of CoNRS)

Mr Jerome Solon, Instituto Biofisika, Leioa

Ms Sylvie Tournier-Gachet, CNRS, Toulouse

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## HCÉRES REPRESENTATIVE

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## REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Arnaud Roffignon, Collège de France

Patrick Blader, CNRS

Keltoum Harouat, Collège de France

Jean Rosenbaum, Inserm

Mme Camille Chaudonneret, Inserm

Mme Delphine Machy, CNRS

## CHARACTERISATION OF THE UNIT

- Name: Centre interdisciplinaire de recherche en biologie
- Acronym: Cirb
- Label and number: UMR 7241
- Number of teams: 18
- Composition of the executive team: Mr Alain Prochiantz, Director from 2011 until 2018, Incumbent Director: Mrs. Marie-Hélène Verlhac; Deputy Director: M. Olivier Espeli

## 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 teams that compose the Cirb do research in several fundamental life sciences and social science disciplines: biology, biophysics, biostatistics, and anthropology. Most Cirb teams work in one of three general areas (proposed to become formal departments): Cellular and Developmental Biology, Neurobiology, and Evolution and Ecology. The institute is therefore multidisciplinary.

## HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The Cirb was created in 2011 by Pr Alain Prochiantz with the aim of bringing together and encouraging the dialogue between a wide range of life science disciplines. It is located in the Collège de France (CdF) in Paris, and funded by Collège de France, Inserm and CNRS. Alain Prochiantz was the Cirb director from 2011 until 2017, followed by the current director, Marie-Hélène Verlhac. Olivier Espeli has been deputy director since 2019. The Cirb was evaluated by Hcéres in 2013 and 2017, with the last report noting a positive evolution of the unit in terms of both scientific excellence and management. The unit has grown in size (167 staff members in 2017, 224 in 2022) whereas the number of teams has remained constant (20 teams since 2017).

## RESEARCH ENVIRONMENT OF THE UNIT

The Cirb is hosted by the College de France, a prestigious higher education and research establishment that offers high-level courses that are free, nondegree-granting and open to all without condition or registration. The CdF is an associated member of the Paris Sciences & Lettres University and Cirb scientists participate in teaching at both the CdF and the university. The Cirb participates in several scientific consortia: Labex Memolife, Q-Life Convergence Institute of PSL University, and C-Brains initiative, fostering the scientific exchange with other researchers working in multiple biological disciplines in the Paris area.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	18
Chargés de recherche et assimilés	25
Personnels d'appui à la recherche	48
<b>Sous-total personnels permanents en activité</b>	<b>97</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	5
Personnels d'appui non permanents	15
Post-doctorants	35
Doctorants	72
<b>Sous-total personnels non permanents en activité</b>	<b>127</b>
<b>Total personnels</b>	<b>224</b>

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

Nom de l'employeur	EC	C	PAR
CNRS	0	26	12
COLL DE FRANCE	4	0	21
Inserm	0	17	10
AUTRES	2	0	3
<b>Total personnels</b>	<b>6</b>	<b>43</b>	<b>46</b>

## GLOBAL ASSESSMENT

The Cirb is an elite multi-disciplinary institute constituted by research teams striving to work at the forefront of their respective disciplines. To promote scientific excellence, teams are hosted at the Cirb for 5-year periods, renewable upon positive evaluation by its supervisory bodies and international Scientific Advisory Board. According to the Cirb Internal Rules (approved in 2019), multiple renewals are possible for senior teams ("rolling tenure" system), whereas junior teams can be renewed only once. At any given time, senior teams constitute at most 25-30 % of all Cirb teams.

Research teams in the Cirb are organised in three main thematic areas, formalised as research departments in 2023: Cell and Developmental Biology, Neurobiology, and Evolution and Ecology. The scientific production of all teams is overall excellent to outstanding. This is demonstrated by high-quality publications in prestigious generalist journals in their different disciplines, including Science, Nature, Cell, Current Biology, elife, The EMBO Journal, Nature Communications, PLoS Biology, and PNAS, among others. Remarkably, this is true across all teams and disciplines, which is a remarkable achievement for an institute of this size.

Reflecting this outstanding productivity, teams in the unit are extremely successful at obtaining competitive research grants at the national and European level, including nine European Research Council grants for all career stages (Starting, Consolidator, Advanced, and Proof of Concept). As a result, and also thanks to the support of the supervisory bodies, the unit has excellent financial resources allowing it to maintain well-equipped imaging and animal facilities.

Scientific interactions between teams have led to multiple collaborations across research themes (now departments), as befits an interdisciplinary institute. However, interaction between unit members remains limited and could be improved. In particular, the committee notes the lack of regular seminars where all unit members can present their results – an exception being the weekly progress reports presented by PHD students and postdoctoral fellows, but that are not regularly attended by career researchers, technical staff or team leaders. Finally, the committee agrees the unit can improve various aspects of its human resource management. The “rolling tenure” system contributes to the dynamism and excellence of the unit, but lack of clarity on renewal requirements can place considerable stress on junior team members. Mentorship programs for junior researchers are still to be established, in spite of previous Hcéres recommendations. Finally, high levels of stress among the administrative staff seems related to the small size of this group, although the committee notes a strong support for the recently appointed General Secretary.

## DETAILED EVALUATION OF THE UNIT

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

The previous Hcéres report made no recommendations on general scientific production and activities, or scientific strategy and projects, which were considered of excellent quality. The previous Hcéres evaluation did raise concerns about the synergy between the two co-leads in the Joliot / Vritz team, and indicated that it would be premature to create a team led by Julia Fuchs (formerly in the Prochiantz team). Motivated by these concerns, the Joliot / Vritz team was not renewed and the Fuchs team was not created.

The recommendations on the unit's organisation and life were:

(A)- *setting up a lab council with elected representatives*

(B)- *improving the mentoring system for PHD students and staff scientists*

(C)- *increasing the number of staff in general administrative support positions*

(D)- *setting-up a welcoming service (including, for example, compiled information for international recruits regarding housing in Paris etc.) for new members of staff at all levels.*

Following these recommendations, a lab council was established in 2019, two new general administrative recruitments were made, and a welcome booklet for new staff was prepared. In contrast, the mentoring system was started but was short-lived, and is currently not operational.

### B - EVALUATION AREAS

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

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

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

The Cirb aims to be an interdisciplinary institute hosting research teams working on multiple aspects of the life sciences. The research themes range from molecular mechanisms in cell, developmental and evolutionary biology, to brain physiology, to palaeoanthropology. The quality of the teams is overall excellent to outstanding. The extent of interaction between teams, necessary to achieve true interdisciplinarity, could benefit from further improvement. The direction aims to develop this aspect thanks to recent new recruitments.

##### Assessment on the unit's resources

The unit has excellent financial resources (approximately 5M €/year, mostly from grants obtained by teams) and occupies 6500 m<sup>2</sup> in two adjacent buildings. Human resources include over 200 personnel whose scientific activity is organised around three major themes, 20 research teams, and well-equipped imaging and animal facilities. Space and equipment are near maximum capacity, suggesting that the development of new directions should be carefully balanced.



## Assessment on the functioning of the unit

Human resources, safety procedures, ethical protocols and data protection are generally organised according to well-defined principles complying with all current legal expectations. In spite of efforts to maintain proper balance in team composition, two teams lack engineers/technicians. There is also a pressing need for an increase in administrative staff.

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

#### Strengths and possibilities linked to the context

A major strength of the unit is the outstanding quality of its individual research teams. This applies across the different themes investigated in the unit. Another equally important strength is the interdisciplinary vocation of the unit. Regardless of the quality of the teams that compose it (which is excellent to outstanding overall), the challenge to achieve true interdisciplinarity is the ability of teams to apply ideas and approaches from multiple disciplines to address research objectives, either within single teams, or in collaboration. In this sense, over 40 papers from the unit are internal co-publications, representing 8% of all publications. These are in the areas of neurobiology, cell and developmental biology, and evolution. This is a trend that should continue to increase. The direction is aware of this need, and advised by its SAB, has sought to strengthen the unit interdisciplinarity through changes in the team composition of Cirb: some teams whose research did not fit well with current themes of the unit were not renewed, while new teams were recruited, with the aim to generate thematic clusters of interactivity. Three major areas have been identified that the unit has recently formalised into departments: 1. neurobiology, 2. cell and developmental biology, and 3. evolution and ecology.

#### Weaknesses and risks linked to the context

The aim to achieve interdisciplinarity may be in tension with the wish to foster research excellence in individual teams. For example, the recently recruited "Paleoanthropology" team performs outstanding research, but it is not clear to what extent it will create synergies with existing teams in the unit. The unit will need to carefully consider future recruitments to maintain the proper balance between these two goals, particularly in regards to space to host teams, which seems limited.

Another potential threat is the decision to create separate departments in the unit. While the committee agrees that this can help improve research excellence and focus, it should not come at the detriment of internal dialogue. Guidelines for the future life of these departments should keep this in mind. Notably, internal scientific seminars to which all unit members participate are currently missing. The committee encourages the unit to institute a common seminar series, and to explore additional initiatives to facilitate internal dialog further.

### *2/ The unit has resources that are suited to its activity profile and research environment and mobilises them nit has resources that are suited to its activity profile and research environment.*

#### Strengths and possibilities linked to the context

The unit has very good financial resources, including 1M EUR / year from CdF, CNRS and Inserm, which is complemented to approximately 5M €/year thanks to grants obtained by teams. The unit staff comprises over 220 personnel including 20 research teams, imaging and animal facilities, and common services. The median size of research teams is 10 members. The unit is housed in two adjacent buildings totalling 3000 m<sup>2</sup> which seems adequate for up to 20 teams (100 sqm each) plus facilities. The imaging facility is equipped with conventional and high-end instruments enabling wide-field and confocal microscopy, stimulated emission depletion (STED), atomic force (AFM), and light sheet microscopy. The animal facility allows for mice, rats, medaka and zebrafish maintenance and has recently been renovated and expanded. Overall, these resources appear to be of high quality and are well-used. The committee noted some problems were encountered following the outsourcing of human resources in the animal facility, due to high turnover in the outsourced staff and low flexibility on requests from researchers.

## Weaknesses and risks linked to the context

In spite of efforts to maintain proper balance in team composition, some teams lack engineers/technicians.

An important issue that came up in discussions concerned the relatively small size of the administrative staff (six full-time positions). While having a slim administration can be beneficial in some conditions, currently the high workload of the remaining staff seems excessive, which creates pressure and stress. Despite this situation, the staff acknowledges that the new General Secretary, in place since 2023, represents a considerable improvement over the previous situation.

Another issue that became apparent during the visit is the lack of clarity for some junior team leaders about the requirements for team renewal, leading to stress and uncertainty about the future among junior researchers, including students and postdoctoral fellows in those teams.

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

## Strengths and possibilities linked to the context

The unit's human resources management follows a set of written internal rules. The unit is mindful of gender parity and this is reflected in the woman/man ratio at all levels: team leaders, researchers and support staff. The unit also upholds non-discrimination principles in training, internal mobility and career development for its staff. Safety procedures, ethical protocols and data protection are all organised according to well-defined principles complying with all current legal expectations.

In particular, the unit has designated nine prevention assistants to ensure safety and health compliance, and one data protection officer to implement open-source data storage and sharing (Omero and Opidor). Volunteers from each group have joined a grassroots collective (Greencom) to advise colleagues on sustainable development aspects: energy consumption, waste production and CO2 emissions.

The unit dealt with a case of sexual harassment among its staff in a swift and efficient manner. Responses from CNRS and Inserm in this case were slow and inefficient compared with the response of CdF. New procedures to handle moral and sexual harassment cases are under consideration as a result of this case.

## Weaknesses and risks linked to the context

No weaknesses identified.

## EVALUATION AREA 2: ATTRACTIVENESS

### Assessment on the attractiveness of the unit

The unit has excellent attractiveness and visibility. It is attractive to researchers because of its excellent scientific research, attested by a high level of success to grant applications at the National and European levels, and its advanced facilities. It has excellent visibility thanks to its participation in multiple consortia with other institutes in the Paris area, by the participation of unit members in meeting organisations, scientific academies, learned societies and editorial boards, and by the award of numerous scientific prizes and honours to unit members.

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

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

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

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

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

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

The unit has excellent scientific reputation thanks mainly to the outstanding scientific research of Cirb teams. Its reputation is strengthened by its participation in multiple scientific consortia, fostering the scientific exchange with other researchers working in multiple biological disciplines in the Paris area (Labex Memolife, Q-Life Convergence Institute, and C-Brains initiative). Group leaders organised international conferences, such as Society for the Study of Blood-Brain Interfaces, SEISC), symposiums of the Federation of European Neuroscience Societies (FENS), European Association for Cancer Research (EACR), Fondation des Treilles, French Society of Cell Biology (SBCF), joint EMBL/Ibems/Cirb. Group leaders also are part of international & national evaluation and founding agencies (ERC panels, ANR, Fondation Bettencourt-Schueller, ATIP/Avenir, ARC Fondation, FRC, Hcéres, CNRS & Inserm recruitment committees, Memolife 2.0 labex of PSL University, among others). Four unit's members are members of EMBO, and others have received honours and prizes including membership of French and Belgian Academy of Sciences, CNRS bronze and silver medals, and CNRS Paoletti prizes.

**2/ The unit is attractive for the quality of its staff hosting policy.**

The unit recruited four team leaders during the evaluation period, including three from outside the Cirb (the fourth PI, originated from Team 10 Cirb team). The unit recruited 21 permanent researchers (CRCN) and employed 87 postdoctoral fellows, 112 PHD students and 87 interns (license and master students). The unit offers a favourable environment for the development of their research activities, such as weekly internal seminars to present their work and the possibility to join the CdF student's association, which organises seminars and other events.

**3/ The unit is attractive because of the recognition gained through its success in competitive calls for projects.**

The unit teams have an excellent track record in obtaining international funding. Nine ERC grants were running during the period of evaluation, and more than 30 ANR projects (coordinated by Cirb teams) were obtained. Grants were also obtained from other French agencies including INCA and charities (such as FRM team labels). The institute has also been able to obtain funding for the acquisition of heavy equipment, notably high-end microscopes for the imaging facility (700 k EUR from Fondation Leduca).

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

The unit has two main facilities: an animal house and an imaging facility, described previously, that are key assets to ensure the attractiveness of Cirb. In addition, there are washing and mechanical facilities.

The imaging facility houses "conventional" instruments such as wide-field, confocal and spinning disk microscopes, and also advanced microscopes such as light sheet, AFM and STED. Staff of seven operates this facility. The budget of this facility is balanced thanks to user fees. The animal facility is subcontracted to an external service (Charles River Laboratories) and its cost to teams is entirely covered by the unit (200 kEUR / year).

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

The mentoring program initiated at the request of the previous Hcéres evaluation was discontinued. Top-down efforts should be made to restart this initiative after a critical analysis of its previous, short-lived iteration.

The number of permanent technical support positions for the imaging facility and research teams is insufficient. Two teams do not have stable engineers or technical support, and one key member of the imaging facility is under a limited-time contract, potentially threatening the stability of the service.

Most of the neurobiology teams working with rodents expressed concern about the current conditions in which to perform sophisticated behavioural analysis. To some degree, these problems are probably compounded by outsourcing the running of the animal facility to Charles River Laboratories, whose staff has limited ability and flexibility to perform advanced animal husbandry/care.

## EVALUATION AREA 3: SCIENTIFIC PRODUCTION

### Assessment on the scientific production of the unit

The Cirb has an excellent to outstanding level of productivity. This is demonstrated by its publications and success in securing competitive funding, including ERC grants for nine teams during the evaluation period, a remarkable indicator of scientific excellence. The number of publications has remained high (more than 50 papers/year since 2017) as well as their quality. Notably, around 20 of these were published in prestigious multidisciplinary journals, including Science, Nature Communications, elife and PLoS Biology.

- 1/ *The scientific production of the unit meets quality criteria.*
- 2/ *The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.*
- 3/ *The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.*

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

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

The overall level of scientific production is excellent (outstanding for 40% of the teams). The volume of publication is commensurate with the unit's size: ca. 500 publications since 2017 (around 250 according to the self-evaluation document) with 40 articles in prestigious multidisciplinary journals such as Cell, Current Biology, elife, The EMBO Journal, Nature Communications, PLoS Biology, PNAS, and Science (with 5 research articles). The unit has been extremely successful in capturing competitive funding, especially European Research Council (ERC) grants (9 grants during the evaluation period). ERC and national grants (National Research Foundation ANR, Clinical Research Hospital Programs PHRC, Unique Ministerial Funds FUI, National Cancer Institute INCa, among others) accounted respectively for 37% and 31% of external funding.

The level of productive internal collaboration is also very good, although the higher-profile papers tended to be authored by single teams. All areas of Cirb interest are well represented in collaborative papers.

#### 2/ **Scientific production is proportionate to the research potential of the unit and shared out between its personnel.**

The scientific production was excellent to outstanding for all evaluated teams, both in quantity and in quality. There was a large variance in the number of articles per team, largely due (as expected) to the difference between theoretical and experimental teams, and to a lesser extent to junior vs established teams. Considering disciplinary practices and disparities between disciplines, scientific production is overall homogeneous between the unit's constituent teams.

#### 3/ **The scientific production of the unit complies with the principles of research integrity, ethics and open science.**

Cirb complies with principles of research integrity, ethics and open science. In particular, more than two thirds of Cirb publications are in full open access journals, and at least eight teams have posted preprints in the bioRxiv server. The unit organised several conferences on Science Ethics and Misconduct.

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

No weaknesses were detected on the quality of the scientific production. The unit teams are encouraged to further adopt the posting of preprints before publication in peer-reviewed journals, as preprints are becoming an essential element in the dissemination of science.

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

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

The unit has a number of activities in place that allow it to make excellent to outstanding (for some teams) contributions to the local community beyond its scientific productivity. Members of the unit are at the origin of twenty patents from at least five different teams, and one startup was founded during the current contract, while another launched shortly before the start of the contract continues to develop. Members of the unit are heavily involved in outreach activities.

- 1/ The unit stands out for the quality and the amount of its interactions with the non-academic world.*
- 2/ The unit develops products for the cultural, economic and social world.*
- 3/ The unit shares its knowledge with the general public and takes part in debates in society.*

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

*1/ The unit stands out by the quality of its non-academic interactions.*

The unit promotes multiple nonacademic interactions at the economic level (producing patents and start-up companies) and at the level of society, sharing its knowledge through multiple mechanisms, as outlined below.

*2/ The unit develops products for the socio-economic world.*

Three Cirb teams have had collaborations with industry: Team 21 with Quantum Genomics, Team 12 with the start-up Braineever, co-founded in 2016 by Team 12 co-PI to focus on neurological diseases, and Team 13 with another start-up, Pannterapi, seeking to develop new treatments for epilepsy, founded in 2021. Furthermore, the imaging facility collaborates with Zeiss for access to technologies.

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

Cirb members have an important involvement in science outreach. For example, Team 1, Team 2 and Team 10 PIs were active in mainstream media during the pandemic period, due to their specific expertise. These activities included TV and radio interviews and publication of podcasts, articles in magazines and popular science books. Other teams (e.g. Team 11) were also very active in their own fields. The Cirb hosted high school students in the Cirb through multiple initiatives, organised among others with the Association "l'Arbre des Connaissances", led by Team 5 PI.

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

None identified.

## ANALYSIS OF THE UNIT'S TRAJECTORY

Since its founding in 2011, the Cirb has aimed to bring together and encourage the dialog between a wide variety of life science disciplines. The unit's success in this objective is clear, managing to host research teams that now work at the forefront of multiple disciplines in the fields of cell biology, neurobiology, and evolution. To reconcile this deliberate lack of thematic focus with the need to foster dialog and collaborations between teams, the unit has recently been restructured into three separate departments, particularly reinforcing the "evolution and ecology" area with the recruitment of several outstanding teams. Although it is too early to say how this reorganisation will affect the functioning of the unit, the committee is optimistic about this change and agrees that its potential benefits outweigh the risks.

Under the current management, the unit's activities are excellent to outstanding at all levels: scientific, valorisation, training and dissemination. In particular, the unit's scientific production during the last five years is of the highest international standard. Several senior and mid-career team leaders are world leaders in their respective fields, and junior team leaders are rapidly establishing themselves as bright stars in their disciplines. In addition, the unit dissemination activities contributed highly to its national profile during the Covid-19 pandemic; the involvement of junior teams working in the evolution and ecology axis was especially notable.

## RECOMMENDATIONS TO THE UNIT

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

The unit has undergone significant turnover in team composition during the last evaluation period, with six teams departing or retiring, and a similar number being recruited at both the junior and senior levels. The committee agrees with the unit's direction that this high turnover, which is enshrined in the Cirb Internal Rules, increases the dynamism and research excellence of the unit. Inevitably, it also generates pressure and stress among the scientific staff, especially in junior teams, which may feel unsure about the near-term sustainability of their projects. To ease these concerns, the committee recommends the unit to specify a clear timeline for evaluations, as well as clear communication of the expectations (key performance indicators) necessary for team renewal, as well as guidelines for leaving teams, such as their conditions to accessing core facilities and other shared resources.

The committee encourages the unit to explore additional initiatives to facilitate internal dialog further. These should include internal seminars where all members of the unit participate and present their results. Other initiatives, such as funding of interdisciplinary, co-supervised postdoctoral fellow or PHD fellowships, could be explored but are depending on favourable financial conditions.

Finally, we advise the unit to formalise guidelines for the duties and rights of researchers and technical staff (such as authorship in publications) in future versions of the Internal Rules.

### Recommendations regarding the Evaluation Area 2: Attractiveness

The mentoring program initiated at the request of the previous Hcéres evaluation was discontinued. Efforts should be made to restart this initiative after a critical analysis of its previous, short-lived iteration. The committee suggests that a top-down approach could be more productive than the previous bottom-up approach: although a participation of younger scientists is essential for this initiative to succeed, the organisation of mentoring activities should be led by the mentors, not the mentees.

Creation of appropriate rooms for behavioural studies in the conventional animal facility, which is a stated priority of the Cirb direction, is likely necessary for the unit is to continue to publish at the top level in neurobiology.

### Recommendations regarding Evaluation Area 3: Scientific Production

The scientific production of the unit is outstanding, so the only recommendation of the committee is to encourage teams to further adopt the posting of preprints before publication in peer-reviewed journals, as preprints are becoming an essential element in the dissemination of science.

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

No recommendations.

## TEAM-BY-TEAM OR THEME ASSESSMENT

**Team 1:** Ecology and evolution of health  
 Name of the supervisor: Mr. Samuel Alizon

### THEMES OF THE TEAM

The team EEH studies the spread of infectious diseases, from an ecological and evolutionary perspective. It is notably interested in understanding how the functioning of within-host microbial communities affects our health, and how public health interventions drive the evolution of pathogens. The ultimate goal is to be able to prevent evolutionary responses that could jeopardise population health. The research of the team is based both on theoretical approaches (mathematical modelling) and on empirical data acquisition and analysis.

### CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team "Ecology and evolution of health" joined the Cirb in 2022. There are no recommendations on the previous report regarding this team.

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

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

### EVALUATION

#### Overall assessment of the team

Outstanding research, at the interface between ecology, evolutionary biology, and epidemiology, with a fruitful combination of theoretical approaches (mathematical modelling, e.g. 2017: Plos Comp Biol, 2021: eLife & Plos Path) and data acquisition (e.g. 2023 Mol Ecol). Pioneer in phylodynamics, the team has been a key actor to analyse the Covid pandemic in France, and made remarkable contributions to diffuse knowledge towards the general public (journals, radio, TV) and to inform public health agencies and decision-makers.



## Strengths and possibilities linked to the context

Team 1 develops innovative research axes at the interface between ecology, evolutionary biology, and epidemiology, with a fruitful combination of theoretical approaches (mathematical modelling) and data acquisition. Notably, the team has been pioneering in the development of phylodynamic approaches, i.e. methods based on the analyses of sequence diversification along phylogeny to infer key parameters of the diffusion of pathogens in the population (e.g. 2017: *Plos Comp Biol*, 2021: *elife*, *Plos Path*). Another important achievement is the implementation of the Papclear cohort at the CHU of Montpellier, which allowed a longitudinal study of 189 women between 2016 and 2020 (2020 *Vaccine*, 2021 *Immunol Res.*). This cohort already led to original results regarding risks of vaginal fungal infections (2023 *Mol Ecol*), and is expected to yield to new findings concerning the dynamics of HPV infections, of the vaginal microbiote, and of sexually transmitted infections.

From the beginning of March 2020, the team was fully mobilised to participate in the fight against the covid19 pandemic. They developed models which allowed the first estimate of the virus reproduction rate in France, a key parameter to inform strategic choices in public health policy (containment). They coordinated a national epidemiological study, and were the first to detect the spread of the Delta variant in France (2022 *Eurosurveillance*). In this period of great uncertainty and confusion (in particular linked to inopportune speeches by certain pseudo-experts), Team 1 PI and his team members have carried out an extraordinary popularisation work towards the general public (and notably the journalists), to explain what it is possible to predict, regarding the evolution of the pandemic and the impact of intervention strategies (containment, vaccination, etc.). This explanatory work, carried out with a clear view of the strength and limits of mathematical models, involved an enormous investment from Team 1 PI and his colleagues (development of a website to disseminate their research reports, guaranteeing the reproducibility of the analyses; numerous interviews for newspapers, radios, television; interventions with parliamentarians, with the justice, with public health agencies). The commitment of these scientists during the pandemic, and their determination to diffuse knowledge is really exemplary. This is all the more impressive that in parallel, the team managed to maintain its fundamental research activity, attested by publications in excellent journals. The success of their commitment perfectly illustrates the importance of developing a pluri-disciplinary expertise, at the interface between theoretical biology and public health. In that prospect, the team has been at the initiative of the creation of a new CNRS GDR (Phylodyn), dedicated to the field of phylodynamics.

## Weaknesses and risks linked to the context

None identified.

## Analysis of the team's trajectory

The team's research project is in logical continuation of its previous work, around three main axes. The first is dedicated to modelling the epidemiology of human viruses (herpesviruses, SARS-CoV-2, sexually transmitted infections). The second is aimed at improving phylodynamic methods, notably to investigate the spread of HIV in France. The third one aims at investigating the impact of the vaginal microbiote on women's health. These projects rely on data acquired from the Papclear longitudinal cohort, or via collaborations with hospitals and with an industrial partner. These projects will benefit from local collaborations within the Cirb (e.g. with Team 2 and Team 10).

## RECOMMENDATIONS TO THE TEAM

Try to attract new researchers to increase the critical mass of the team.

**Team 2:** Evolutionary epidemiology of infectious diseases  
 Name of the supervisor: Mr. François Blanquart

## THEMES OF THE TEAM

This is a relatively small team (6 members at the time of evaluation) which was created in 2022. The main research axis is the study of the spread of infectious diseases using evolutionary epidemiology in-silico approaches. The team mainly focuses on E. coli as major commensal and opportunistic pathogen but has also been working on HIV-1 and SARS-CoV-2.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Not applicable as the unit was not there during the past evaluation.

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

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

## EVALUATION

### Overall assessment of the team

The team productivity is excellent, with 38 articles and three reviews over the evaluated period (4 as last and corresponding author), ten of which have been published since its creation in 2022. Main results were produced on the analysis of a large cohort of commensal E. coli over a 30-year period (App Env Microbiology 2022). The PI has secured competitive funding as coordinator (ERC starting 2021-2026, momentum CNRS 2019-2021). Many members of the team are actively involved in teaching.

### Strengths and possibilities linked to the context

The team is very interdisciplinary and collaborative. It has a strong connection to the clinics and the projects are well aligned with current public health challenges.

## Weaknesses and risks linked to the context

The team relies on a single major grant (ERC starting). There is no permanent staff (researcher or engineer). The publication rate is high, but not in generalist journals. A substantial number of publications (17) come from collaborations without a first or senior authorship.

## Analysis of the team's trajectory

The project of the team is well conceived and will continue along the lines developed recently, notably on the ecology of *E. coli* and the development of mathematical models.

## RECOMMENDATIONS TO THE TEAM

Focus more on publishing as lead author and with team members. Increase international visibility with invitation to conferences and collaborations. Foresee other types of funding for when the ERC ends. Recruit at least a permanent researcher or engineer.

**Team 3:** Molecular control of neuro-vascular development  
 Name of the supervisor: Mrs. Isabelle Brunet

## THEMES OF THE TEAM

Team 3 studies neurovascular development using the mouse as a model organism, as well as the perivascular macrophages in the brain. Their main interest is the coordinated neural and vascular development and the interaction between the two systems, but also dysfunctional neurovascular interactions in human pathologies.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

*The committee recommends prioritizing the publication of the recent work (as senior author) to establish the leadership and international recognition of the PI.*

Two original articles have been published with the PI in leader position.

*Based on the risk that is inherent to projects on animal models, one could think of alternative strategies that are less risky and time-consuming. This issue has been addressed by the introduction of zebrafish models. No in vitro models have been developed and the use of zebrafish was not pursued.*

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

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

## EVALUATION

### Overall assessment of the team

The team "Molecular control of neuro-vascular development" is a young team with excellent national and international reputation, as demonstrated by numerous invitations to meetings. Attractiveness is outstanding, with the recruitment of one CR in 2018 and the arrival of two DRs in 2023 and 2024. The team obtained grants from ANR, charities and Labex, which is excellent. The scientific production is very good, with two original papers in *elife* and *J Cereb Blood Flow Metab* as leader author. The team produced a proof-of-concept in the field of cancer chemotherapy that is currently tested in collaboration with a clinical unit.

## Strengths and possibilities linked to the context

This is a relatively young team created in 2016, who started with the PI and a PAR. Since then, one young researcher has been recruited in 2018 at Inserm and two DRs will join the team in 2023 and 2024, showing the outstanding attractiveness of the team. Four PHD students and three postdoctoral fellows were hired by the team during the last contract. Hence, there will be a very positive balance of tenured and temporary scientists for this team in the near future. The PI is frequently invited in international (7) and national (10) meetings, and she obtained awards and rewards from Inserm (5), as well as from the Gefluc and Vaincre Alzheimer foundation. Students obtained several prizes (8) in national and international meetings for posters or talks. The three researchers (PI and the two DRs) have an HDR, which will increase the possibility to recruit PHD students. The team participated to teaching, to PHD (18) and HDR (3) committees, as well as PHD student mentoring (10). This is thus a very good contribution to scientific education. In addition, the PI was a member of the CSS4 at Inserm during five years, and was an expert for Hcéres. In addition, the team participates to different scientific networks in neuroscience and angiogenesis. Team 3 is thus well inserted into its scientific network, participates to student education and to various expertise at Inserm, in Universities and Hcéres.

Team 3 obtained a large number of grants, mainly from charities, ANR (one as coordinator and one as co-coordinator) or Labex. Altogether, 651 k€ were spent in six years (142 k€/y), which was sufficient for its functioning. In addition, several salaries for short-term researchers (PHD students and postdoctoral fellows) were acquired.

Team 3 published two original papers as corresponding authors in specialist (J Cereb Blood Flow Metab) and generalist journals (eLife), and the PI was co-authored in several additional papers (Circ Res, two eLife, Cell Reports). Some of these articles were co-published with Yale University where the PI was postdoctoral fellow, hence showing a productive link with her previous lab. They also published a preprint in Biorxiv and two reviews in Med Sci. Altogether, the scientific production is very good.

The PI is very active in understanding the action of oxaliplatin on the dysfunction of the blood-nerve barrier during tumour treatment with this drug. Her preliminary data are encouraging and show that vasodilators may help prevent tissue damage. This finding was shared with the medical community (Med Sci review) and with the general public (Youtube video). Importantly, the PI is connected to hospital units and to a medical consortium to perform a clinical trial to test vasodilators on oxaliplatin-treated patients. The team also participated to scientific events, such as Fête de la Science... targeting the general public or high school students.

## Weaknesses and risks linked to the context

Productivity of PHD students and postdoctoral fellows was uneven, as each of the three PHD students that left the lab authored only one first-author paper (one of which was available exclusively in Biorxiv at the time of evaluation), and the post-doctoral fellows (present in the team for only 2 years) have not yet published any first-author papers during the evaluation period.

## Analysis of the team's trajectory

The team's projects are in the continuity with those of the previous contract, and are largely extended with the arrival of two researchers (level DR).

A major research axis will aim at understanding the contribution of brain perivascular macrophages in tissue drainage, and their pathophysiological role in amyloid plaque formation and brain edema. This project is important and several approaches will be undertaken with French (notably Cirb Team 4) and international collaborators. It is founded by the Inserm AgeMed program and Vaincre Alzheimer Foundation and will involve five people from the lab.

The second project is linked to the etiology of oxaliplatin-induced peripheral neuropathy and its therapy. Both projects are well focused, original and scientifically sound, with potential benefits for public health.

## RECOMMENDATIONS TO THE TEAM

The major recommendation of the committee to team members is to maintain their effort and pursue their own scientific projects. They should provide major findings on the topic of neurovascular interface and brain drainage, and thus increase publication output.

The number of publications of PHD students and postdoctoral fellows could be improved. In this regard, the arrival of two senior researchers with HDR should be helpful to provide additional mentoring in the team

We strongly recommend to pursue the translational research on the use of vasodilators for oxaliplatin-treated patients.

**Team 4:** Physiology and physiopathology of the gliovascular unit  
 Name of the supervisor: Mrs. Martine Cohen-Salmon

## THEMES OF THE TEAM

The team focuses on astroglial regulatory functions at the brain vascular interface under both physiological conditions and in pathological settings. These inquiries were evaluated using cutting-edge molecular, cellular and in-vivo techniques.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

*The committee recommends attempting to consolidate the team using third party funding that is already initiated.*

Several external fundings were obtained, securing the functioning of the team.

*The committee recommends focusing on the expertise on the in vivo mouse models and on the excellent (core) field of research that will give rise to excellent publications, and finding a balanced way of networking activities and collaborative outreach.*

Team 4 publications are well balanced with some excellent articles from the team and several articles in collaboration.

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

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

## EVALUATION

### Overall assessment of the team

This is a very dynamic team studying the interaction of astrocytes with brain vessels in pathophysiological settings, a field for which they produced pioneering data. The reputation of the team and its attractiveness are excellent, as demonstrated by invitations at meetings, excellent funding level and collaboration network. The publication level is excellent to outstanding, with 20 articles in prestigious journals, both as corresponding authors and as collaborators. The team knowledge on pathological mechanisms within the gliovascular unit could be exploited for therapeutical strategies.

## Strengths and possibilities linked to the context

The team has an excellent national and international reputation, as demonstrated by numerous invitations to international (4) and national (20) meetings or seminars, for which both the PI and the CR were invited. Six PHD students were hired during the contract, and two postdoctoral fellows, showing the attractiveness of the team, and its capacity to obtain fundings for staff, and high-level students with doctoral grants. The team obtained 769 k€ of funding in five years (154 k€/y), mostly from ANR (2 as partner), from FRM (2 as coordinator, 1 as partner) and from other charities, Cepr and Labex, as coordinator. This is an excellent funding for a team of this size, and it shows the attractiveness for Team 4 projects in competitive grants.

The PI teaches in three masters and was a member or president in numerous theses, HDR and mid-PHD committees. In addition, she is a member of the Senat at PSL University and of the steering committee of the Cirb animal facility, indicating her participation to local organisation. She also interacted with high-school students in the framework of Declics and Apprentis chercheur.

Team 4 published twenty original articles during the last contract, including nine where team members were in leader positions. Among the latter papers, one was in a generalist journal (Cell Discovery) and four in prestigious journals such as *elife* and *Cell Rep*. Collaborations lead to major publications in *J Clin Invest*, *PLoS Biol*, *PLoS Pathog*, *Mol Metab*. In addition, they published three reviews and one methodological paper. Altogether, this is an excellent to outstanding publication level for a team of this size. Each of the three PHD students with defended thesis, published 5.7 papers in average during their stay in the lab, among which 2.0 in average as first author. This indicates that students were well supervised and their work well valued. In addition, the PHD students and a postdoctoral fellow obtained 3 best oral and 3 best poster prizes at meetings, further indicating the importance of the data presented and the preparation of the students.

Team 4 brought insight into pathological mechanisms of Alzheimer disease and hemochromatosis, showing a very good interest for translational research.

## Weaknesses and risks linked to the context

As they mentioned in their self-evaluation report, the field is "at the interface between fundamental and translational research". They produced excellent data in basic science, but their effort in translational research could be improved.

Work from postdoctoral fellows could be better valued in publications.

## Analysis of the team's trajectory

The Team will pursue their studies in astrocyte biology, notably the local translation in astrocytic processes, and the contribution of astrocytic dysfunction in two diseases, MLC and brain vessel calcification, using transgenic mice models. These lines of research are in perfect concordance with their previous work and are highly relevant.

## RECOMMENDATIONS TO THE TEAM

The main recommendation of the committee is to pursue their studies in this very relevant field and to maintain or even increase the publication level.

More interaction with the general public and the socio-economic world could be considered.

As mentioned in the project, their study on brain vessel coverage by astrocytes may lead to a therapeutic strategy for MLC disease. As viral targeting in the brain is not a simple therapeutic intervention, the committee encourages the team to explore additional, alternative options in that direction.

**Team 5:** Nuclear organisation and post-translational control in physiology and APL physio-pathology

Name of the supervisor: Mr. Hughes De The / Mrs. Valérie Lallemand-Breitenbach

## THEMES OF THE TEAM

Co-directed by two PI, the team is split between the Cirb and St. Louis Hospital. The team located in Cirb, evaluated here, focuses on the biology of the Promyelocytic leukaemia (PML) protein and its role in PML nuclear bodies. The team in St. Louis focuses on acute promyelocytic leukaemia (APL), which is driven by a fusion between PML and the Retinoic Acid Receptor alpha (RARA) protein.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No recommendations were made on the scientific production and activities (criterion 1) or on the scientific strategy and projects (criterion 3) as these were considered outstanding to excellent.

The team's organisation and life (criterion 2), was not evaluated due to lack of information on how activities between the two halves of the team (located in Cirb and St. Louis) are coordinated. Clarifications on this point were provided by the team in an addendum to the previous report, and to some extents are maintained in the current self-evaluation document: the projects carried out in the two sites are related but well separated.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	2
<b>Sous-total personnels permanents en activité</b>	<b>6</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	3
Doctorants	4
<b>Sous-total personnels non permanents en activité</b>	<b>7</b>
<b>Total personnels</b>	<b>13</b>

## EVALUATION

### Overall assessment of the team

This is an outstanding team and an internationally recognised leader in the leukaemia field, that has made seminal contributions on the molecular mechanisms of leukaemogenesis and targeted therapies. Its productivity and funding in the evaluation period were excellent to outstanding, including articles in Cancer Discovery and Nature Communications, and an ERC Advanced grant. The team also demonstrated high involvement in outreach activities and is highly visible in this sense at the national level.



## Strengths and possibilities linked to the context

The team is scientifically recognised internationally for their contributions to the APL field, and has also made fundamental advances to the understanding of PML body biology.

The productivity of the team during the last period has been excellent to outstanding, with two articles provide important insight into the basis for the therapeutic response of acute myeloid leukaemia to Actinomycin D (Cancer Discovery 2021) and on PML function in sumoylation control in nuclear bodies (Nature Communications, 2022). Additionally, more than 20 articles (mostly in specialised journals, including J Exp Med, Blood among others) in which team members are in a first or corresponding author position, and multiple articles in collaboration.

The team has also maintained its outstanding international reputation through reviews and presentations in highly visible venues, and been very successful in funding acquisition. The level of funding is outstanding, with grants from ERC Adv, INCa, ITMO Cancer, among others.

An important commitment to award-winning science outreach activities further contributes to the visibility of this outstanding team.

## Weaknesses and risks linked to the context

The departure of Team 5 co-PI will affect the management and scientific direction of the team at College de France, which will be led by one PI and will reduce its focus on the role of phase transitions on PML body biology. This change will also affect the team outreach efforts, which were driven in great part by the leaving Team 5 co-PI.

## Analysis of the team's trajectory

The scientific project explores exciting questions on i) the roles of RARA and retinoids in acute myeloid leukaemia ii) Cell biology of PML and its functions in chemotherapy response iii) basis for response of human AMLs to conventional chemotherapy.

## RECOMMENDATIONS TO THE TEAM

No recommendations.

**Team 6:** Chromosome dynamics

Name of the supervisor: Mr. Olivier Espeli

## THEMES OF THE TEAM

The "Chromosome Dynamics" group investigates the molecular mechanisms involved in the transfer of genetic information during chromosome segregation in bacteria. The group focuses on characterising the mechanisms of chromosome folding and segregation. More recently, the group has begun to study the adaptation of the cell cycle to environmental stress in the host cell of pathogenic bacteria.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

There was no specific recommendation other than to consider putting some effort into the structural characterisation of Recn to confirm its cohesion like nature. This line of research was not initiated by the team.

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

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

## EVALUATION

### Overall assessment of the team

The "Chromosome dynamics" team (Team 6) is outstanding both in terms of scientific production, obtaining funding for the team, or participating in training through research. The quality of the published articles is remarkable, with five published articles with the team leader as the last author in high-profile journals such as Nature Communications in 2017, NAR in 2022 or PLoS pathogens in 2019. The team has received numerous national grants including ANR (three as coordinator and two as partner), FRM and "fondation" ARC.

### Strengths and possibilities linked to the context

The team develops two topics in parallel. The group's expertise in the first topic (bacterial organisation and dynamics) is internationally recognised. Indeed, the PI has been invited to present his work at Gordon conferences, EMBO workshops, and ASM general meetings. Regarding the team's second theme (host-pathogen interaction), which is more recent, the group's reputation is growing. The fact

that two members of the Team, represent France in the COST action EuromicropH, which deals with bacterial adaptation to low pH environments, confirms the scientific recognition of the team in this field. One of the strengths of running these two topics in parallel is the possibility of overlapping them, increasing the visibility and attractiveness of the team, and favoring interdisciplinary research. Of note, the team already has collaborations with physicists (Grenoble University and MNHN) on the bacterial chromosome topic, which led to an outstanding joint publication with colleagues from Grenoble and Paris-Saclay Universities (Cell 2018), while on the host-pathogen interactions topic, collaborations with clinicians (Clermont-Ferrand Auvergne University), mathematicians (ENS Paris) and chemists (ENS Paris) also led to excellent publications (Commun Biol 2021, PLoS Pathogens 2019).

Team 6 PI is actively involved in the teaching and administrative organisation of the PSL University in addition to being deputy director of the Cirb.

In particular, he has been involved for the last eight years in the organisation of the Frontiers in Microbial Systems module of the Imalis Master of ENS. This involvement of Team 6 PI in teaching is a clear strength since it may be one of the reasons for the attractiveness of the team for PHD students and postdoctoral fellows. The training through research is outstanding since from 2017 the team has supervised the PHD thesis of ten students.

The quality of the team's published articles is outstanding, with five articles published with the team leader as last author in journals such as Nature Communications in 2017, NAR in 2022 or PLoS Pathogens in 2019. The team has received numerous national grants, including ANR (three as coordinator and two as partner), FRM and ARC foundation.

## Weaknesses and risks linked to the context

The main weakness identified by the Committee is the retirement (in 3 years) of the only permanent researcher in the team and who was largely involved in the second topic "host-pathogen interaction". This could affect the execution of this project, which had gained momentum in recent years. Especially considering the number of responsibilities that the team leader has within the management of the Cirb and the Boards of Directors of the PSL University.

## Analysis of the team's trajectory

The goal of the team is to maintain its research activity around two main axes:

1) Mechanisms of sister chromatid pairing in the normal and pathological bacterial cell cycle. In this first axis, the team aims to provide a comprehensive analysis of sister chromatid pairing in bacteria. They will also study how sister chromatid pairing integrates and affects other cellular events, and an interesting aspect of the project is to study cell cycle dynamics of non-conventional E. coli strains.

This axis will benefit from the close collaborations already established with the Rivoire, Barre and Modesti labs (Bach ANR project), with the Cornet, Koszul and Junier labs (Sisters ANR project) and with the Lamour lab. (Topo-RNAP ANR project).

2) Organisation and dynamics of intracellular bacterial communities.

Based on the team's recent discovery that an AIEC LF82 strain forms colonies inside phagolysosomes and that a protective biofilm-like matrix surrounds each LF82 in the colony, the group aims to characterise LF82 life within intracellular bacterial communities. An FRM grant, the Weizmann Foundation and Labex Memolife are currently funding this axis of the project.

The two axes of the proposed project are carefully designed, innovative and well focused. The team will use state-of-the-art interdisciplinary approaches based on molecular and computational biology, genetics, biochemistry and advanced imaging. Overall, the Committee judges the scientific strategy outstanding.

## RECOMMENDATIONS TO THE TEAM

The committee recommends that the team continue its studies with the two research axes in parallel, maintaining the outstanding publication level in the first axis and even increasing the level in the second axis.

A critical aspect will be to attract new permanent researchers to maintain the success of axis 2 of their research.

The recruitment strategy of the team should also aim at recruiting or sharing an engineer with another Cirb team, which should be a priority for the Institute, considering the involvement of the team leader in the management of the Cirb.

**Team 7:** Neurobiology and Immunity  
 Name of the supervisor: Mrs. Sonia Garel / Mrs. Morgane Thion

## THEMES OF THE TEAM

The team is studying how neuro-immune interactions contribute to the proper development of forebrain circuits that enable sensory perception, motor responses and cognition. Forebrain circuitry develops during embryogenesis and can be disrupted by changes in the maternal environment, such as inflammation, leading to neurological disorders such as autism spectrum disorders and schizophrenia. The team's main objective is to decipher how interactions between microglia, resident brain macrophages, and neuronal and vascular players contribute to this process, focusing on the early development and diversity of microglia, as well as their prenatal functions.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was created in 2022 and was not evaluated in the previous report.

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

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

## EVALUATION

### Overall assessment of the team

The team "Neurobiology and Immunity " has an outstanding scientific production, with five published papers with the team leader as senior author in top-ranking journals (Cell Reports, Nature Communications, Cell...) and review articles in very high-profile journals (Nat Rev Neuro, Science and Nat Neurosci...). The originality and quality of the research team are also acknowledged by the considerable support from european and national fundings (ERC, ANR, FRM...), strong collaborative network leading to remarkable publications (Cell, Immunity...) and international recognition of the team co-leader.

## Strengths and possibilities linked to the context

The team studies the integrated molecular mechanisms governing the establishment of functional forebrain neuronal circuits, enabling sensory perception, motor responses and cognition during development. They notably showed that the thalamocortical projections are guided and organised by a small population of guide neurons located along their path. In particular, the contributions of neuronal activity, microglia and environmental signals to wiring have been studied.

The team has a high international visibility and an exceptional level of publications and funding with a total of eleven publications, including five publications where the team leader is the senior author in journals that ensure the visibility of the team's work (Cells Reports, Cell, Nature communications...). The team is extremely well financed thanks to national and European funds.

The major findings over this evaluation period are that 1) the developmental mechanism of the striatal projection neuron mosaicism relies on an intrinsic transcription factor for cell type specification and intermixed cellular migration, 2) Cajal-Retzius cell migration and maintenance are controlled by pre and post-natal neuronal activity, 3) there is a period of time after birth during which mistargeted embryonic thalamic axons can be rescued under the regulation of serotonin and time of birth, 4) prenatal lack of microglia or prenatal inflammation have a two-step impact on parvalbumin interneurons wiring onto their excitatory target neurons in the barrel cortex (in collaboration with Institut de Génomique Fonctionnelle, Montpellier), 5) microglia contribute to maintain tissue structural integrity by promoting repair and secreting osteopontin, 6) microglia lie at the interface between the microbiota and developing neuronal circuits, relaying environmental signals in a sex- and age-dependent manner (in collaboration with Institut Gustave Roussy).

## Weaknesses and risks linked to the context

One of the co-PI, which was awarded a professorship at the Collège de France in 2022, has been based at Ibens for several years. Since 2022, a second research team co-directed by the two PIs has been set up at Cirb. At the time of this evaluation, each team was relatively small, comprising seven people, but was destined to welcome new members. The separation of personnel and funds between these two teams is not clearly presented in the self-evaluation document this was clarified during the oral presentation. The specificity of research projects of the Cirb team relative to the Ibens team (i.e. projects that are complementary but not redundant) is not clear from the self-evaluation document.

## Analysis of the team's trajectory

The ambitious proposed projects are a perfect continuation of the previous projects. The team will continue its studies on microglia embryonic colonisation by evaluating the contributions of the medial ganglionic eminence niche and peripheral monocytes to microglia repopulation after CSF-1R mediated depletion. The particularities of the different regional niches of microglia accumulation will be studied using transcriptomic, imaging and molecular approaches. The respective and dynamic roles of CSF-1R ligands on microglia proliferation, differentiation and survival will be studied on mutant animal models. The team also proposes to study the functional interactions between microglia and vascular cells during embryogenesis. It will also continue her studies on the impact of microbiota and prenatal inflammation on the development of microglia.

## RECOMMENDATIONS TO THE TEAM

The new co-leader of the team created at Cirb is encouraged to apply for funds at national and European levels as principal investigator and to sign articles in corresponding authorship. Despite the outstanding scientific production of the team, some PHD and post-doctoral students have not signed articles with leading positions yet. The committee recommends that this problem be rectified in the future.

**Team 8:** Paleanthropology  
 Name of the supervisor: Mr. Jean-Jacques Hublin

## THEMES OF THE TEAM

The "Paleoanthropology" team is interested in human evolution from a multidisciplinary perspective and combines anthropology and archaeology with other natural and social sciences to study how hominin biology, culture and ecology structured human evolution.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team leader joined the Cirb in 2022. There are no recommendations on the previous report regarding this team.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	0
<b>Sous-total personnels permanents en activité</b>	<b>1</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	1
Post-doctorants	2
Doctorants	3
<b>Sous-total personnels non permanents en activité</b>	<b>7</b>
<b>Total personnels</b>	<b>8</b>

## EVALUATION

### Overall assessment of the team

The team is outstanding, world leader in its field. Its works have led to major breakthroughs in palaeoanthropology. The team is strongly involved in international collaborative networks. Its projects rely on an efficient combination of multidisciplinary approaches and fruitful excavation sites. The publication track record is exceptional (e.g. Nature 2017, 2019, 2020), and has drawn a lot of interest from the general public.

### Strengths and possibilities linked to the context

The research conducted by the team has led to several major breakthroughs in palaeoanthropology. Just to cite a few: discovery that anatomically modern humans already existed 300 kyrs ago (100 kyrs earlier than previously thought) (Nature, 2017); discovery of a mandible from a Denisovan individual in Tibet (the first fossil attributed to Denisovans, outside of the Denisova cave, Nature 2019); demonstration that H. sapiens already penetrated deep into Europe 46 kyrs ago (Nature Ecology & Evolution 2020, Nature, 2020), and that he was exposed to a subantarctic climate (Science Advances, 2021). The scientific track record of the team is

outstanding, with publications not only in high-quality journals of the field, but also in generalist journals such as Nature, Nature Ecology & Evolution or Science Advances.

The team is strongly involved in international networks, leading or collaborating to various field and laboratory projects in Africa, Europe and Asia. Its projects rely on an efficient combination of multidisciplinary approaches (large-scale paleoproteomics, isotopic analyses, ancient DNA analyses, 3D imaging, ...) and fruitful excavation sites.

The quest for the origins of humanity is a fascinating topic, and the important advances made by the team have drawn a lot of attention from the media. The PI also participated to the making of several documentaries on human evolution (e.g. for Arte).

The Balzan prize awarded to the PI last September and a recently accepted ANR grant will secure the funding of the team for the next years.

### Weaknesses and risks linked to the context

None identified.

### Analysis of the team's trajectory

The team will pursue its line of research by developing exciting new areas: they will analyse the evolution of brain metabolism and energetics expenditure. To do so, the rate of cerebral blood flow will be addressed through the analysis of the carotid canal in fossil crania using different technics such as computed tomography and high-resolution 3D imaging. They will also analyse at the molecular scale (DNA, proteins, amino-acids) different remains in order to better understand mankind evolution. Besides, human evolution will also be analysed through the lens of cultural and environmental evolution. To this end, several excavation projects have been set up around the world (Africa, Middle East). These different lines of work promise exciting new findings.

## RECOMMENDATIONS TO THE TEAM

There is no specific recommendations. We wish to congratulate the team for its work.

**Team 9:** Evolution and Development of Germ Cells

Name of the supervisor: Mr. Jean-René Huynh

## THEMES OF THE TEAM

Team 9 is interested in the development of germ cells and more specifically in the way these cells divide by examining several molecular levels and using complementary model organisms to gain knowledge by comparing reproduction strategies.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

N/A

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

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

## EVALUATION

### Overall assessment of the team

The scientific production of the "Evolution and Development of Germ Cells" team is outstanding. The quality of the research team is also recognised by the considerable support it receives from national funding agencies, and its attractiveness is excellent to outstanding reflected in the impressive recruitment of CRCN researchers, enabling it to provide good supervision of current research projects. The team enjoys excellent national and international recognition and its non-academic activity is excellent with regular initiatives aimed at communicating with the general public.

### Strengths and possibilities linked to the context

The team is very dynamic and draws on the solid experience of researchers who obtained a post-doctoral degree and continued their research projects immediately afterwards as permanent CRCN researchers. The scientific achievements (8 Research articles - 4 Reviews) are highly relevant in the field of germ cell development and meiosis, with influential publications in generalist journals (Science, Science Advances). Among the main recent discoveries, The "Evolution and Development of Germ Cells" team has identified a mechanism of deubiquitination underlying the incomplete division of germ cells keeping them connected through cytoplasmic bridges (Science 2022).



The laboratory's other strength is the successful use of three different model organisms: drosophila, medaka and jellyfish, which provides evolutionary aspects that reinforce the laboratory's research objectives. The team's level of funding is also excellent, with grants from the ANR, the FRM and the Bettencourt Foundation. The team's funding has enabled it to recruit several postdoctoral fellows and ITAs. Recently, a CRCN of Team 9 was awarded an ANR-JCJC and JRH an ANR PRC, guaranteeing funding until 2026.

### Weaknesses and risks linked to the context

There are no major weaknesses, although it will be necessary to ensure that the projects pursued are rapidly supported by new funding. However, the quality of publications should make this possible.

### Analysis of the team's trajectory

The team's trajectory is very coherent, consisting of the continuation of recently published work and new, well-structured and well-funded projects (e.g. ANR JCJC). Each project is supervised either by CRCN researchers or by talented postdoctoral fellows, which should enable rapid progress. For some projects, collaborative work is planned, particularly for evolutionary aspects involving the use of non-Drosophila model organisms, which is undoubtedly a good strategy.

## RECOMMENDATIONS TO THE TEAM

We recommend increasing the number of HDRs in the team. Only the PI has his HDR, whereas there are four CRCNs in the team and only one PHD student in training at the moment. Funding resources, while substantial, are mainly obtained (except one ANR JCJC) through the team's PI. It would probably be important for the team's CRCNs to be able to obtain their own funding and quality of publications should allow targeting international funding agencies.

**Team 10:** Stochastic models for the inference of life evolution

Name of the supervisor: Mr. Amaury Lambert/ Mr. Guillaume Achaz

## THEMES OF THE TEAM

The Smile team lies at the crossroads of mathematics, population genomics and bioinformatics. Its members develop innovative probabilistic models for inferring evolutionary processes such as speciation, diversification, epistasis and cancer evolution. In addition, the evolutionary epidemiology of several pathogens is studied, notably SARS-CoV-2.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Although the previous committee considered the Smile team to be highly competitive, a few recommendations were made, notably to increase the dissemination and impact of the team's work by considering publications in higher-impact journals and providing more user-friendly resources to the community.

This objective has been partially achieved, for example, through the dissemination of tools for constructing species partitions from single locus sequence alignments (i.e. barcode datasets). This software published at the end of 2020, has already been cited a remarkable 400 times. As far as the journal impact is concerned, production is in line with the previous time window, i.e. excellent journals in the field but few journals with a large audience.

Nevertheless, in the eyes of the current committee, providing useful tools and knowledge to the scientific community is the most important value of scientific work, and the Smile team has an excellent impact on this point.

Encouragement to collaborate with more experimental groups was also expressed. This was taken into account by the establishment or continuation of collaborations within Cirb (Team 11) and outside Cirb (E. Rocha, Institut Pasteur and C. Tomasetti, Johns Hopkins Univ).

The team achieved the point of giving the students of the group more opportunities to interact with people working outside their field of interest through the recurrent organisation of conferences ("Evolution in Paris").

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

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

## EVALUATION

### Overall assessment of the team

The Smile team is excellent to outstanding in terms of scientific output, including highly cited papers (ex: Puillandre et al. 2021, 400 citations in 2 years). The attractiveness of the group is outstanding with the involvement of numerous postdoctoral fellows (9) and PHD students (13) during the period. The Smile team strongly contributed to the national and international scientific animation, has been dedicated to increase the teaching offer in Paris (Master EvoGEM) and was involved in scientific outreach especially during Covid-19 pandemic.

### Strengths and possibilities linked to the context

The Smile team has an excellent to outstanding scientific output in both quantitative (n=70 articles, 39 of which are first or last author) and qualitative terms (eLife, MBE, Nature, Systematic Biology...).

The Smile team established an outstanding visibility and attractiveness in at a national and international scale. The team has a strong mentoring activity involving all four permanent members as supervisors (9 postdoctoral fellows, 13PHD), revealing a high level of attractiveness. The Smile team enjoys national and international recognition.

The team's national reputation is attested by its numerous committee memberships (32 PHD committees, 13 hiring committees) while international recognition is attested by numerous international co-publications and the management of the international Redcode consortium.

In addition, team members make a significant contribution to national scientific activities (i.e. direction of the GDR AIEM by GA).

This remarkable activity was supported by several competitive grants, including an ERC starting grant to Team 3 PI (who left the group in 2022) and additionally more than 800 k€ to other members of the group. In addition to a strong teaching activity (>600h per year), the two PIs have been strongly involved in the creation of the new EvoGEM Master program and also in excellent outreach featuring (20 interviews in mainstream media, including on Covid pandemics, and >10 seminars for the general public).

### Weaknesses and risks linked to the context

The team does not suffer any evident weakness on the scientific ground. The unique point of potential future weakness is the decrease in the number of permanent research staff (from 4 at the beginning of the mandate to 2 at the end).

With the departures of all full-time researchers, hiring ideally a full-time researcher should be a priority to maintain the high level of scientific production.

The team is aware of this weakness.

### Analysis of the team's trajectory

The team will pursue its main lines of research in population genomics (including conservation biology), biodiversity dynamics and pathogen evolution. The structuring of an additional axis on somatic evolution is also proposed. This axis will draw on the team's expertise in understanding evolutionary processes to provide insights on somatic evolution, including carcinogenesis. The project offers new opportunities for potentially fruitful collaborations through shared PHD tutorship (at Cirb: Team 11 on colour evolution, outside Cirb: Pasteur Institute the evolution of antibiotic resistance, abroad: Johns Hopkins University on the evolution of cancer). In addition, the project aims to strengthen the team by hiring a permanent young researcher or a teacher researcher, while maintaining and developing involvement in the teaching offer on the evolution and challenges induced by climate change.

In designing its projects, the team is concerned with main current societal issues such as the erosion of biodiversity, or the preventive medicine, through the study of somatic evolutionary processes applied to carcinogenesis and tumorigenesis phenomena or the evolution of human pathogens (emergence of antibiotic resistance or the discovery of their evolutionary history and origins). All of these trajectories have the potential to shed significant light on our understanding of the living world and into some current societal issues.

## RECOMMENDATIONS TO THE TEAM

Following the recent evolution of the team (2021), the committee strongly encourages the team to continue on the same dynamics and to try to attract a full-time researcher.

**Team 11:** Formation and Evolution of Skin Patterns

Name of the supervisor: Mrs. Marie Manceau

## THEMES OF THE TEAM

The team addresses evo-devo questions on feather and colour patterns in birds, using natural interspecific variation as raw material. Specifically, the team study the mechano-chemical processes which produce positional information and shape the phenotypic landscape of natural patterns. A special attention is given to developmental mechanisms ensuring pattern fidelity, but still allowing pattern diversification during evolution. This is achieved through drug treatments on cultured skin explants, live imaging histological techniques, hetero-specific grafting, RNAseq analyses and theoretical modelling. The two model systems, feather patterns and colour patterns, are complementary with different predominance of self-organisation processes versus use of pre-featuring embryonic landmarks.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No recommendation was made, other than to translate the excellent results into published articles. This has been done, and very well since excellent to outstanding papers were published on the two main research axes (4: Science 2018 ; PlosBiol 2019 ; PlosBiol 2022 ; Sci Adv 2022) as well as a number of reviews (inc. in Curr Op Genet Dev). We also note that several points raised in the previous report were addressed; e.g. the PI obtained her HDR and proved the efficacy of her network at collecting bird eggs from different species (previously judged as a fragile strategy).

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

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

## EVALUATION

### Overall assessment of the team

The team has an outstanding scientific output, both quantitatively and qualitatively, with fourteen publications including papers in generalist journals, such as Science). This success stems from the unique niche of the team in comparative developmental biology, establishing various functional experiments and handling multiple species. The team's attractiveness, visibility and outreach are all excellent to outstanding, with prestigious grants and awards, keynote lectures at international conferences and participation in scientific committees.

### Strengths and possibilities linked to the context

Research projects are very efficiently managed, as seen in the well-balanced productivity of the two main projects, with two excellent/outstanding papers each (Science; Science advances; Plos Biology x2). Most postdoctoral fellows and PHD students have signed first-author research articles at the end of their contracts, which testifies to good supervision. The PI also involved three of them in writing reviews (3, including in Current Opinion in Developmental Biology).

Part of this success relies on the team having efficiently developed their technical abilities to perform functional experiments both adapted to the model system and the questions, and developing fruitful collaborations with modellers. This way, the team has worked to decipher and test principles of development inferred from natural variation, such as 1) how a cryptic template, which is inherited from earlier steps of embryonic development, is used to establish colour patterns in the plumage of finches, and how this conserved template is differentially reused to generate colour diversity in nature 2) the team proposed a unified model for feather formation with a wave of self-organisation, acting on a species-specific prepatter, and progressing according to different proliferation rates. Moreover, early cell shape anisotropy in the dermis was correlated to fidelity of the final pattern, opening new questions.

Research has been very well funded thanks to the acquisition of highly competitive grants (more than 1 M€ following the 1.5M€ ERC starting grant obtained in 2015)

The team has attracted a high number of PHD Students and Postdoctoral fellows over the period (5 PPHD, 3 postdoctoral fellow). This is well suited for a single PI in the team, and has been remarkably stable over the years, also reflecting the fluid transition between funding resources.

The quality of the research has been recognised by national institutions (5 prizes for the PI including CNRS bronze medal, Académie des Sciences; Bettencourt Schueller foundation, Schlumberger Foundation), and contributions to scientific committees (ANR, cercle FSER) and the PI's work enjoys international recognition (e.g. invited speaker at 22 international conferences; including two keynote talks, academic editor for Developmental Biology).

The PI and its team have also an impressive record of scientific outreach and art/science initiatives, including national radio interviews ("La tête au Carré" « Les savanturiers », France inter) and popular articles in the mainstream press (Pour la Science, Elle).

The team is well integrated in the Cirb, with starting internal collaborations, and forms a nice bridge between the developmental biology and the evolutionary biology departments.

### Weaknesses and risks linked to the context

We do not identify real weaknesses at the moment, but one point merits attention.

One possible risk for the future is that the team hosts only one permanent researcher. This is has not been a problem so far, as shown by the very efficient management of the team over the last five years, in terms of science, human resources and funding. However, the team's future project, extending to more evolutionary questions, may benefit from another permanent researcher with an evolutionary background, which would nicely complement the PI's background.

### Analysis of the team's trajectory

During the last period, the team showed that feather patterning fidelity is controlled by species-specific initial conditions of cell shape anisotropy and motility. The next period will be dedicated to elucidate the origins of

these differences in initial conditions, and clarify their role in pattern fidelity. The ambition is to disentangle the role of external forces (e.g. tissue deformation following body growth), tissue material properties linked to species-specific extracellular matrix, and active forces resulting from local cell behaviours. This will be done through a series of experiments probing the histology and the mechanical properties of the tissue, with already developed protocols and in collaboration with recognised experts (ex. IBDM, Marseille). This is original and ambitious because multiple feedback may obscure causal relationships.

In a second axis, the team will study at an unprecedented scale of the diversity in colour patterns (~3000 species) thanks to collaborations with national history museums and with phylogeneticists, including with Team 10 at Cirb. The hypothesis is that a basic cryptic template is conserved across the avian phylogeny. This will be tested by reconstructing the phylogenetic history of cryptic and apparent colour domains, and by performing lineage tracing experiments and hetero-specific grafting which are mastered by the team. By introducing ecological data, this may eventually reveal how the developmental constraint interacts with environmental (adaptive) constraints to produce the diversity patterns. The team has proved its capacity to get eggs from different species. In this more constrained phylogenetic context, access to the most relevant species may be more difficult yet is possible through a network of collaborators in zoos.

The aim of the third axis is to identify the molecular determinants which instruct the colour pattern according to the template, with a number of candidate genes already identified, and gain- and loss-of-function experiments. Finally, the team will study late mechanisms for colour pattern formation, resulting from spatiotemporal variations in pigment production. This will be done in species well mastered by the team, trying to correlate spatiotemporal expression of pigmentation master genes to the colour pattern through a combination of mathematical modelling and experimental manipulations. A phylogenetic study of pigmentation genes will be correlated with the above-mentioned phenotypic data. This is mainly done in collaboration with other teams, including some present in the Cirb.

The project is ambitious, with approaches ranging from in-depth developmental analysis in particular species to broad analysis of diversity in more than 3000 species, and genome analysis. Success in this project will require the full involvement of multiple team members (the PI and several PHD students, postdoctoral fellows) and intense collaborations for the evolutionary sections.

## RECOMMENDATIONS TO THE TEAM

The team should continue on the same outstanding dynamic, including efforts to collaborate across departments with other teams in Cirb. The team should pay attention to possible conceptual dispersion, as the model may not be sufficient to unify very different research questions. Recruiting another permanent researcher in the team would obviously be a good strategy to ensure this richness remains a strength.

**Team 12:** Development and Neuropharmacology

Name of the supervisor: Mr. Alain Prochiantz/Mr. Ariel Di Nardo

## THEMES OF THE TEAM

The team's main interest is the study of homeoprotein transcription factor transfer during physio-pathological conditions, and specifically the functions of these transcription factors in brain development, plasticity and neuroprotection during neurodegenerative diseases.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

There was no specific recommendation for this team

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

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	3
<b>Sous-total personnels permanents en activité</b>	<b>8</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	3
Post-doctorants	1
Doctorants	5
<b>Sous-total personnels non permanents en activité</b>	<b>11</b>
<b>Total personnels</b>	<b>19</b>

## EVALUATION

### Overall assessment of the team

This is an excellent team in terms of scientific production (Mol Psychiatry 2021; Int J Mol Sci 2022), industrial interaction (patents; start up) and public outreach (many shows such as 'France Culture'). The team has an outstanding international and national recognition (invited to prestigious conferences, including EMBO). The team will focus on the role of the plexus choroid and the transfer of homeoproteins during brain homeostasis. Projects are well defined and funded. One PI will be more involved in the industrial projects and the second PI will take the lead on the academic side.

### Strengths and possibilities linked to the context

The team benefits from the great environment offered by the Collège de France and the excellent teams present at the Cirb. The team is recognised internationally. This is a very productive team in terms of academic research but also given the number of patents they produced.

Moreover, the team is led by an emeritus professor from Collège de France. He has an excellent sense of interaction with the public and he is strongly involved in the interaction between the academic world, industry (through Labcom) and the public: notably he is one of the founders of the PAUSE initiative that helps scientists



in danger to relocate to France to pursue their work. In the coming years, the second PI will take the lead on the academic side of the projects. He has already shown great ability to acquire funding (mainly ANR grants) and to publish high quality work (among others he is the lead author on 2 articles published in Molecular Psychiatry). The projects developed by the team are challenging but very exciting, as they focus will be on the role of plexus choroid derived homeoproteins in brain homeostasis during development and in the mature system.

## Weaknesses and risks linked to the context

Compared to the last evaluation, the current team mainly relies on PHD students. During the current evaluation period, only three postdoctoral fellows joined the team and they left after two years. Since 2020, there are no postdoctoral fellows in the lab. It is clear since the pandemic, there is a shortage of well-qualified postdoctoral fellows.

Moreover, one permanent researcher has left the team. Therefore, the axis developed under her supervision will also end. With this departure, the team will have only male scientists.

The team's international recognition and interaction with the public rely strongly on the most senior co-PI. However, the other co-PI shows great potential as a leader, since he is obviously able to secure funding (ANR grants) and to publish high-profile articles (Mol Psychiatry)

## Analysis of the team's trajectory

The team allowed the emergence of new independent scientists (Julia Fuchs).

It appears that in the coming years there will be a major shift in the group, as one co-PI will be involved more with Labcom, and the other co-PI will be in charge of the academic side of the team. Hence, there will be a change in team dynamics. This shift of balance might bring some new challenges but the team is stable enough to overcome them.

In this context, there was a major effort to focus the projects of the team. There are now clearly two research axes in the group and one axis that has a more industrial focus. Each of these axes has its own funding. Even if the two academic axes are independent, there are still some overlaps that will allow synergy across projects.

## RECOMMENDATIONS TO THE TEAM

There are no particular recommendations. The team leaders have shown over the years the ability to manage projects and a lab. However, there will be a change in the dynamics of the group, as one co-PI will take the lead on the academic side and the other co-PI on Labcom. They should be careful to maintain the high standards and quality of their work and the quality of interactions within the team. Moreover, the team needs to be vigilant in the gender ratio among scientists. As of 2019, there is no female in the group; among PHD students, this ratio is almost 50/50.

**Team 13:** Neuroglial interactions in cerebral physiopathology

Name of the supervisor: Mrs. Nathalie Rouach

## THEMES OF THE TEAM

The team works to determine the role of astrocytes and astrocyte-neuron interactions in information processing in the brain, in physiological and pathological conditions, with a specific focus on the role of connexins, pannexins and calcium signalling.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous comments noted that most publications were being published in specialised journals, that the load of team management appears heavy for the team leader, that teaching output could be increased, and that the permanent members of the team could be more engaged in non-academic interactions.

In the latest review period, the team has published studies in generalist journals demonstrating a critical role for astrocytes in early life plasticity (Ribot et al., *Science*, 2021), and a role for pannexins in human epilepsy (Dossi et al., *Sci Transl Med*, 2018). The study on critical period biology in particular led to significant interest among the general public, with high-profile articles in the general press (e.g. *Le Monde*), radio shows etc. Outreach has been further helped by one tenured lab member taking the lead in these activities.

Issues of team management and teaching were not meaningfully addressed in the self-evaluation report, but are likely to become more significant issues with the departure of a permanent member (and colleagues/subteam) for an independent position.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	3
<b>Sous-total personnels permanents en activité</b>	<b>6</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	7
Doctorants	9
<b>Sous-total personnels non permanents en activité</b>	<b>17</b>
<b>Total personnels</b>	<b>23</b>

## EVALUATION

### Overall assessment of the team

Outstanding. The team published some outstanding studies addressing key issues in the field (incl. Ribot et al., Science). These enhanced the international profile of the team, resulting in a (high) number of invited talks at institutes and conferences (e.g. GRC). Training is excellent, with many studies originating from students, and senior lab members securing research grants (incl. ERC) and external positions. The team has strengthened its outreach activities. A discovery on pannexins and circuit excitability is being explored in epilepsy, leading to the creation of a spin-off company (Panntherapi).

### Strengths and possibilities linked to the context

Building on their previous work, the team made significant discoveries on the role of astrocyte channels (connexins and pannexins) in the control of CNS metabolism (Cheung et al., Nat Commun, 2021), circuit excitability (Dossi et al., Sci Transl Med, 2018; Hardy et al., Glia, 2021) and plasticity (Ribot et al., Science, 2021), including in human systems. The team appears to make extremely good use of the multidisciplinary nature of Cirb and maintains excellent local, national and international collaborations. Funding to date (national and European) has been impressive and includes industrial contracts. The team has been actively involved in IP generation and creation of a spin-off company.

### Weaknesses and risks linked to the context

No major weaknesses are detected.

Minor issues which may need to be considered are as follows:

The team no longer has ERC funding, but is well placed for an ERC Advanced application, which should be made within the next evaluation cycle, to supplement existing ANR grants.

The team should aim to be a 'first choice speaker' at international astrocyte conferences (particularly US-based ones, such as CSHL and GRCs). Alternatively, the team could leverage its international standing to organise a major conference, or satellite symposium, on astrocyte-neuron interactions.

The transition of a permanent member to an independent position could lead to excessive management load falling onto the team leader in the short-to-medium terms, and academic conflicts-of-interest arising in future. Therefore, this issue needs to be actively managed – although the experience gained from the successful transition of the present team leader to an independent position suggests that this will be skilfully handled and not present a significant issue

Spin-off creation and management (Panntherapi) is to be applauded, but success is by no means guaranteed and could prove a resource drain long-term on the lab.

### Analysis of the team's trajectory

Based on its expertise and strong recent findings, the team has decided to further strengthen their research lines on (i) astroglial regulation of the critical period (Science, 2021), (ii) astroglial perisynaptic process excitability and role in neuronal activity (in both mouse and human) (Nat Neurosci, 2014; Cell Rep, 2021) and (iii) the role of human astrocytes in the pathogenesis of epilepsy (Sci Transl Med, 2018).

The questions proposed position the group at the forefront of international astrocyte research. While technically demanding, requiring skills from molecular to behavioural analysis, the track record of the group and access to significant funding suggest that substantial progress will be made along all these lines during the next evaluation cycle – although the lack of dedicated molecular biology skills within the group and issues with mouse housing/access to dedicated behavioural analysis suites need to be carefully managed.

## RECOMMENDATIONS TO THE TEAM

The committee compliments the team on its excellent performance and encourages it to continue in the same manner.

**Team 14:** Name of the team  
 Name of the supervisor: Mrs. Fekrije Selimi

## THEMES OF THE TEAM

The team studies the mechanisms that control the molecular identity of excitatory synapses in the olivopontocerebellar network and its modulation by both activity-dependent and neuron-specific mechanisms. The team is interested both in physiological neurodevelopment, as well as synaptopathies such as schizophrenia or autism spectrum disorders.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

There were no specific recommendations made in the previous report

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

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

## EVALUATION

### Overall assessment of the team

Very good scientific production, with five original articles published during the reference period (3 as last author in *elife*, *PNAS* and *Biotechniques*) and one review article signed as last author, and three articles posted on *Biorxiv* in 2023. The team leader has an excellent international visibility and her ability to secure competitive funding is outstanding. The scientific quality of the work is excellent, with the identification of several molecular mechanisms that control synapse formation and identity. The small size of the team with only one permanent researcher is a threat for the future.

### Strengths and possibilities linked to the context

The PI has a unique expertise in synaptic organisation during development and uses well-suited model to address her research questions. The team leader has an excellent international visibility, as demonstrated by several international conferences (FENS, Gordon conference, society for Neurosciences). She is also actively involved in her research community at the national level as President and co-founder of the 'Club Cervelet' (The French Cerebellum Club) and has an excellent network of national collaborations.

She has demonstrated an outstanding capacity to obtain highly competitive funding (ERC consolidator 2017–2023) and has secured significant funding up to 2026 (2 ANR and 1 INCa) which should allow the team to run efficiently. This is an important point since the team heavily relies on external funding for salaries of non-permanent staff. The scientific quality of the work is excellent, and the team uses a large panel of models to study the functional roles of molecular targets they have identified such as C1QL1 or SUSD4. They further identified a unique combination of genes involved in synaptic development. Another strength of the work is the study of both physiological and pathological conditions such as schizophrenia and identified an unforeseen role for the cerebellum in the pathophysiology of this disease.

The team is also implicated in spreading an ethical and responsible research culture, notably by the ambassador role of the PI for the ALBA network (promote equity and diversity in the brain sciences) and by the implication of the permanent engineer in ethics committee on animal experimentation and its participation to the 'Structure du Bien-Etre Animal' of the Cirb.

## Weaknesses and risks linked to the context

A main concern is the very small size of the team, which is essentially composed of PHD students. Two PHD students are scheduled to defend in 2023, possibly leaving the team with only one permanent researcher, one permanent engineer, one PHD student and one non-permanent research engineer.

Given the amount of funding that has been obtained during the last period, scientific production is very good and of very high quality (two papers published by the PI as last author in high visibility journals: PNAS, elife) but could be increased. However, it must be noted that 3 articles are underway (posted on Biorxiv in 2023). One article posted on Biorxiv in 2018 (Expression and role of Galectin-3 in the postnatal development of the cerebellum) does not seem to be published so far.

There seem to be only one international collaboration with the former postdoctoral fellow lab of the team leader during the reference period.

Another side effect of the small size of the team is the low contribution of their research activities to society. However, the team participates as much as possible in spreading scientific culture by participating in some scientific popularisation events.

## Analysis of the team's trajectory

The project coherently builds on the previous achievements of the team and is organised around three axis: 1) to further dissect the molecular code of synapse formation. 2) to identify the molecular heterogeneity of granule cells and its functional consequences. 3) to identify the role of Adamtsl3, an extracellular matrix protein secreted by neurons and risk factor for schizophrenia in shaping synapse specification.

The project is excellent, and the research theme is highly relevant to our understanding of the molecular mechanisms that determine synapse formation and identity. The proposed work at the single synapse/molecule level is elegant and internationally competitive. The team has all the necessary expertise to reach the proposed goals and funding has been secured. Given the ambitious nature of the proposed work and the techniques to be used, the team should ensure that the turnover of non-permanent staff (e.g. PHD students) may not be an issue to reach the proposed objectives in a timely manner.

## RECOMMENDATIONS TO THE TEAM

We recommend working on increasing the size of permanent members in the team. Because obtaining permanent positions for technicians and engineers is now a major issue in all institutions, one way to reach this objective could be to attract promising postdoctoral fellows that could compete for a permanent researcher position at CNRS or Inserm. Increasing the number of international collaborations would also strengthen the international visibility of the team leader.

**Team 15:** Multiscale Physics of Morphogenesis

Name of the supervisor: Mr. Hervé Turlier

## THEMES OF THE TEAM

The team 'Multiscale Physics of Morphogenesis' investigates the physics of biological systems at multiple scales. It is particularly interested in developing physical models of cavities or lumen formation in early animal development, providing new physical of cellular cortex leading to different cell shape and behaviour and developing methods to infer physical forces from experimental videomicroscopy images. The team is theoretical and work essentially in collaboration with internationally renowned experimental groups.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has been created in 2017 and this is the first evaluation of the team.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	0
<b>Sous-total personnels permanents en activité</b>	<b>2</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	4
Doctorants	4
<b>Sous-total personnels non permanents en activité</b>	<b>10</b>
<b>Total personnels</b>	<b>12</b>

## EVALUATION

### Overall assessment of the team

The team 'Multiscale Physics of Morphogenesis' (Team 15) develops outstanding research lines at the interface between physics and cell and developmental biology. The scientific output is outstanding, with articles signed as lead authors in high-profile journals such as Cell (2022), Science (2019) and PloS Computational Biology (2021). Attractiveness and visibility are also outstanding, as this young PI has been awarded multiple grants including an ERC StG (2021), invitations to lectures and teaching at ENS, and has developed a network of renowned international collaborators.

### Strengths and possibilities linked to the context

Team 15 is an outstanding emerging team in the field of physics of biological processes. In a few years, the team has already performed significant scientific achievements, leading to publications with high visibility. The group successfully developed quantitative models at the scale of multicellular embryo (Science 2019) or at the intracellular scale in the context of cortex mechanics (Journal of the Mechanics and Physics of Solids, 2022) and

membrane cortex interaction (Cell, 2022) These elegant models were nicely used to explain fundamental biological questions such as lumen/cavity formation in development or membrane tension propagation in protruding cells. In addition, the team 'Multiscale Physics of Morphogenesis' has initiated strong effort to tackle the complex problem of force inference during morphogenesis. With international collaborations, using several model systems (mouse embryo, *c. elegans* and ascidian embryos), team 15 developed methods to infer mechanical forces in multicellular organisms, which has the potential to be an essential methodology in the future for the field of developmental biology. Overall, the group is developing original lines of research that resulted in several publications in high visibility journals. The group got awarded by prestigious grants and awards (ERC, ANR...) and the group clearly does excellent science at the international level and has the potential to be leading in the field of mechanobiology.

They already have a developed and large network of collaborations with different very well-known experimentalists giving rise to many successful projects. The PI's profile of the 'Multiscale Physics of Morphogenesis' fits perfectly in the Cirb and we would expect additional collaborations in the institute in the future.

### Weaknesses and risks linked to the context

The team 'Multiscale Physics of Morphogenesis' does not present main weaknesses. As a recently incorporated team, the team seems to have developed only few initiating collaborations with groups in the Cirb. They should continue their effort in building interaction through collaborations with groups in the Cirb.

### Analysis of the team's trajectory

The trajectory is outstanding. The 'Multiscale Physics of Morphogenesis' team succeeded in securing very competitive funding in the last years and to build a coherent group of scientists with very strong expertise. The projects developed by the team already gave rise to excellent publications in high-profile journals. Team 15 appears as a new key player in the field of mechanobiology that have already achieved remarkable contributions and started promising new research lines.

## RECOMMENDATIONS TO THE TEAM

No special recommendation except to perhaps encourage the team to pursue their effort in creating scientific interactions with teams in the Cirb.

**Team 16:** Dynamics and Physiopathology of Neuronal Networks  
 Name of the supervisor: Mr. Laurent Venance

## THEMES OF THE TEAM

The team works on identifying the mechanisms underlying synaptic plasticity (particularly spike-timing dependent plasticity) in the striatum and their implications for procedural learning, goal-directed behaviour and habit formation. Such work is performed at a multi-scale level, from molecular (e.g.: Gaba, BDNF, endocannabinoid), to cellular (ex: astrocytes, interneurons) and circuit mechanisms (cortical and thalamic inputs), together with mathematical modelling.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team should keep their very good level of publication. Trying to reach very high impact journals should be the next objective. Implementation of more integrated approaches, which is ongoing would without doubt help to further improve the level of publication.

- These points have been addressed: the team has published in generalist journals, with several articles published in Nature Communication with team members as first/last author. Several integrated approaches have been successfully implemented such as in vivo electrophysiology (including patch clamp & multichannel recordings), optogenetics or 2-photon imaging.

The team should seek to attract a permanent researcher to reduce its dependency on young trainees

- This point has been addressed: one permanent researcher (CRCN Inserm) joined the team in 2019 and implemented 2-photon imaging and one postdoctoral fellow of the team has been recruited as a research engineer (permanent position)

An effort to develop a conceptual breakthrough would help to reach outstanding publication level.

Projects could be strengthened by developing novel hypotheses.

- This point has been addressed with the development of a collaborative network involving computational neuroscientist and mathematicians

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

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



## EVALUATION

### Overall assessment of the team

This is an outstanding team in terms of productivity and attractiveness. It has developed a successful growth strategy (1 permanent researcher & 1 engineer) and expanded its technical expertise by developing several integrated approaches. The team is internationally competitive in the field of synaptic plasticity in the basal ganglia and has excellent funding. The proposed projects for the next contract are coherent and ambitious with implications for both basic and clinical research. There is no concern regarding the feasibility and strong impact of the work proposed for the next contract.

### Strengths and possibilities linked to the context

The team has grown in size with the arrival of one permanent researcher and one research engineer. It has markedly expanded its technical expertise with the implementation of multiple approaches that are complementary to its original electrophysiological expertise on brain slices (in vivo electrophysiology, including patch-clamp and multichannel recordings, optogenetics and 2-photon imaging, computational modelling). Such impressive broadening of the team's technical expertise, together with the development of a conceptual framework and predictive models was an excellent strategy that has proven rewarding, as shown by an outstanding scientific production and an excellent capacity to obtain funding. Such developments have contributed to increasing an already excellent international competitiveness of the team and allow for the development of innovative, ambitious and integrative projects. The team leader is internationally recognised for his expertise in synaptic plasticity in the basal ganglia and has an excellent network of national and international collaborations. The team is not only interested in basic science but also committed to develop translational projects with potential clinical applications in Parkinson's disease. Training of young researchers, interactions with the general public, open-science policy and valorisation (1 patent) are excellent.

### Weaknesses and risks linked to the context

No major weakness or risk identified.

### Analysis of the team's trajectory

The projects coherently build on the team's expertise and previous achievements. One goal is to investigate beyond spike-timing dependent plasticity by defining input-timing dependent plasticity maps in the striatum and determine how coordinated activity of striatal ensembles evolve during the transition from goal-directed behaviour to habits. A second project aims to investigate how endocannabinoid-mediated LTP previously identified by the team can contribute to fast learning. A third and translational project will investigate how different types of Gabaergic interneurons in the primary motor cortex may contribute to the beneficial effects of deep brain stimulation in Parkinson's disease and how these neurons may be directly targeted to reproduce the effects of DBS using non-invasive stimulation methods. The proposed projects are ambitious and rely on cutting-edge technical approaches that are available in the team (ex: 2-photon imaging in behaving mice). The integrated approach incorporating multiple levels of recording of neuronal activity, behaviour, mathematical modelling and investigation in parkinsonian patients is outstanding. There is a strong potential for groundbreaking results and publications.

## RECOMMENDATIONS TO THE TEAM

The team should be commended for its achievements. There are no specific recommendations other than to pursue such an ascendant trajectory.

**Team 17:** Oocyte Mechanics and Morphogenesis  
 Name of the supervisor: Mrs. Marie-Emilie Terret/Mrs. Marie-Hélène Verlhac

## THEMES OF THE TEAM

The team works to elucidate the phenomena taking part at the end of mouse oocyte maturation, and their impact on future zygote development and quality. They specifically study the role of actin structures for nuclear and meiotic spindle positioning, oocyte cortical tension regulation, chromosome segregation and gene expression.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous recommendations consisted in encouraging the team to continue with their outstanding work. In accordance, the team pursued well its remarkable scientific production keeping at the same time an excellent team's organisation and a strong scientific strategy.

The only minor remark concerning the lack of funding by European or international grants remains unaddressed.

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

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

## EVALUATION

### Overall assessment of the team

The team is excellent to outstanding. Its scientific production is outstanding, comprising some remarkable publications and key discoveries. The team maintained its excellent implication in various scientific activities such as in the organisation and participation to international meetings, scientific outreach by different popular media and an excellent level of training. The quality of the PIs is well established by the recognition of prestigious awards and grants (e.g. CNRS Silver medal to the co-Leader of the Team). European funding and industrial interactions are lacking.

### Strengths and possibilities linked to the context

Following their previous work, the team made significant discoveries in the field of mouse oogenesis and consolidated its international leadership with an excellent interdisciplinary scientific production including some

world-class publications. During the evaluated period, the team remarkably studied a variety of processes related to oocyte maturation and morphogenesis including: 1) the forces transmitted from the cytoplasm to the nucleoplasm and its influence on mRNA processing during oocyte maturation (Al Jord, A., Letort, G., Chanet, S. et al.; Nature Communications, 2022), 2) the mechanical properties of the cortex and their relationships to aneuploidies i (Bennabi, I., Crozet, F., Nikalayevich, E. et al. ; Nature Communications, 2020). 3) The mechanisms of nuclear centration (Colin et al. J Cell Biol 2020) 4) The regulation of transcriptional dynamics (Almonacid et al. Dev Cell 2022).

The team takes advantage of a remarkable combination of multidisciplinary scientific approaches, including live cell imaging, modelling, biophysical measurements and gene expression profiling. The funding ID and training record and international reputation is outstanding.

### Weaknesses and risks linked to the context

No major weakness or risk were detected. The only minor weaknesses are the current lack of large European funding (e.g. ERC) and industrial interactions.

### Analysis of the team's trajectory

Based on their expertise and on their recent findings, the team will develop further three axes that have the strong potential to bring a better comprehension of oogenesis and zygote development but also to apply them to clinical and technological contexts in the field of reproduction medicine. The first axis will compare how cytoplasmic forces are transmitted to the nucleoplasm before and after fertilisation, as nuclei exhibit different compliance. The second axis will expand previous findings on the role of cortical tension on chromosome segregation, by notably analysing a strain defective in Arp2/3 regulation. The last aim will shift the team towards human oocytes and zygotes and the use of AI-based image analysis to identify novel descriptors or oocyte quality.

The team's trajectory follows well the previous excellent achievements, and promises to bring outstanding knowledge into the mechanisms of mammalian oocyte maturation and developmental potential.

## RECOMMENDATIONS TO THE TEAM

The committee compliments and encourages the team to continue its impressive scientific production.

The committee also encourages the team to improve industrial interactions with patents or industrial contracts and to expand its sources of funding at the European level.

**Team 18:** Brain Rhythms and Neural Coding of Memory

Name of the supervisor: Mr. Michael Zugaro

## THEMES OF THE TEAM

The team's goal is to gain a deeper understanding of how brain oscillations in hippocampal networks, in tandem with cortical and striatal assemblies underlie memory formation, consolidation, and impact motivated behaviours.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

*Recommendation 1: The outstanding publication quality will have to be maintained concerning the project on memory formation and consolidation and increased concerning the project on spatial navigation and decision-making. Given his track record, the team leader could apply to an ERC grant scheme. European and international collaboration has to be strengthened during the next contact.*

The publication quality of the team was significantly increased during the last evaluation cycle with two papers in Science and three in Current Biology.

*Recommendation 2: The number of postdoctoral fellows and master students should be increased. Recruitment of additional postdoctoral fellows should be actively forecasted for the next contract.*

Thirteen PHD students and five postdoctoral researchers were hired in the considered period.

*Recommendation 3: The team should reduce the number of projects planned: douze projects, which does not match perfectly with the number of team members. Although some of the projects involve national or international collaborators, securing European or International funding would definitely allow the team to fulfil its objectives.*

The number of projects has been reduced but this recommendation is still relevant considering the relatively small size of the team.

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

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

## EVALUATION

### Overall assessment of the team

The overall scientific output, reputation, appeal, as well as interactions with the non-academic word are all excellent to outstanding. This assessment is justified quantitatively by the number of very high-quality publications (including two papers in Science during the considered period) and fundraising.

### Strengths and possibilities linked to the context

Using state-of-the-art techniques, the researchers of the team have been instrumental in identifying the contribution of brain rhythms in memory formation and consolidation.

The team has obtained an impressive amount of competitive grant funding during the last evaluation cycle: one ANR as coordinator, three as a partner, a Labex grant and 'Equipe FRM' grant. This reflects impressive fundraising for a team of this size. Twelve PHD students and five postdoctoral researchers (3 of them were former PHD students in the team) were recruited during the period considered showing the high attractiveness of the team.

The scientific track record of the team is outstanding. The team has published nine original articles during the last evaluation cycle, including seven where team members are in senior author positions. The majority of them were published in prestigious generalist journals: two papers with a maximum of three authors (all team members) were published in Science, and three in Current Biology. In addition, they published 6 reviews in highly visible journals, such as Nature Comm and Progress in Neurology.

PIs of the team have contributed to research dissemination activities and scientific life and are strongly involved in editorial activities, grant evaluation and review activities.

### Weaknesses and risks linked to the context

The main weakness of the team is that it currently consists of only one permanent researcher and an emeritus research director. As mentioned in the previous Hcéres report, the PI should actively seek to recruit/attract permanent positions.

Considering the substantial number of PHD students recruited, and the successful acquisition of funding, we could anticipate a higher number of published papers by students and post-doc. It is worth noting that data from some PHD students who left the lab several years ago, is not yet published.

Based on the research grants obtained (and those to be submitted), numerous projects are planned that involved national and international collaborations. This is a positive development as the team published no collaborative papers during the last evaluation cycle, except with Pr. Sara. However, the direct involvement of the PI, the only permanent member of the team, in these different projects could be detrimental to the main thematic of the team.

### Analysis of the team's trajectory

The working programme is very ambitious and appropriate in view of the team's expertise. The team has been awarded an Equipe FRM grant to investigate the functions and network mechanisms of hippocampal sequences in freely behaving rodents and epileptic patients. Other projects involving collaborations (both intra- and extra Cirb) with national or international teams will be conducted. Care has to be taken to not add too many different projects. The team leader will apply for an ERC advanced grant.

## RECOMMENDATIONS TO THE TEAM

The team leader's productivity seems to have experienced a slight decline over the past two years. Besides problems with construction work impacting mouse colonies, the team appears to be grappling with the pursuit of extremely ambitious and lengthy projects, which have the potential to be published in highly prestigious journals. This is a point that needs to be considered in the team's future publication strategy, especially for students and postdoctoral fellows.

As emphasised in the previous Hcéres report, the team should concentrate its efforts on a select few projects to avoid diluting the team's visibility and productivity.

The team's recruitment strategy will be a key element of its future success and sustainability. The integration of permanent researchers could well be essential. Also, the fresh recruitment (or the sharing with another Cirb team) of an engineer should be considered and considered a priority for the institute.

## TEAMS NOT INCLUDED IN THE NEXT CONTRACT

**Team 19:** Role of matrix proteins in hypoxia and angiogenesis  
 Name of the supervisor: Mr Stéphane Germain

### THEMES OF THE TEAM

Team 19 research is centred on angiogenesis and vascular biology. They developed three axes of investigation: 1/the cardioprotective effects of ANGPTL-4, 2/amphiregulin in vascular permeability and 3/lysyl oxidase-like-2 in the organisation of the vascular basement membrane. They used different models from 3D culture models to mice and zebrafish, participated to clinical investigations and developed lines of translational research.

### CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No recommendations in the previous report.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
<b>Sous-total personnels permanents en activité</b>	<b>4</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	4
<b>Sous-total personnels non permanents en activité</b>	<b>7</b>
<b>Total personnels</b>	<b>11</b>

### EVALUATION

#### Overall assessment of the team

Team 19 has an excellent interaction with national and international labs, as shown by invitations to meetings and numerous participations to scientific committees in France and abroad. Their publication level is excellent with some articles in high-range journals as main authors or as collaborators. They have several fruitful interactions with clinical units. In addition, they filed two patents and established a collaboration with two industrial partners. Altogether, their translational research activity is outstanding.

#### Strengths and possibilities linked to the context

Team 19 was a pioneer in investigating the role of ANGPTL-4 in the cardiovascular system. The team has a national and international reputation in the fields of cardiology and angiogenesis, as attested by numerous

invitations of the PI and two researchers to national and international meetings. They participate to scientific or steering committees of charities, the French Cardiology Society (the PI was president of its research group, GRRC), a Labex and Silab foundation. The PI was president of the CSS3 at Inserm and was expert for several international founding agencies.

The team obtained six ANR grants as coordinators, one as partner, from charities and medical foundations, from a Labex, and through collaborations with two industrial partners, which is remarkable for a team of this size.

Publication level is very good to excellent, with seventeen original publications in the 2017–2022 period, including seven publications in leader position. Articles were published in high-range (Biomaterials, Biofabrication, as corresponding authors and EMBO Mol Med, Arthritis Rheumatol as collaborators) and mid-range (Matrix Biol, J Clin Endocrinol Metab, Faseb J...) journals. All researchers were authors of publication, except the PUPH.

The three researchers participated to teaching activities in several Master classes in Paris area and they supervised eleven Master 2 students during the period, which is a very good contribution to scientific education. The team developed innovative research in the cardiovascular field, notably they filed two patents on the use of 1/ANGPTL-4 as a treatment against cardiac remodelling after infarction and 2/Amphiregulin to treat vascular permeability. The latter patent was licensed by a biotech company. The team has several collaborations with cardiology, odontology, intensive care and endocrinology units, for which they have obtained specific ANR grants.

### Weaknesses and risks linked to the context

The PHD students published two original papers in average during their PHD (0.7/student in average as first author), which is relatively low number. Similarly, few postdoctoral fellows were co-authors in papers during their stay.

### Analysis of the team's trajectory

Not evaluated by this committee.

## RECOMMENDATIONS TO THE TEAM

The recommendation of the committee is to pursue their outstanding translational activity.



**Team 20:** Statistical Biology  
 Name of the supervisor: Mr Olivier Rivoire

## THEMES OF THE TEAM

Team 20 investigates how physical and evolutionary constraints can lead to biological function at the molecular scale. The groups particularly focus on developing statistical physics models to explain molecular interaction and evolution such as the emergence of allostery and patterns of evolution of proteins or catalytic efficiency using elastic network models. In addition, the group developed quantitative experiments to assess the biophysical and evolutionary properties of proteins or gene regulation in bacteria.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The group was positively evaluated as performing excellent research at the previous evaluation. The SAB advised the group to relocate in a more suitable centre. The group is now located at the ESPCI Paris-PSL.

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

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

## EVALUATION

### Overall assessment of the team

The research developed in the SB group is excellent with the development of simple statistical physics model to uncover fundamental principle explaining evolution and regulation of protein function. The research led to several very good publications as main author published in renown journals (Phys Rev E, Plos Comp Biol, Cell systems, J. Chem B.) The group also attracted competitive funding with several grants such as ANR or FRM.

### Strengths and possibilities linked to the context

The group presents expertise in statistical physics modelling. The models developed by the 'Statistical Biology' team are generic and aimed to reveal fundamental emerging properties of the biological function of proteins. Along these lines, the group developed statistical physics model explaining emergence of allostery (Phys.Rev E 2019; Arxiv) and physical models of catalysis based on elastic networks (J. Phys Chem B). The group also

developed quantitative experiments to investigate antibody selection for antibody libraries based on different scaffolds (Plos Comp Biol 2021). The team also developed projects in collaboration to investigate allostery or gene regulation (Cell Systems 2023; Cell Reports 2019). The group was successful in attracting several funding (FRM, ANR, Qlife, IRIS PSL) during this period. The group is now located in ESPCI.

### Weaknesses and risks linked to the context

The main potential weakness of the group is the relatively low number of publications compared to the number of lab members. Four PHD students appears to not have published during their PHD.

### Analysis of the team's trajectory

The trajectory is very good. The group develop original research in between theory and experimental science with several projects that led to good publications. The group has moved to ESPCI and should continue on similar lines in their new institute.

## RECOMMENDATIONS TO THE TEAM

No particular recommendations

**Team 21:** Central Neuropeptides in the Regulation of Body Fluid Homeostasis and Cardiovascular Functions

Name of the supervisor: Ms Catherine Llorens-Cortes

## THEMES OF THE TEAM

The team leader worked as a neuropharmacologist and cardio-vascular researcher at the Cirb, where she led a very successful research group until her retirement and team closure in 2020. The team was interested in role of neuropeptides in the regulation of body fluid homeostasis, and in the development of drugs to treat cardiovascular and hypertensive disorders.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report encouraged the development of strategies to continue the research program after the retirement of the team leader, either in the Cirb or in a different unit. This was ultimately not successful, and the team closed at the end of 2020 after the mandatory retirement of the team leader.

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

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

## EVALUATION

### Overall assessment of the team

This outstanding team led successful research projects aimed at identifying potential therapeutic targets and small molecules to treat hypertension and cardiovascular diseases. Productivity and visibility remained excellent during the evaluation period, with more than ten research papers in prestigious specialised journals, multiple reviews and book chapters, meeting organisations and awards to team members. Most notably, the team developed a partnership with the Quantum Genomic Company and developed drugs that went through successful clinical trials.

### Strengths and possibilities linked to the context

The team continued its characterisation of aminopeptidase A (APA), the enzyme responsible for the formation of angiotensin III, which controls blood pressure and cardiac function, and of Apelin, a vasoactive

neuropeptide. In collaboration with the Quantum Genomics company, the team contributed to the development of a clinically efficient APA inhibitor (Firibastat, assessed in phase II clinical trials) and worked on the discovery and characterisation of Apelin analogues with therapeutic potential. These research lines led to 22 research papers in respected generalist and specialised journals (including Nature Communications, The FASEB Journal, Journal of Hypertension, Biochemical Journal) of which more than half are led by team members. The visibility of the team, and in particular of the team leader, remained high with the organisation of/invitations to multiple international conferences, publication of reviews and book chapters, and memberships in numerous French scientific societies and in the European Academy of Sciences. Finally, the team leader received multiple scientific prizes, including the Prize of the National Academy of Medicine in 2021.

### Weaknesses and risks linked to the context

No weaknesses identified.

### Analysis of the team's trajectory

The team 'Central Neuropeptides in the Regulation of Body Fluid Homeostasis and Cardiovascular Functions' closed in 2020 after an outstanding trajectory in both fundamental and applied sciences. The self-evaluation report does not include information on the current status of permanent researchers formerly associated with the team, and the committee did not meet with former team members during the on-site visit. The PI was awarded the Applied Sciences Medal from the French Scientific Academy in 2023.

## RECOMMENDATIONS TO THE TEAM

Not applicable.

## NEW TEAMS IN THE NEXT CONTRACT

**Team 22:** Gene regulation during mammalian development  
Name of the supervisor: Mr Denis Duboule

### THEMES OF THE TEAM

The team has a longstanding interest in the study of the regulation of Hox genes in space and time during mammalian embryo development. Most of their achievements over the past 30 years was done in mice, but the lab has recently completely switched to the use of ES-cells derived gastruloids.

### CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

This is a newly opened team, which was not evaluated in the previous round.

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

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

### EVALUATION

#### Overall assessment of the team

The team is outstanding, with a unique reputation and a set of achievements. The PI was for instance awarded two consecutive ERC advanced grants and many other prestigious awards. The publication record over the past five years is outstanding with 28 published papers in excellent journals (Nature, Nat Comm, Genes and Dev, PNAS, elife...). The PI is also highly involved in science organisation, interaction with the general public, editorial boards, and has an outstanding training record.

#### Strengths and possibilities linked to the context

The team has an outstanding reputation and the PI is an established world authority in the genetic regulation of mammalian development. Their installation at the CRIB is an excellent opportunity for the institute, not only in terms of visibility, but also in terms of scientific gains, with the development of gastruloids as a new model to study early development and gene regulation.

#### Weaknesses and risks linked to the context

No major weaknesses were identified. The PI installs a new team at the Cirb moving from the Swiss to the French system, which constitutes a potential risk of delaying scientific progress. This is offset by the maintenance of the Swiss lab during the initial years of installation in France.

#### Analysis of the team's trajectory

The main project of the team will be to study the regulation of the Cyp26a1 gene a negative regulator of Retinoic Acid signalling during embryo development, using gastruloids as a powerful tractable system. The team will notably explore (i) the transcriptional regulation of this gene using single cell RNA-seq, ATAC-seq and Hi-C approaches, and (ii) the function of this gene in body axis elongation. The project builds on many years of optimisation of the gastruloid system and on the extensive expertise of the team in addressing genetic regulation of early mammalian development; and is therefore likely to bring outstanding new insights into the mechanisms of gene regulation in mammalian development. This project will also provide a very good example for how work in a relevant *in vitro* model system can be used to more specifically target experiments to be done with animals: what are the strength and the drawbacks of replacement strategies. This is an important point regarding all the current debates.

## RECOMMENDATIONS TO THE TEAM

The committee compliments and encourages the team to continue its impressive scientific trajectory now at the Cirb.

**Team 23:**

Ecology and evolution of trait and species diversification

Name of the supervisor: Violaine Llaurens

Ms Violaine Llaurens

## THEMES OF THE TEAM

The team focuses on how colour patterns evolution in butterfly wings favours speciation events, and reciprocally. Colour patterns are submitted to complex selective pressures, as they form the basis for mate choice within the species or in hybrids, but also for the evolution of mimicry with distasteful species. The project of the team aims at integrating these different selective pressures to explain the diversification of colour patterns and species, from the micro to the macroevolutionary scale.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

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

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

## EVALUATION

### Overall assessment of the team

The team carries outstanding integrative research in evolutionary biology, focusing on identifying feedback between trait and species diversification, here colour pattern evolution and species diversification in butterflies. The group's work ranges from fieldwork to molecular studies and includes genetic, phenotypic (including behavioural) approaches and mathematical modelling.

### Strengths and possibilities linked to the context

This evaluation is based mainly on the project, and a few additional facts reflecting the past of the team, as the new team did not need to provide a self-assessment.

The team carries outstanding integrative research in evolutionary biology, focusing on identifying feedbacks between trait and species diversification, here colour pattern evolution and species diversification in butterflies. The idea is that, on the one hand, wing colour patterns may be involved in mate choice and thus in the speciation process, and, on the other hand, sympatric populations of different butterfly species tend to evolve mimicry (because predators can learn to avoid distasteful prey such as these butterflies, a phenomenon known as Mullerian mimicry). The evolution of these so-called 'magic traits', which are involved in both local adaptation and reproductive isolation, is the main topic of the group. The group's work ranges from fieldwork to molecular studies and includes genetic, phenotypic (including behavioural) approaches and mathematical modelling.

The team will benefit from a recently awarded ERC grant (2023). The publication record of the group is excellent and includes high impact journals (Science, PLoS Biology, Nature Communications) and the scientific project is exciting. Finally, the arrival of the team will clearly strengthen the Department of Ecology and Evolution. Interactions with Team 11 and Team 10 should be natural, as well as with groups in the neurology department on the behavioural side.

### Weaknesses and risks linked to the context

No specific weakness was identified in the project.

### Analysis of the team's trajectory

The team has been awarded with a consolidator ERC grant, which will start as the team will move to Cirb in October 2023. This was obtained on the basis of previous research on an original case of colour pattern

convergence observed in the genus *Morpho*. In this genus, an iridescent motif on the wings shows striking parallelism in the diversification of different species, suggesting Müllerian mimicry. The idea is that iridescent motifs make their flight hardly tractable for predators, and serve as a signal for low chance of capture success. The project will determine the genetic and developmental basis of pattern convergence; use field experiments to characterise the ecological interactions at work and model mathematically the eco-evolutionary feedback between the colour pattern and the interaction within species and among sympatric species. The work on convergent evolution in particular will synergise with other projects in the institute, e.g. with Team 10 and Team 11 who are also working on the detection of molecular convergent evolution.

Another project focusing on the *Morpho* genus (where up to 13 species with different ecology can be observed in sympatry) is currently asking how ecological interactions may reinforce different traits (niches in terms of circadian rhythm and iridescent patterns) that act as barriers to gene flow and further contribute to speciation. It involves a PHD student (Joséphine Ledamoisel 2022–2025). Although colour patterns in bird feathers and butterfly wings will have very different determinism, Team 23 and Team 11 may somehow synergise there.

Other projects of the team involve the evolution of Papilionidae, quantifying pattern variation with machine-learning approaches and developing statistical phylogenetic tests, to determine how much mimetic interactions (here with distasteful species) promote pattern transitions and contribute to the general pattern of species diversification. It involves another PHD student for the period 2021–2024,

## RECOMMENDATIONS TO THE TEAM

No specific recommendation. The committee encourages the team to continue to perform outstanding integrative research in the new environment of the Cirb.



## CONDUCT OF THE INTERVIEWS

### Dates

**Start:** 11 October 2023 at 9 a.m.

**End:** 12 October 2023 at 6.00 p.m.

**Interview conducted: on-site or online**

### INTERVIEW SCHEDULE

#### Wednesday October 11

8:30 AM Preliminary meeting of the expert committee (closed hearing)  
8:45 AM Presentation of the Hcéres evaluation to the unit (SO)  
9:00 AM Presentation of the research unit by the Director (40' +20' questions)  
10:00 AM Platforms (20' +5' )

10:25 AM Break

10:45 AM Espeli/Brunet  
11:15 AM Zugaro/Terret · Verlhac  
11:45 AM Duboule/Llaurens

12:05 PM *subcommittee debrief*

12:35 PM Lunch

1 h 20 Alizon/Achaz · Lambert  
1:50 PM Blanquart / Manceau  
2:20 PM Hublin / Turlier  
2:50 PM Garel · Thion / Cohen-Salmon

3 h 20 *subcommittee debrief*

3:50 PM Break  
4:20 PM Di Nardo / de Thé  
4:50 PM Rouach / Venance  
5:20 PM Huynh / Selimi

5 h 50 *subcommittee debrief*  
6:20 PM *committee debrief*

7:20 PM end of day

#### Thursday October 12

8:30 AM Meeting with technical and administrative staff (in French)  
9:15 AM Meeting with thesis students and post-docs  
10:00 AM Meeting committee and supervising bodies

10:45 AM Break

11:00 AM Meeting with researchers and professors  
11:45 AM Visit of the Lab

12:15 PM Lunch

1:30 PM Meeting with the head of the unit/deputy director

2:45 PM *subcommittee: overview of all teams*  
3:30 PM *committee meeting/final debrief: overview of all teams*

5:00 PM End of day

## PARTICULAR POINT TO BE MENTIONED

N/A

## GENERAL OBSERVATIONS OF THE SUPERVISORS



**Thomas Römer**

*Administrateur*

Paris, le 29 février 2024

Monsieur Eric Saint-Aman  
Directeur du Département de l'évaluation  
de la recherche - Hcéres  
2, rue Albert Einstein  
75013 Paris

Monsieur le Directeur,

Je fais suite au courriel en date du en date du 9 février 2024, par lequel vos services ont sollicité les observations des tutelles sur le rapport d'évaluation DER-PUR250024556 - Centre interdisciplinaire de recherche en biologie (CIRB, UMR 7241).

En premier lieu, je souhaite remercier le comité pour l'attention portée au CIRB. Je souhaite ensuite apporter les quelques précisions suivantes :

- L'assertion (page 9 du rapport) selon laquelle il n'y aurait pas de séminaires scientifiques internes à l'unité, associant l'ensemble de ses membres, est inexacte : des séminaires externes sont régulièrement organisés les mardis et, tous les vendredis, des séminaires internes permettent aux étudiants et aux post-docs de présenter leurs travaux. Par ailleurs, un « chalk board lunch » rassemble les PI et les chercheurs tous les mois. Enfin, une retraite du CIRB est organisée chaque année, une retraite des étudiants et des post-docs tous les deux ans, et une retraite des professeurs de biologie et des PI du Collège de France tous les deux ans également.
- S'agissant du stress que générerait, chez certains chefs d'équipe juniors, l'insuffisance de clarté des conditions de renouvellement des équipes (page 10 du rapport), des précisions ont été apportées au comité, notamment à l'occasion de son entretien avec l'équipe de direction du CIRB. Le comité a ainsi été informé que ce sujet serait abordé à l'occasion d'une table ronde rassemblent les chefs d'équipe, les Professeurs de l'Institut de biologie du Collège de France ainsi que l'Administrateur du Collège de France, dans le cadre d'une retraite scientifique prévue à l'abbaye de Royaumont au mois de novembre 2023. De nouvelles règles pour le renouvellement des équipes sont ainsi en cours de rédaction par un groupe de chefs d'équipe et de Professeurs de biologie du Collège de France, avant d'être présentées à l'Administrateur.
- La considération selon laquelle l'équipe « Evolutionary epidemiology of infectious diseases » aurait un taux de publication élevé mais pas dans des revues généralistes est inexacte : entre 2019 et 2022, François Blanquart a publié 1 article dans Science, 3 dans eLife, 2 dans Nature Communications, 1 dans Proceedings B, soit quasiment deux publications par an, ce qui représente un taux raisonnable de publications dans des revues généralistes.

- Pour ce qui concerne les recommandations formulées à l'attention de l'équipe « Neurobiology and Immunity » (page 29 du rapport), co dirigée par la Pr Sonia Garel et Mme Morgane Thion, il me semble utile de préciser que Mme Morgane Thion s'est d'ores et déjà vue attribuer une ANR (ANR JCJC en 2023) et candidate actuellement à une ERC. Par ailleurs, tous les étudiants et post-doctorants ayant rejoint l'équipe depuis sa création en 2008 ont de fait publié au moins un article en premier auteur (à l'exception de l'un d'entre eux, pour des raisons médicales). Le fait de parvenir à faire publier et reconnaître les travaux de chacun constitue d'ailleurs l'une des fiertés de l'équipe.
- L'assertion selon laquelle l'équipe « Development and Neuropharmacology » n'accueillerait plus de femmes depuis 2019 (page 40 du rapport) est inexacte. Si un déséquilibre existe s'agissant des chercheurs statutaires et CDI (4 hommes et 2 femmes), l'équipe compte à ce jour 6 hommes et 9 femmes et reste attentive à maintenir la parité.
- Il est indiqué page 41 que la précédente évaluation avait mis en évidence que la charge de la gestion de l'équipe « Neuroglial interactions in cerebral physiopathology » semblait lourde pour sa responsable, qui ne reconnaît pas ses propos dans cette appréciation. De la même façon, la charge de la gestion de l'équipe ne se verra pas alourdie avec le départ d'un membre permanent de l'équipe, dans la mesure où il n'y contribuait pas. S'agissant toujours de cette même équipe, l'assertion selon laquelle elle n'aurait plus de financement ERC (page 42 du rapport) est inexacte : l'équipe a obtenu en octobre 2022 un financement ERC « Proof of concept ». Enfin, la recommandation faite à l'équipe (page 42 du rapport) de s'efforcer d'être un « orateur de premier choix » lors des conférences internationales sur les astrocytes (en particulier celles qui se déroulent aux États-Unis, telles que celles du CSHL et du GRC) (page 42 du rapport) ne tient pas compte du fait que la responsable de l'équipe a de fait donné plusieurs conférences aux Gordon Research Conferences (GRC) ainsi qu'un « open plenary lecture » dans un congrès international (15th Göttingen Meeting of the German Neuroscience Society, <https://www.nwg-goettingen.de/2023/default.asp?id=8°>).
- La préoccupation exprimée par le comité page 44 du rapport concernant la petite taille de l'équipe « Molecular Identity and Diversity of SYNapses in the Brain (MIDISYN) » doit être nuancée : en effet, l'équipe a su attirer de nouveaux personnels et inclut désormais deux post-doctorants supplémentaires ainsi qu'un étudiant en master appelé à postuler sur un contrat de doctorant.
- Le tableau des effectifs de l'équipe « Central Neuropeptides in the Regulation of Body Fluid Homeostasis and Cardiovascular Functions » figurant page 58 du rapport est établi au 31 décembre 2022 alors que l'équipe a fermé en décembre 2020. Cela donne une fausse idée de sa composition.

Je vous précise que le CNRS, qui assume la cotutelle de l'unité, a répondu par courriel à notre sollicitation, nous indiquant qu'il n'émettrait pas de réponse institutionnelle de type « observations de portée générale ».

Souhaitant avoir apporté quelques éclaircissements utiles à la lecture de ce rapport, je vous prie de recevoir, Monsieur le Directeur, l'assurance de mes sentiments les meilleurs.



Thomas Römer

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