

EVALUATION REPORT OF THE UNIT
Phyma - Physiologie moléculaire et adaptation

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Muséum national d'histoire naturelle - MNHN,
Centre national de la recherche scientifique -
CNRS

EVALUATION CAMPAIGN 2023-2024
GROUP D

Rapport publié le 04/04/2024



In the name of the expert committee :

Alan Dobson, 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.

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:

Mr Alan Dobson, University College Cork Ireland

Experts:

Mr Frédéric Brunet, École normale supérieure de Lyon (representative of supporting personnel)

Ms Pascale Crépieux, CNRS - Centre national de la recherche scientifique, Mouzilly (representative of CoNRS)

Mr Jerome Gay-Queheillard, Université de Picardie Jules Verne – UPJV (representative of CNU)

Ms Marie-Pierre Moisan, Inrae - Institut national de recherche pour l'agriculture, l'alimentation et l'environnement Bordeaux

HCÉRES REPRESENTATIVE

Ms Birke Bartosch

REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Mrs C. Prip-Buus, CNRS

Mrs C. Bernard, MNHN

CHARACTERISATION OF THE UNIT

- Name: Phyma - Physiologie moléculaire et adaptation
- Acronym: Phyma
- Label and number: UMR 7221
- Composition of the executive team: Mr. Laurent Sachs (Unit director), Ms. Marie-Stéphanie Clerget-Froidevaux, Mr. Jean-Baptiste Fini, Mr. Fabrice Girardot, Nicolas Narboux-Nême, Mr. Hervé Tostivint (Members of the executive committee)

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

All three teams of the unit have a common interest in development, evolution, phenotypic plasticity, endocrinology, behaviour and functional genomics. The **team 1 BBC** has focused on brain-body crosstalk during adaptive processes to understand how changes or stresses in the internal or external environments modify integrated processes such as metabolism, behaviour, reproductive strategy and adult neurogenesis. The **team 2 Rodeo** has interests in the molecular and cellular responses to environmental challenges to understand the physiological consequences of exposures to environmental changes related to life cycles transitions, stress and endocrine disruptors. The **team 3 DESYNE** has analysed the development and evolution of neuro-secretory systems to understand how the physiology is regulated by peptides secreted by the central nervous system. Because of the complementarity of the three teams, the main goal of this unit is to understand, define and explain how integrated systems adapt to environmental changes at molecular and cellular levels and affecting whole body homeostasis.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The Molecular Physiology and Adaptation (Phyma) Unit UMR7221 was originally founded in 1837 as the Laboratory of Physiology at the Museum National d'Histoire Naturelle (MNHN) and more recently has been renamed "Evolution des régulations endocriniennes" and is one of the five units of the MNHN Department of Adaptations du Vivant at the MNHN and belongs to the CNRS Institute of Biological Sciences (INSB) section 24 of the CoNRS "Physiology, Aging and Tumorigenesis".

RESEARCH ENVIRONMENT OF THE UNIT

The Phyma unit is hosted at the National Museum of Natural History (MNHN) in the "Jardin des Plantes" Campus in Paris and by the CNRS Institute of Biological Sciences (INSB). The MNHN has for a number of years been dedicated to the description and understanding of the living and mineral world and of past and present environments, including the relationship between humans and nature. The MNHN explores the interactions between living organisms and their environment and their skills cover the disciplines of life sciences, ecology, earth sciences, archaeology and anthropology. Their scientific policy enables them to contribute to studies in veterinary research, primatology, ethology or paleontology. The unit has an executive team consisting of the Unit Director and four other team leaders and one assistant professor, which collectively are involved in the decision-making processes within the unit. The unit has a Laboratory council which includes the Unit Director, eight elected members of staff and six appointed staff, coming from the different research, PhD and support staff coheres from within the unit. The unit also has a Scientific Advisory Board, which was constituted in 2021 consisting of eleven external scientists, which provide advice on the strategic scientific direction of the unit. The unit consists of three different teams totalling 45 people, including 31 permanent staff including fifteen tenured researchers, fifteen support staff and one maintenance staff member; together with three non-permanent personnel, twelve PhD students and two Emeritus researchers. The unit has access to appropriate imaging, molecular biology and phenotyping equipment together with access to bioinformatic support through servers. In addition, they have access to animal facilities consisting of a 220 m² aquatic facility and 110-m² mouse facility.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	4
Maîtres de conférences et assimilés	7
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	19
Sous-total personnels permanents en activité	33
Enseignants-chercheurs et chercheurs non permanents et assimilés	3
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	7
Sous-total personnels non permanents en activité	12
Total personnels	45

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
MNHN	10	0	14
CNRS	0	3	5
AUTRES	1	0	0
Total personnels	11	3	19

GLOBAL ASSESSMENT

The unit has very relevant scientific objectives involving the characterisation of biological processes of the adaptation of living organisms to their environment, which are excellent. The unit has a high-quality international reputation, with the overall standard of the research being conducted in the unit being very good to excellent; overall with team 2 being excellent to outstanding in this respect. There are some examples of scientific outputs that have made significant advances in the field such as the work on the potential health problems associated with exposure to endocrine-disrupting chemicals in the environment. The unit has been successful in obtaining a high level of research funding relative to its quite modest size, from a variety of different funding sources. Examples include funds obtained by team 2 of 555k€ and €398k€ for the H2020 projects Athena and Ergo respectively. The attractiveness of the unit is overall excellent but the unit needs to attract more PhD students. The scientific production of the unit is overall very good to excellent with articles published in high quality journals, and in particular by teams 1 and 2. The unit needs to increase collaborative activities between the teams and thereby further increase the number of inter-team publications, while team 3 needs to publish their scientific outputs in a much timelier fashion. The unit has access to important key animal facilities, including fish and mouse facilities, but the costs associated with these facilities is unequally distributed among the unit teams. The unit is very well organised and the overall functioning and management of the unit is excellent.

There was clear evidence of a very high level of collegiality during the interactions between the committee and the different levels of personnel, including the research and technical staff as well as the PhD students. The renewed scientific focus of the unit, initiated through the recommendations of the SAB is a positive and should be accompanied by an effort to more clearly define the scientific identity of the unit, which will facilitate its interactions with other units within the museum and increase its overall attractiveness to help in the recruitment of PhD students in particular. The unit has access to state-of-the-art animal facilities, but in the longer term needs to address its requirements in the bioinformatics area.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Regarding the recommendation of a midterm evaluation of the unit's scientific outputs, following a meeting with their SAB in 2021 the unit received a number of recommendations which they have acted upon or are acting upon. The unit has revised the way in which they presented their research taking cognisance of the context, objectives, strategies and impact. They are gradually redefining their strategic policy and will discontinue their scientific activities in certain areas. In addition, they plan to reconfigure researchers from different teams within the unit to focus on a small number of key research questions.

They have not acted on the recommendation from the previous report to hire new team leaders, but have chosen instead to act on the recommendation of the SAB and their governing bodies to reinforce existing teams. With the acquisition of new space, they are planning to attract new researchers.

Regarding the development of an outreach plan, the unit has instigated the use of a number of new communication tools, including the web site and the use of social media but have not yet developed a strategy to increase their national and international visibility. Regarding the use of external mentors for grant writing. The unit have addressed this to some extent through involving emeritus and external collaborators in sharing their experiences with some team leaders; however, the recommendation about the establishment of Grant study groups has not been implemented. The recommendation for unit members to take leadership roles in collaborative projects, has been addressed to some extent, but efforts to fully address this recommendation need more effort.

The recommendation that the new team leaders and the director should be allowed to develop their own scientific direction has been acted upon.

The recommendation for mouse and aquatic facilities has been acted upon and is reflected in their two facilities being approved for use by the appropriate veterinary authorities. Some limited progress has been made regarding the recommendation to involve technical personnel in the animal facilities in the projects within the unit and to hire one new technical staff at a senior position to undertake a leadership and training role. While a technical staff, member at a higher level has been hired and promotions of two technical staff, this recommendation still needs to be fully implemented.

Regarding the recommendation of developing a scientific strategy on which emerging technologies would have largest synergies and help productivity, they have embarked on the use of omics and single cell and behaviour/metabolism-based approaches and have leveraged their geographical location to access other technologies, while investing in new equipment for behaviour or metabolism.

Regarding in recommendation of increased exchange between researchers and an increased bioinformatics capacity, this has been addressed to some extent with new research projects involving members from different teams. While the bioinformatics is now also more widely used.

B - EVALUATION AREAS

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

Assessment on the scientific objectives of the unit

The unit has relevant scientific objectives, which involve the characterisation of biological processes of the adaptation of living organisms to their environment. In particular, the unit focuses on elucidating the physiological processes controlling tissue development and tissue homeostasis in vertebrates in both normal and modified conditions. They are very focused on their scientific objectives, which are overall excellent.

Assessment on the unit's resources

The unit has excellent financial and human resources. The teams have been very successful in obtaining grants totalling around 4.9M€ for the period, particularly from European contracts (46% of research funding) and national grants including ANR (42% of research funding). Unit members were PIs on 33% of the European contracts and 57% of the national contracts respectively. The staff are of a very high scientific quality, although expertise in bioinformatics needs to be strengthened. The unit has access to appropriate equipment and to important key animal facilities, including mouse and fish facilities. However, the financial aspects regarding the costs for these facilities is unequally distributed among the unit teams.

Assessment on the functioning of the unit

The direction and management structure of the unit is very well organised. The Director leads an executive team, which consists of four team leaders and one assistant professor. The unit has a laboratory council consisting of members from different relevant groups including researchers, technical staff and PhD students. The executive team is advised by a Scientific Advisory Board on the strategic scientific direction of the unit. Both the researchers and support staff are very satisfied with the functioning of the unit. The unit complies with health and safety issues, with booklets and training; together with a prevention assistant involved in risk assessment activities. The overall functioning of the unit is excellent.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The unit has relevant scientific objectives, which involve the characterisation of biological processes of adaptation of living organisms to their environment. The unit's scientific objectives have become more focused around how organisms cope with exposome variations.

Weaknesses and risks linked to the context

There are no weaknesses regarding the scientific objectives of the unit. However, the unit needs to further refine its scientific objectives to more clearly define an overall scientific identity and to communicate this identity to its relevant stakeholders.

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

Strengths and possibilities linked to the context

The unit is supported by both the CNRS and the MNHN with salaries for research personnel (~692K€ in 2022) and with infrastructural support. The unit has access to appropriate equipment and important animal facilities, which include a mouse animal house with the capacity to accommodate up to 3,000 mice and a fish facility. The unit has recently gained access to another 110m² of research space, which will allow it to expand. The teams are overall well-funded and have been successful in obtaining grants, particularly from European grants (46%) and from national grants including ANR (42%). The staff are of a very high scientific quality and the human resources are quite well distributed within the unit. The unit level of gender equality is positive, which is reflected in 51% of the permanent staff and 42% of the full-time researchers being female.

Weaknesses and risks linked to the context

The financial aspects regarding the costs for the animal facility are not equitable for the three teams within the unit. There is a lack of bioinformatic expertise within the unit, which will be important for the future sustainability of the unit in the longer term. The age of buildings in which the unit is housed, necessitates frequent maintenance.

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

Strengths and possibilities linked to the context

The direction and management structure of the unit is very well organised. The Director leads an executive team which consists of four team leaders and one assistant professor. A Scientific Advisory Board advises the executive team on the strategic scientific direction of the unit. A laboratory council consisting of members from different relevant groups including researchers, technical staff and PhD students also advises the Director.

The cohesiveness of the unit is facilitated not only by its small size, but also by the collegiate environment within the unit. Gender parity is reflected in the permanent staff, and in the full-time researchers, with a female professor being targeted to assume the role of deputy director in the future. Training courses are available for different levels of staff and clear career development opportunities exist within the unit.

The unit has very clear systems in place with respect to hygiene and safety aspects associated with working there, including booklets and training; together with a prevention assistant (PA) who is involved in risk assessment activities. Both Business continuity and emergency plans are also in place if required. The direction actively promotes a working environment that is conducive to collegiality, which is reflected in the researchers and support staff being very satisfied with the functioning of the unit.

Weaknesses and risks linked to the context

None identified.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The unit has a high-quality international reputation, in endocrine disruption, thyroid hormone signalling, neuropeptide evolution, morphogenesis and functional genomics. The unit has been successful in obtaining a total of 3.794M€ in grants supporting eight post-docs and eleven PhD students. This is reflected in the number of invitations at international meetings and its involvement in European projects such as Thyrage and Endpoints.

Members of the unit have presented their work at both, national and international congresses. The attractiveness of the unit overall is excellent.

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

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

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

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

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

The unit has a high-quality international reputation, which is evident from the number of invitations to give oral presentations (110), with 71% of these being at international meetings and in the organisation of national (1) and international scientific meetings (4). They have also been involved in the organisation of six symposia. Thirteen unit members are also involved in editorial duties for internationally recognised journals, four as associate editors, two editors and one as a senior editor. Members have also been involved in reviewing 346 manuscripts.

Two unit members have received awards: in 2018 Commander of the National Order of Merit and in 2022 Foundation Yves Cotrel prize.

A structured system is in place for newly recruited researchers, including information from the administrative office on the information systems, together with a very modest funding allocation. Similar training and information is also provided to research support staff.

During the period, the unit hosted six visiting researchers including four PhDs and two PIs.

The unit has been successful in obtaining a total of 3.793M€ in funding from various funding sources. Examples include funding obtained by Team 2 of 555k€ and €398k€ for the H2020 projects Athena and Ergo respectively. The unit is well equipped with standard laboratory equipment, which allows them to measure variation at genomic, cellular, tissue and whole organism levels. The unit has access to two important platforms, while involve animal experimental facilities, one for mice and the other for amphibians and fish. Five technical personnel run the two platforms. For bioinformatics, the unit has access to support from the MNHN Adaptation department and calculation cluster.

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

The unit has difficulty in attracting PhD students because of a lack of visibility within the doctoral school.

The unit also has difficulty in attracting post-doctoral researchers, again due to poor visibility.

There is a lack of official support for PhD students, with respect to their career development.

There is an over reliance on EU funding schemes and alternative sources should be considered.

The visibility and profile of the unit within the museum is not optimal which hinders it in leveraging human resources for the unit.

Technical support positions within the unit that become vacant due to retirements are not always filled in a timely fashion, which results in an increased work load for the remainder of the technical workforce.

The national and international visibility of the team leaders and scientists within the unit is not optimal. This is negatively affecting the overall attractiveness of the unit.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of the unit is overall very good to excellent with articles published in journals such as eLife and the Lancet, PNAS, Science, reporting on a number of key findings in their scientific fields. For example, Team 1 have reported that DLX5/6 deletion specifically in GABAergic neurons in mice increase lifespan by 33% and leads to a phenotype of hyper-vocalisation and hyper-socialisation. Team 2 have reported that pregnant women are commonly exposed to mixtures of endocrine disruptors exceeding the regulatory doses of each individual EDC, and that this is correlated with adverse consequences for the age of language learning of the progeny. The team for their part reported that the signalling pathway involving Urp1 and/or Urp2 and their receptor represent a conserved mechanism that controls spine morphogenesis in jawed vertebrates. In addition, all the team leaders actively publish in their respective scientific fields.

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

The unit has produced a total of 168 journal articles with around 84% of these with Phyma researchers as either first or last author. The quality of the peer-reviewed articles is reflected in the fact that 52 % and 37% of these

articles were in the excellent or the best journals in their respective fields. The publication by team 2 in PNAS (2019) is an example of such a high quality scientific output. They have also produced five books, ten book chapters. Beyond the number of publications, the unit has disseminated their research activities through a number of presentations at congress (109) and through poster presentations (54). In addition, they have contributed to increased knowledge in their respective fields of research such as an increased understanding of how organisms are affected by environmental changes and in the generation of important scientific knowledge in the fields of metabolic, neurodegenerative and cardiac diseases. The unit is clearly leveraging both its national and international collaborations as is evident from the number of journal articles (83) co-authored with international partners, which constitutes 49% of their total journal articles. A clear example of this is the Science paper (2022) involving Team 2 members.

All PhD students and post-doctoral researchers typically publish at least one paper during their time at the unit. This is reflected in 39 and 38 journal articles involving doctoral research and post-doctoral researchers respectively, with the latter being first author in 24 publications. The unit gives fair consideration to younger researchers regarding co-authorships on publications. All research staff within the unit have published during the period. In addition, research support staff have also been involved as co-authors (26) or first author (2) in unit publications. The panel noted that 30% of the total publications from the unit were from a PRMu in Team 1. Clear systems are in place to ensure the traceability and reproducibility of the scientific work, involving laboratory notebooks and backing up of large volumes of data sets. The unit employs FAIR principles with respect to data access and usability. All publications are published as Open Access, either directly or as prepublications on the Open Access French HAL website. Regarding the research activities undertaken in the animal facilities within the unit, are subject to appropriate ethical approval.

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

There are no clear policies in place to ensure the integrity of the scientific work.
 There is some but quite limited evidence of inter-team publications, or scientific exchanges between teams within the unit.
 Notwithstanding its modest size, the overall productivity in terms of publications of team 3 is less than that of the other two teams.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The unit's contribution to society is overall very good. There is clear evidence that the unit has been active in disseminating their work particularly the work on endocrine disruption (ED) research to the general public. Various appropriate communication avenues have been employed. However, apart from the ED research area there is limited evidence of activities in other areas in the context of interactions in the cultural, economic and social world.

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

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

The unit has continued its collaboration with the WatchFrog laboratory in the area of assays for thyroid hormone disrupting compounds. They are also involved in a collaboration with L'OREAL in the area of new markers of thyroid disruption and are involved in the European Ergo consortium with this company in identifying markers of thyroid disruption in fish as well as in the supervision of a PhD student on a cifre contract.

The unit interacts with the OECD (Organisation for Economic Co-operation and Development) and with Pepper a non-profit association and a public-private platform dedicated to the pre-validation of endocrine disruptors characterisation methods; in the evaluation of methods developed for the testing of endocrine disruption. They also interact with EFSA (European Food Safety Authority) and ANSES the French agency for food, environmental and occupational health safety in evaluating the endocrine-disrupting properties of chemicals, through their involvement in working groups on endocrine disruption (<6 meetings per year).

The unit clearly defines its role in being involved with these partnerships as facilitating the development of new approaches in the regulatory use of standardised test guidelines and in the development of Endocrine Disrupting Chemicals (EDC)-free products which will ultimately benefit both the environment and human health. There is clear evidence that the unit has made an active effort to disseminate their work on endocrine disruption research to the general public. Various communication avenues have been employed including radio interviews (23), TV appearances (27) and press releases (10). They have also participated in Science festivals by hosting primary, middle and high school students. The unit also communicates their activities on social networks through twitter/x and LinkedIn and through their website. Some of the Team leaders and research scientists have demonstrated an excellent to outstanding level of activity in presenting their research to the general public.

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

No valorisation of results from the unit has taken place during the reporting period.

There is little if any evidence of the unit developing products for the cultural, economic or social world.

Apart from their activities in the endocrine disruption area, there is little evidence of activities in other areas in the context of interactions in the cultural, economic and social world

ANALYSIS OF THE UNIT'S TRAJECTORY

During the on-line presentations, members of the three teams outlined their research plans for the next contract. The committee were convinced that the unit's trajectory is overall very good and is realistically in line with their ongoing activities. However, the unit needs to continue to define an overall scientific identity, particularly through a reduction in the number of its research topics during the next contract. The interconnectivity from a scientific perspective between team members within some teams within the unit also needs to improve. The proposed ongoing interactions with the socio-economic world is to be welcomed. The unit are also expanding their scientific approaches to study the impact of methylome variations in the presence of thyroid hormones and glucocorticoids on metamorphosis and adaptation to environmental changes and new models such as sea cucumbers will be studied

RECOMMENDATIONS TO THE UNIT

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

The unit is recommended to continue to implement the remainder of the recommendations from the SAB, in particular to increase the attractiveness of the unit to foster the recruitment of new research scientists and PhD students.

The unit is recommended to simplify its management structure, while ensuring a good flow of information of management decisions to the personnel within the unit.

The unit is recommended to find a more equitable solution to cover the running costs for the animal facility.

While a post-doctoral researcher with expertise in bioinformatics, financed by MNHN will be recruited for the next two years; a longer-term solution to address the unit's requirements in the bioinformatics area is required.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit needs to identify new team leaders who will replace retiring personnel.

The unit needs to replace retiring technical staff in a timelier fashion.

The unit is encouraged to implement formal support structures for PhD students and post-doctoral researchers, with respect to their career development.

Team leaders and scientists within the unit should further increase their national and international visibility to enhance their attractiveness, which will help in attracting both PhD students and post-doctoral researchers.

The unit is encouraged to continue to build on the visibility of the Health/Environment group within the museum.

This will facilitate the better integration of the unit within the museum, improve the communication channels, and promote potential collaborative interactions with other units within the museum.

The unit needs to further increase its visibility within the doctoral school to help attract more PhD students.

The unit needs to further diversify its funding streams, which are currently over reliance on EU funding schemes.

Recommendations regarding Evaluation Area 3: Scientific Production

The unit is encouraged to continue its very good to excellent level of scientific production.

The unit is encouraged to further maximise the impact and visibility of their research outputs by choosing to publish in journals with a better scientific reputation and record of accomplishment within their scientific fields.

The unit is encouraged to further increase the number of inter-team publications.

Members of team 3 within the unit are encouraged to publish their work in a timelier fashion.

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

The unit is encouraged to explore the possibility of generating patents from some of their exploitable results, such as for example the tests being developed for the detection of endocrine disruptors.

The unit is also encouraged to leverage the outstanding communication skills with the general public by some of the unit members, to train other unit members to further highlight the research activities and outputs from the unit as a whole. This will have the added benefit of increase the unit's attractiveness for students, postdocs and new researchers.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Brain-body crosstalk during adaptive processes

Name of the supervisor: M.-S. Clerget-Froidevaux and N. Narboux-Nême

THEMES OF THE TEAM

Team 1's general theme is on Brain-body crosstalk during adaptive processes. The team studies the links between genetic diversity (allelic variations and differential gene expression) and plasticity (morphological, metabolic, behavioural or cognitive) to unravel adaptive processes in response to environmental constraints and to understand the marks of evolutionary pressure.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Following the recommendations of the previous report, the scientific production, funding and visibility have been maintained and work on thyroid hormone signalling has been continued. The involvement in teaching and training is still strong and both team leaders as well as another PI of the team hold an HDR. Interactions with non-academic partners have been reinforced since 2019 with several interventions in school or in Science festival as well as participation to radio or TV programs. The interconnectivity between the various axes of the team is gradually improving. Elaboration of projects in common have started with the acquisition of an ANR project in 2021 (Metabrain) involving various PIs of the team.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	9
Enseignants-chercheurs et chercheurs non permanents et assimilés	3
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	2
Sous-total personnels non permanents en activité	7
Total personnels	16

EVALUATION

Overall assessment of the team

The overall assessment of the team is excellent.

Strengths and possibilities linked to the context

Researchers of the team are well recognised in their fields with participation to conferences (17 invitations to congresses such as the annual meeting of the European Thyroid Association, European Congress of Endocrinology, editorial activities (e.g. *Frontiers in Endocrinology*, *Functional Ecology*, *Scientific Reports*), responsibilities in scientific societies (council of French Endocrine Society), evaluation activities (jury member for HDR, PhD thesis, professor recruitment, technician promotion). Scientific production (96 articles in peer-reviewed journals) is excellent with publications in very good (*Stem cell Reports*, *Scientific Reports*, *Endocrinology*, *Frontiers in Endocrinology*) to excellent (*Molecular metabolism*, *Elife*, *Thyroid*, *Molecular Biology & Evolution*) journals and commentary/reviews in outstanding journals (*The Lancet*, *Diabetes & Endocrinology*). Members of the team are first or last author on 70% of the publications and 52% of the publications are in Open Access. Major scientific discoveries include the finding that DLX5/6 deletion specifically in GABAergic neurons in mice increases lifespan by 33% and leads to a phenotype of hyper-vocalisation and hyper-socialisation. Very interestingly, this DLX5/6 genomic region plays a role in human evolution since a specific Neanderthal haplotype was identified and found introgressed in 12.5% of European individuals and under-represented in semi super-centenarians (>105 years of age) (*Mol Biol Evol* 2021). Another major finding is the demonstration that transient hypothyroidism, characterised by absence of TRa1 expression and overexpression of Dio3, favours the generation of myelinating oligodendrocytes from neural stem cells of the sub-ventricular zone. These findings unveil a new mechanism of adult brain lineage decisions, and provide potential insight into demyelinating disorders (*eLife* 2017). This work was further developed by showing that induced hypothyroidism during early postnatal life, e.g. due to exposition to endocrine disruptors, modifies subventricular zone neuron/glia output impacting the development of olfactory interneurons and impairing short-memory odor tests, showing the sensitivity of this developmental window regarding EDC acting on thyroid signalling (*Stem cell reports* 2022). The use of different vertebrate models, linked to the MNHN context is original and represents a strength for the team.

The team collaborate internationally (Japan, USA, Australia, Spain, UK, Hungary, Belgium) and they have been well funded (> 30 contracts (European H2020, ANR, ANSES-EST, etc.) 3000 k€ total over the period). A collaboration with a non-academic partner has very recently been initiated, namely with the company Valgo to evaluate the toxicity of PFAS (per- and polyfluoroalkyl substances) on myelination processes in the central nervous system. Outreach activity is excellent. Team members performed 26 interventions in schools or in science festivals (15) as well as in media (TV, radio, journals).

A new assistant professor was recruited in 2023. Six researchers in the team currently hold an HDR, including two HDR defences within the evaluation period. The team has trained six PhD students over the period among which four have passed the PhD and are now employed as either postdoctoral researcher, technical manager or scientific consultant. Five postdocs were recruited during the evaluation period among which two obtained a tenured position in the team, one is a researcher in Napoli, Italy and one is postdoc in Nantes.

Weaknesses and risks linked to the context

The team has lost one permanent researcher during the period and another researcher, a CR CNRS will be leaving soon. Although a new MCU was recruited, there is a need for an additional researcher to keep the balance.

Emeritus professors obtained several important fundings during the evaluation period. There is only one postdoctoral fellow at the moment.

Interaction with non-academic partners is weak and may only start to evolve with the collaboration with Valgo.

Analysis of the team's trajectory

With the two new team leaders, the BBC team has maintained a high level of scientific production and good funding as well as attractiveness. The interconnectivity with the other axes is however still not obvious. Although a project leader has left, a new assistant professor replaces him. An effort to reduce research topics is being made. With the departure of a permanent researcher (PR) the project related to "in natura observation of physiological adaptations to anthropic impacts" has disappeared. The departure of the CR will lead to the drop out of studies on cranial and neural tube morphogenesis. Therefore, for the next contract the team will focus on the consequences of early-life events on adult fitness, with specific examination of genetic, hormonal and molecular determinants of brain-body crosstalk establishment during the prenatal and perinatal period and its impact on adulthood, as well as adaptive mechanisms promoting healthy aging.

RECOMMENDATIONS TO THE TEAM

The committee encourages the BBC team to continue their excellent research activity. The excellent scientific production should continue to be maintained at this level over the next contract, despite the departure of two highly productive researchers. The departure of these researchers and the arrival of the new assistant

professor is an opportunity to have more focused researched themes. Recruitment of a CNRS researcher should be a priority. The team also needs to make an effort to continue to obtain high-level funding from European contracts and national calls for projects (H2020, ANR, ANSES). The team, through its manager, must ensure that all researchers are able to respond to calls for projects. The number of doctoral and post-doctoral students must also be maintained or even increased. The committee encourages more collaborations with the other teams of the unit.

Team 2: Molecular and cellular response to environmental challenges
 Name of the supervisor: L. Sachs and J.-B. Fini

THEMES OF THE TEAM

The scientific objective of the Rodeo (Réponses moléculaires et cellulaires aux défis environnementaux) team is to determine the mechanisms whereby environmental changes, whether natural (embryo-larvae transition and metamorphosis) or chemical (endocrine disruptors), affect aquatic organisms at the molecular, cellular and organismal levels. A particular emphasis is placed on the mechanisms whereby thyroid hormones (TH) regulate the Amphibian life cycles, and how the latter can be affected by endocrine perturbations.

The scope of these themes extends beyond academic research, with strong applications to public health, and to the preservation of ecosystems, including endangered aquatic species.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Wherever possible, the main recommendations of the previous Hcéres committee have been followed: 1/ another leader has now emerged and has encountered a very good success rate in funding calls as a partner. This scientist is now the Rodeo co-leader, in addition to the previous leader who is also now the director of Phyma; 2/ the observed deficit in PhD supervision is no longer relevant, with five theses defended in the assessment period, and six still ongoing. However, the team still failed to attract foreign visitors and post-docs; 3/ the unit has not been able to recruit a new support staff in bioinformatics, hence one scientist of Rodeo bears the workload needed for the bioinformatic analyses of the large-scale data this team has generated; 4/ with respect to publications, the position of the team members as PDC has notably improved, as recommended.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	9
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	4
Total personnels	13

EVALUATION

Overall assessment of the team

The Rodeo team is considered excellent to outstanding. It is widely recognised for its studies on the molecular mechanisms governing aquatic animal life cycles and for their expertise in genome-wide analyses. Their studies on endocrine disruption on specific animal models are unique. Their emphasis on thyroid hormone disruption is original and elegantly capitalizes on the knowledge they have gathered over the years on the developmental regulations by these hormones. The team members are highly solicited by non-academic partners, whether institutional or industrial, by the media or by public authorities.

Strengths and possibilities linked to the context

During the assessment period, the Rodeo team has had excellent scientific production. Altogether, they published 50 articles, of which 27 as PDC. Two publications were co-authored with BBC members and two others with DESYNE members. The quality of journals the team published in ranks from very good (Endocrinology, Frontiers in Endocrinology) to excellent (Environmental Pollution, PNAS) to outstanding (Science). The team has demonstrated that during *Xenopus* metamorphosis, the methylome is regulated much more extensively by both T3 (the tissue remodelling hormone) and glucocorticoids (the stress hormones that accommodates to the level of environmental changes) than the transcriptome (Cells, 2021), and could potentially be targeted by deleterious effects. Importantly, the team also reports that pregnant women are commonly exposed to mixtures of endocrine disruptors exceeding the regulatory doses, and that this is correlated with adverse consequences for the age of language learning of the progeny (Science, 2022).

The Rodeo team extensively interacts with non-academic partners, essentially to contribute to chemical risk assessment for living organisms. For example, they have developed a strong expertise in the evaluating of more than 20 EDC for national (ANSES) and international (EFSA) chemical risk assessment agencies, and to provide endpoints to respond to the OCDE guidelines.

The Rodeo team is an essential player in the field of public health and preservation of ecosystems in Europe, since over the period, they have procured 1451 k€ in funding (22 contracts in total including 7 European and 6 national contracts) for the team, on projects all of which are focused on endocrine disruption. Outside of Europe (USA, Chile, Mexico), their international visibility has been established on their historical studies on thyroid hormone signalling and functional genomics during Amphibian life cycles, and their genome-wide studies on these non-conventional organisms. They have been involved in the organisation of nine international workshops/congresses (International Congress of Comparative Endocrinology, International Symposium on Amphibian and Reptilian Endocrinology and Neurobiology, etc) and participated at national and international grant evaluations and other kinds of expertise (ANSES, OECD, Pepper, etc).

Rodeo team members are in charge of many tasks related to the common functioning of Phyma or of the MNHN (bioinformatics support, computation). Hence, the Rodeo team appears as a very dynamic team, with excellent scientific productivity and outstanding interactions with the non-academic world.

Recently, the team has promoted the emergence of a new leader, recruited in 2020 as PR MNHN, who now co-leads the team.

Weaknesses and risks linked to the context

Involvement of the Rodeo team in non-ED studies is declining, likely due to the strong financial support they have obtained from EU funding sources on ED. While the team has received impressive research funding during the evaluation period, large-scale financial resources are not secured for the next years: only the PARC EU project which finishes in 2027, but the amount being allotted to the team was 133 k€ for five years. No post-doctoral researcher has been recruited on the team's EU projects, and no foreign visiting scientist has been hosted.

On the operational level, the Rodeo team has relatively little technical staff, with only one IE allotted full-time to the team and one TR 60 % in the team, which is of concern particularly given the huge amount of omics data that the team has gathered and needs to analyse. The integration of a new incoming MCU, whose expertise (physiology of reproduction of large mammals) is not directly related to the team's research activities, needs to be carefully organised and overseen.

Analysis of the team's trajectory

The next project will be carried out as a continuation of the current project with an emphasis on homeostasis/adaptation in amphibians. A major effort will be put on the impact of methylome variations in the

presence of thyroid hormones and glucocorticoids on metamorphosis and adaptation to environmental changes. The team will also deepen its studies of the impact of exposure to TH-disrupting or enhancing agents, to chemical cocktail, on the development (especially brain, metabolism and reproduction repro). New models such as sea cucumbers will be studied.

The team will also continue to improve knowledge of their amphibian model. For example, they will generate data to better understand the heterochrony of developmental processes regulated by TH, and how these changes influence sensitivity to environmental changes. They will be part of the Guyana CRB Program for the Conservation of Endangered Species Semen. They will further sustain their interactions with the socio-economic world, with the project of a Labcom with L'Oréal.

A new statutory researcher would be required in the next period to ensure supervision of the team's research activities.

RECOMMENDATIONS TO THE TEAM

The committee encourages the Rodeo team to continue its excellent research activity. It is recommended to equilibrate activities between expertise in chemical evaluation, multiple and heavy tasks devoted to the MNHN or unit functioning and grant writing to secure the financial support of the group for the next period.

Since one CR will not be present during the next period, one PI is co-leader of the group and another PI is Director of the unit, it will be crucial to reinforce the training capacity of the team by recruiting a new CR or a new MCU. Another possibility is to reinforce the collaborations within Phyma, especially with the BBC group, given the interest of this team in adaptative processes to environmental changes and in thyroid signalling dysregulations.

Team 3: Development, evolution and functions of neurosecretory systems
 Name of the supervisor: H. Tostivint and G. Pezeron

THEMES OF THE TEAM

The team works on the development and evolution of neurosecretory systems in vertebrates, with the main scientific research goals dealing with comparative neuroendocrinology. More specifically, three themes are developed being: 1. the evolution of neuropeptides multigene families, 2. the roles of the peptides of the urotensin II and somatostatin families, 3. the development, evolution and functions of the caudal neurosecretory system. Their objectives are the description of the neuropeptide diversity, regarding both their history and functions, as well as the developmental origin of neurons producing them by using animal models as zebrafish, clawed frog and dogfish.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has addressed the recommendation of publishing their research findings in journals with higher visibility. It has however not to any great extent addressed the recommendation to engage with the media to promote their work, or undertaken outreach or public engagement activities. The team has not recruited more PhD students as recommended, but has improved communication and interactions with other teams in the unit. The team has addressed the recommendation of continuing the pursue receptor characterisation.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

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

EVALUATION

Overall assessment of the team

This small team has recently expanded and is made up of four permanent staff with a comfortable teaching activity and two technicians. The team is good to very good in terms of scientific publications and in obtaining funding for research projects.

Strengths and possibilities linked to the context

The team is actively involved in research and in the supervision of students. One strength of the team is data analysis of several new vertebrate species to provide insights into the origin and evolution of neuropeptide families with a special focus on the urotensin 2, somatostatin and gonadotrophin-releasing hormone (GnRH) families. These data provide essential information in the field of evolutionary molecular genetics. Several of their key discoveries were made possible by collaborations with researchers from national and international research teams. The research theme in molecular evolution of peptide families is a particular focus of the team, with three articles in this area in preparation and another two cited references coming from their international collaborations.

During the evaluated period, the team has published a total of seventeen articles, including twelve original papers, three reviews, two popular articles and 34 communications and presented 22 posters, eight oral communications and four popular lectures. The ratio of articles/ researchers is about 4.25 over the entire evaluation period.

The theme of the functional properties of urotensin II and somatostatin family peptides is firmly anchored within the team, with significant publication activity, including some in high profile journals such as *Front Neurosci*, *Sci Rep*, *Peptides* and *Physiol rev*, which again highlights the value of their international collaborations.

The team has also demonstrated an ability to obtain research funds, either through two national contracts (ANR, 182k€), two contracts financed under the PIA (175k€) and many others by local authorities or charity (75k€); totalling 470 k€.

The team have developed a close collaboration with the Rodeo team in the generation of KO tadpoles lacking a Ull receptor subtype (CRISPR) mainly by sharing animal models and techniques. This collaboration has resulted in an article published in *Open Biol* (2021). The team has also developed a collaboration that is still ongoing with the BBC team in order to investigate the role of the peptides of the Ull family during lizard development. These internal collaborative activities are to be fostered.

Due to the small number of researchers in the team, the research themes within the team have been reduced in order to concentrate their activities on these themes and avoid dispersion, which is a very positive development.

It is important to note that the human resources of this team doubled over the period covered by this current evaluation, with two assistant professors and one new technician, which suggests that the team is gaining strength.

Weaknesses and risks linked to the context

The small size of the team is a concern from a future sustainability standpoint. There are only four permanent researchers in this team. The team leader is a professor, with three assistant professors, one who arrived in Nov. 2014 and has published four articles and two reviews, with the team leader. The two other assistant professors who arrived recently, Jan. 2019, and Sept. 2022, have not yet published any papers. None of the assistant professors yet holds the HDR, which negatively affects the ability of the team to supervise Master 2 and PhD students, particularly as the only person with a HDR is the team's PI.

Albeit the exchanges with the unit, it remains difficult to evaluate the quality of the work of the team in the molecular evolution of peptide families' area as all publications are still in preparation.

Analysis of the team's trajectory

For the new contract, the team will continue their focus on two key themes. The first is the study of the functional properties of peptides in the urotensin II family. The second theme is the study of the development, evolution and functions of the caudal neurosecretory system. This area of research should enable the team to obtain the funding it needs to ensure its continued existence. To better anchor this theme within the team and to render it productive in terms of publications, the assistant professor recently recruited in the team is now involved in the study of the functional importance of the Caudal NeuroSecretory System in zebrafish, assisted by the assistant professor who has been in place for the past nine years. The submission of an ANR project will ease the feasibility of this theme.

RECOMMENDATIONS TO THE TEAM

The two recently arrived assistant professors must strive to establish themselves within their position in this small team to facilitate its growth.

The number of HDR in the team needs to increase as a matter of urgency in order to increase the number of PhD students.

If possible, the team should continue to expand in terms of researchers and/or research support staff. In addition, increasing the number of publications with higher profiles and visibility, as well as the number of national and international grants to be obtained, should remain the team's guiding principle, while maintaining the collaborations already undertaken in the past, whether these are national or international.

The functional properties of peptides in the urotensin II family research theme needs to be maintained at a sufficiently high level to maintain/increase national or regional funding; otherwise, it may not be able to survive within the team.

As recommended by the SAB, the team should continue to look for possibilities for interactions with non-academic entities.

To ensure the future sustainability of the team and the continuity of its work, the team needs to continue to search and develop the best leadership strategy to adopt before the team leader retires.

CONDUCT OF THE INTERVIEWS

Date

Start: December 13, 2023 at 08:00 AM

End: December 13, 2023 at 7:00 PM

Interview conducted: on-site or online

INTERVIEW SCHEDULE

Visio conference, 13th Dec

8:50-9:00 Hcéres Rules and procedures

9:00-9:30 Administrative and Scientific presentation of the Unit by L. Sachs

9:30-10:00 Presentation Team 1: by M.-S. Clerget-Froidevaux and N. Narboux-Nême

10:00-10:30 Presentation Team 2: by J.-B. Fini

10:30-11:00 Presentation Team 3: by H. Tostivint

11:00-11:30 Debriefing committee (closed door meeting)

11:30-12:10 Meeting with ITAs (in French)

13:00-13:20 Meeting with researchers in the absence of DU and DUA

13:20-13:40 Meeting with researchers in the absence of any managing staff (DU, DUA, team leaders and members of the executive committee)

13:40-14:20 Meeting with post-docs and students in the absence of any managing staff

14:20-14:30 Debriefing committee (closed door meeting)

14:30-15:00 Meeting with institution representatives (closed door meeting)

15:00-15:20 Debriefing committee (closed door meeting)

15:20-16:00 Meeting with Management team of the Unit

PARTICULAR POINT TO BE MENTIONED

N/A

GENERAL OBSERVATIONS OF THE SUPERVISORS



MUSÉUM NATIONAL D'HISTOIRE NATURELLE

Direction de la Recherche

Direction Générale Déléguée à la Recherche, l'Expertise, la Valorisation et l'Enseignement-formation
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UNITE : PhyMA - Physiologie moléculaire et adaptation

SOUS TUTELLE DES ÉTABLISSEMENTS ET ORGANISMES :

Muséum National d'Histoire Naturelle - MNHN

Centre National de la Recherche Scientifique - CNRS

Réponse générale de la tutelle Muséum au rapport d'évaluation :

D2025-EV-0753494R-DER-ER-DER-PUR250024313-SVE3-PhyMA-RT

The Muséum National d'Histoire Naturelle would like to thank the HCERES evaluation committee of the UMR 7221 MNHN-CNRS "Molecular Physiology and Adaptation" (PhyMA) for carrying out an in-depth evaluation, appreciate very much the quality of very comprehensive report and the constructive comments and recommendations, particularly on the future trajectory proposed by the unit and its teams.

This external evaluation by the experts of the HCERES committee is very useful to the parent institutions (MNHN & CNRS) in supporting the unit and its teams for the next 2025-2029 contract, in order to strengthen its visibilities, which are essential for our scientific policy in the fields of development, evolution, phenotypic plasticity, endocrinology, behavior and functional genomics in order to achieve relevant scientific objectives which involve the characterization of biological processes of adaptation of living organisms to their environment by focusing on how organisms cope with exposome variations.

The Museum takes good note of the recommendations made to the PhyMA unit and its teams, and will carefully support the unit, particularly by strengthening skills and competencies on bioinformatics and genomic analyses.

C. Bernard

Directrice de la Recherche, DGD-REVE

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