

ERE - Évolution des régulations endocriniennes

Rapport Hcéres

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agence d'évaluation de la recherche
et de l'enseignement supérieur

Department for the evaluation of
research units

AERES report on unit:

Evolution of physiological regulations

Under the supervision of
the following institutions
and research bodies:

Muséum National d'Histoire Naturelle

Centre National de la Recherche Scientifique



January 2013



agence d'évaluation de la recherche
et de l'enseignement supérieur

Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head

Pierre Glaudes



Grading

Once the visits for the 2012-2013 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).

This score (A+, A, B, C) concerned each of the six criteria defined by the AERES.

NN (not-scored) attached to a criteria indicate that this one was not applicable to the particular case of this research unit or this team.

Criterion 1 - C1: Scientific outputs and quality;

Criterion 2 - C2: Academic reputation and appeal;

Criterion 3 - C3: Interactions with the social, economic and cultural environment;

Criterion 4 - C4: Organisation and life of the institution (or of the team);

Criterion 5 - C5: Involvement in training through research;

Criterion 6 - C6: Strategy and five-year plan.

With respect to this score, the research unit concerned by this report and its in-house teams received the following grades:

- Grading table of the unit: **Evolution of physiological regulations**

C1	C2	C3	C4	C5	C6
A	A+	A+	A	A+	A+

- Grading table of the team: **Integration of thyroid hormones signalling**

C1	C2	C3	C4	C5	C6
A+	A+	A+	A	A+	A+

- Grading table of the team: **Molecular regulations of morphogenetic processes**

C1	C2	C3	C4	C5	C6
A	A+	A	A	A	A+

- Grading table of the team: **Function and mechanisms of thyroid hormone receptors**

C1	C2	C3	C4	C5	C6
A	A	B	A	A+	A+

- Grading table of the team: **Development and evolution of neurosecretory systems**

C1	C2	C3	C4	C5	C6
NN	NN	NN	NN	NN	B



Evaluation report

Unit name:	Evolution of physiological regulations
Unit acronym:	
Label requested:	UMR
Present no.:	UMR 7221
Name of Director (2012-2013):	Ms Barbara DEMENEIX
Name of Project Leader (2014-2018):	Mr Giovanni LEVI

Expert committee members

Chair: Mr Philippe CHEMINEAU, INRA

Experts:

- Ms Ana ARANDA, C.S.I.C- Universidad Autónoma de Madrid, Spain
- Mr François BOUCHER, Université Joseph Fournier (representative of CNU)
- Ms Valérie CREPEL, INSERM
- Ms Joëlle DUPONT, INRA (representative of CoNRS)
- Mr Miguel LOPEZ, Universidad Santiago de Compostella, Spain
- Mr Gilles SALBERT, Université de Rennes 1
- Mr Stéphane VINCENT, INSERM

Scientific delegate representing the AERES:

Mr Hubert LEVEZIEL

Representative(s) of the unit's supervising institutions and bodies:

Mr Gilles BOEUF, MNHN

Mr Jean-François FERVEUR, CNRS



1 • Introduction

History and geographical location of the unit

This unit has a long and prestigious history in the Muséum National d'Histoire Naturelle in Paris. Created by Frédéric CUVIER (brother of the paleontologist) in 1837, it was directed by famous scientists such as Jean-Marie FLOURENS and Claude BERNARD. During the 20th century, Maurice FONTAINE initiated the interest for comparative endocrinology and associated the laboratory to CNRS. This history is still very present among the people working in the unit who are very proud of its filiation.

The Unit "Evolution des régulations endocriniennes" is located in the historical buildings of MNHN, at 7 rue Cuvier, Paris 5° and composed of 4 teams, 2 of them being recently created. A majority of scientists are Enseignants-Chercheurs at the MNHN; this means that they have teaching duties in addition to research activities.

Management team

Ms Barbara DEMENEIX (BD) PR-CE MNHN is director of the unit for 2008-2013 and Mr Giovanni LEVI (GL) DR1 CNRS is proposed for the period 2014-2018.

AERES nomenclature

SVE1_LS4, SVE1_LS3

Unit workforce

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	6 (5.2)	6 (5.2)	6 (5.2)
N2: Permanent researchers from Institutions and similar positions	6	7	6
N3: Other permanent staff (without research duties)	16 (15.8)	16 (15.8)	
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)			
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	6	6	6
N6: Other contractual staff (without research duties)	5 (4.5)	5 (4.5)	
TOTAL N1 to N6	39 (37,5)	40 (38,5)	18 (17.2)
Percentage of producers	100 %		



Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	8	
Theses defended	12	
Postdoctoral students having spent at least 12 months in the unit*	5	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	5	6



2 • Assessment of the unit

Strengths and opportunities

Strengths

- This unit has very strong scientific accomplishments, clearly apparent when looking at the rationale of its objectives and programs, at the number, level and quality of publications and at the place that the unit is holding in the economy and society.
- The current director of the unit has a strong and uncontested international and national position in the field of Thyroid Hormones (TH) and has a real impact on general physiology in various species. She is a strong motor of the unit, and she allies scientific excellence, human qualities and a very efficient dynamism.
- The unit is also internationally recognized in its field.
- The unit is strongly supported by the two institutions MNHN and CNRS.
- The unit thematics are now well integrated within MNHN priorities and provide to this institution new concepts and new lines of work which are not explored elsewhere.
- The creation and further development of a spin-off, which has now 15 employees, a turnover of 1 Million Euros and clients in Europe, Japan and USA, is a tangible proof of the implication of the unit in the socio-economic tissue. This is based on a patent licensed exclusively by MNHN and CNRS to this spin-off.
- Relationships with Human clinicians and agricultural research also demonstrate the interest of the programs and results of the unit.
- Due to its recognized excellence and to the international networks initiated by the two leader scientists this unit is ranked 1st at MNHN in terms of external fundings. This includes several EU projects, some of them led by the unit.
- The strength of the unit is based on the strength of its teams and on the cohesion of all the members of the unit where engineers, technicians and students share the enthusiasm and dynamism of the scientists.

Opportunities

- The existence of a strong potential for the emergence of new teams among the present members of the unit.
- The foreseen recruitment of high quality Associate professor and Professor on the positions provided by MNHN this year and their possible insertion in 2 of the existing teams.
- The renewing of approaches and concepts, as well as tools, in the areas of physiology, evolution, ecotoxicology and transcriptional regulation.

Weaknesses and threats

Weaknesses

- Desequilibrium among teams both in size and scientific production.
- Low number of post-docs, especially foreign ones.

Threats

- Risk of insufficient transmission of network contacts to the young unit members to maintain in the future international leadership in European consortia.



Recommendations

- Continue the reflection and the efforts to re-equilibrate the size of the teams by increasing that of the smallest ones.
- Maintain the former director, at least for some years, in a (even non-official) position aside to the new director, within the management board, to facilitate the transmission of her contacts and know-how.
- Define collectively within the unit a strategy for attachement to doctoral schools (to maintain student flow and increase HDR number).



3 • Detailed assessments

Assessment of scientific quality and outputs

The unit has produced major breakthroughs in the field of TH receptors during the period (for instance: role of TH in regulation of the MC4R gene, in neural stem cell emergence and in regulation of neurogenesis; genes and factors controlling craniofacial development; histone methylation in gene regulation by TH) and would be able to continue to do so in the future by developing new concepts and ideas about the relationship between environment and physiology of living organisms (for instance: effects of endocrine disruptors on obesity, evolution of neurosecretory systems). The scientific production in terms of publications reaches the highest international standards with journals of very high IF (Cell Stem Cell IF 25), prestigious general journals (PNAS), and an average IF of published papers higher than 5 (Development, HMG, Endocrinology). This deliberate policy of publishing in excellent scientific journals is done while maintaining an average of more than one publication per scientist per year, with all scientists publishing during the period. The unit is clearly a leading unit in the field. The tools and methods are of very high international standard and some of them (for instance those used by Team 3) should provide new insights into “old” questions.

Assessment of the unit's academic reputation and appeal

The unit has clearly an outstanding level in this domain. Scientists are invited to present communications at major international conferences (about 40 during the period) and one of them received international awards for the work done in the unit as a mentor. The unit is leading 2 major European networks and participates in 8 other ones. The unit welcomes numerous foreign scientists for sabbatical stays. The unit participates in 7 projects funded by the “French National Research Agency” (ANR : Agence Nationale de la Recherche) (6 as coordinator), to 4 projects funded by the “French Muscular Dystrophy Association” (AFM : Association Française contre les myopathies) and one project funded by a “Pôle de compétitivité” set up in the “Ile-de-France” Region. The unit has co-organized an international conference on endocrine disruptors and a national conference on nuclear receptors.

Assessment of the unit's interaction with the social, economic and cultural environment

The unit is at the origin of the creation and the success of a spin-off company which creates and develops amphibian models for *in vivo* detection of the endocrine disruptor activity of chemicals and cosmetics for environmental risk assessment and drug discovery. It has now 15 employees, a turnover of 1 M€ and contracts in different EU countries, USA and Japan. The original test is currently in the process of validation by OECD (Organisation for Economic Co-operation and Development), which may insure its probable worldwide development. The company has been licensed by MNHN and CNRS the right to use a patent deposited by the unit.

All members of the unit aim to share their objectives, projects and results with the general public and have achieved this goal through original events and productions (theater play, cartoons, participation in MNHN activities etc.).



Assessment of the unit's organisation and life

- The governance is recognized by all members of the unit as efficient and all members share the scientific objectives of the unit.
- The Laboratory Council meets regularly and on exceptional occasions if necessary. Collegial decisions regarding the life of the Unit are being taken.
- Rooms hosting the mammalian part of the animal facilities were recently renovated and the technicians of both animal facilities are responsible and efficient in their work.
- Management of the personnel (technicians, students and postdocs) follows adequate rules. Scientific temporary personnel recognized that the Direction of the Unit is doing efforts to follow their career, even after departure from the unit.
- The proposition done for the renewal of the director of the unit was discussed among the scientists, the putative director for the period 2014-2018 (presented a project for managing the unit for the next five years, and a vote has been organized during a General Assembly which expressed a strong consensus for the perspective proposed.
- However, the committee wants to stress that conditions of work in the different laboratories are very variable, some labs having been renovated recently, while others have not.
- The committee wants also to point out that there is only one administrative personnel to manage the numerous contracts obtained by the unit. This situation could be dangerous.
- Finally, a plan of action in case of flooding by the Seine river exists (a centennial flood would submerge the ground level of about 1.5 meters which would be catastrophic for animal facilities and deep-frozen samples), but this plan is not well known by every member of the unit.

Assessment of the unit's involvement in training through research

- The unit has a deliberate strategy to monitor students' activities and careers.
- All Master and PhD students are carefully followed during their stay in the lab.
- PhD students are stimulated to present their results in international conferences.
- PhD grants with the industry using the CIFRE ("Conventions Industrielles de Formation par la REcherche") system, allow the students to discover the industry and the differences between basic and applied sciences.
- All students are able to follow specific courses of the different doctoral schools to which the scientists of the unit are attached.
- After the defense of their PhD, young Doctors are followed by the direction of the unit who knows exactly where they are and in which position, after helping them to find a post-doc, if required.



Assessment of the five-year plan and strategy

- The scientific strategy is excellent, based on an ambitious and innovative programme. The combination of emerging ideas and new tools is expected to produce new and fruitful results for the next contract, mainly because their feasibility has been already explored.
- The new ideas and directions, at the interface between physiology/endocrinology and environmental toxicology, are especially interesting and may provide novel insights to help explain the profound and permanent effect of endocrine disruptors on phenotypes.
- The next project seems very feasible to the committee because it will be run by highly qualified scientists who already proved their engagement and dynamism as project leaders, and because of the existence of already established technical and/or bioinformatic tools required to reach the objectives of the proposed project.
- Due to its participation in high profile networks and because the unit pilots some of them, the unit has a very good knowledge of its scientific and technical assets and this will be especially useful for exploring new lines of research during the next contract.
- The follow-up of the spin-off company with the present Director of the unit acting as the principal scientific advisor, associated to the rapid development of the company, especially abroad, could be of major interest for the whole project of the unit. It is answering an important demand in the area, both from governmental bodies and industrial companies, and may help to provide resources to the unit and to ensure the progress of techniques for monitoring the environment.



4 • Team-by-team analysis

Team 1 : Integration of thyroid hormones signalling

Name of team leader: Ms Barbara DEMENEIX

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	2	2	2
N2: Permanent EPST or EPIC researchers and similar positions	4	6	4
N3: Other permanent staff (without research duties)	5	5	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	2	2
N6: Other contractual staff (without research duties)	3	3	
TOTAL N1 to N6	18	18	8

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	3	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	3



• Detailed assessments

Assessment of scientific quality and outputs

The scientific production of the team was good at the beginning of the evaluated period and has become very good during the past three years. Altogether 21 articles have been published, among which a major contribution on the role of thyroid hormone on stem cell signaling (Cell Stem Cell) and 3 articles in scientific journals with a very high impact factor (Methods Mol Biol and PNAS). Most of the recent articles of the team are published with young researchers as senior or co-senior authors indicating a very good transmission of the leadership.

The unit, via this team "Integration of thyroid hormones signalling" is recognized as an international leader in the field of endocrine disruption involving thyroid hormone. In particular, it has a very high potential for identifying new targets and generating new tools for studying thyroid hormone availability and detection of pollutants. Members of the team have participated to the organisation of an International Symposium on Endocrine Disruption in Melbourne (Australia) in 2008. In addition to this scientific output, the team is also involved in scientific communication with the general public, through the publication of several flyers and comic strips with the MNHN.

Assessment of the team's academic reputation and appeal

The team leader is regularly invited to meetings in France and abroad and her international scientific reputation is high. Recently (in 2011), she has received an award from the very famous Nature publishing group for her outstanding efforts to mentor young researchers. Moreover, the team has an exceptional ability to establish collaborations and get fundings. Over the past 5 years it has participated in 8 European networks (2 as co-ordinator), and in projects funded by ANR (2, including 1 as co-ordinator), by AFM (2 projects) and by a pôle de compétitivité. This national and international visibility brings a high attractiveness to the team and allows the recruitment of scientists on MC (Maître de Conférences) and post-doctoral positions.

Assessment of the team's interaction with the social, economic and cultural environment

The team has created a Small to Medium Enterprise (SME) spin off that generates in vivo amphibian models for pharmaceutical screening and environmental monitoring. The company employs 15 people and has a turnover of more than 1 M€ from Europe and USA. It holds a license to exploit a major patent from the team, which has been extended to Japan in 2011. Very recently (2012) Team 1 has identified early embryogenesis as a new developmental window for thyroid hormone action. From these findings, a novel OECD test is currently under development (Xenopus Embryonic Test Assay).

During the evaluated period, the interaction with industrial environment has provided collaborations and 2 PhD grants to team 1. Finally, the members of team 1 are very active in the diffusion of knowledge to the general public through their activities in the MNHN and through open days (Fête de la science, specific publications).

Assessment of the team's organisation and life

The management of the team is very good. However, it could be better by improving communication among scientists of the team. Indeed, the Friday meetings are maybe not sufficient to discuss other scientific points such as the submission of proposals (ANR...). Moreover, during the discussions, the committee felt some concern of scientists on the future of the team. The leader of the team has a very strong relational network with the different EU projects that she obtained; maybe she should begin to transmit this network to the future team leaders. The associate professors from MNHN have also claimed a better recognition of all their missions, especially for teaching, by the team leader. Finally, the committee has noted very good relationships between scientists, technicians, students and post-docs.



Assessment of the team's involvement in training through research

The committee has noted that the students and post-docs were very happy to work in this team. There is an excellent supervision or co-supervision by the scientists and the team leader. Each PhD student or post-doc has his/her own project and there is no overlap in the projects (so it means no competition between students). Thus, there is a good working atmosphere among the students of the team. The PhD students and post-doc participate in international events and are involved in Master teaching. The team leader is very involved in the "after thesis" for the PhD students to find them a postdoc and also in the career of the post-docs. Some post-docs wish to come back in the lab. The committee strongly think that the scientists could support their HDR (it's a real pleasure to defend his or her HDR !).

Assessment of the five-year plan and strategy

The project proposed by this team is excellent, very innovative and feasible since the team has already obtained or showed its capacity to get national or international grants. The team has developed an original approach on iPS (induced Pluripotent Stem) cells but we can regret that it is not exploited in the strategy. At the national level, the team has the leadership in the thematic "T4 hormone and aging", it will be a very good opportunity for the new professor to be in charge of this thematic.

Conclusion

- Strengths and opportunities:

The team has demonstrated its exceptional ability to find significant financial resources and has good opportunities for international collaborations. Its scientific activity is very good and innovative. The team leader is one of the key opinion leaders in the field of thyroid hormone and endocrine disruption, at the interface between Environment and Physiology.

Moreover the team has participated to the creation of a SME (Small to Medium Enterprise) spin off, and developed fruitful relationship with industry over the past years. Finally, the research topics of the team are part of the scientific priorities of the MNHN.

Team 1 develops two axes of research, the first one on central hypothalamic control of metabolism and a second one on stem cell function during development. The future recruitment of a new professor is expected to strengthen one of these axes, and might eventually allow the emergence of a new autonomous team.

- Weaknesses and threats:

The sub-division of the team into sub-groups corresponding to the different axes of research weakens the communication between researchers within the team. Paradoxically, some of the members of team 1 communicate more with researchers from other teams than with those of their own team. The strong international recognition of the team leader might obstruct the development of other senior researchers of the team. The transmission of the leadership could lead to a decline in the international visibility of the team and to a decreased ability to obtain funds.

- Recommendations:

The committee recommends improving communication among the researchers of the different sub-groups of the team. The team leader will have to continue helping senior researchers to become autonomous (defend their HDR) and to find a significant place in international networks. Finally, a profound reflection will have to be engaged on the future of the team after the recruitment of the new professor, possibly by proposing the creation of two independent teams emerging from the current axes of research.



Team 2 : Molecular regulations of morphogenetic processes

Name of team leader: Mr Giovanni LEVI

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	1
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	1
N6: Other contractual staff (without research duties)	3	3	
TOTAL N1 to N6	7	7	3

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1



- Detailed assessments

Assessment of scientific quality and outputs

This team has had a very good record of publications, publishing in very specialized journals (one publication being awarded by the James G. Wilson Publication Award of the Society for Teratology, an award for the best publication in the journal Birth Defects Research) but also in more general journals top rated in the field of Developmental Biology or Human Genetics (2 Development, 2 PNAS, 1 Human Molecular Genetics, 1 American Journal of Pathology). This team is working on a very specialized area (Dlx5/6 genes and cranio-facial morphogenesis in the mouse embryo), having many years of expertise in the field of molecular genetics of the development of the mouse embryo and having a very good connection with clinics leading to publications with a clinical impact. A true asset of this team is a surgeon (PUPH), working part-time, who is a recognized expert in the field of craniofacial development, malformation and repair: his expertise in the manipulation of chicken embryo complements very efficiently the mouse molecular genetics. The candidate gene approach and the analysis of the phenotype of the mutant followed by this unit has open new areas of studies that led to publications. This process has been supported by very active and productive collaborative works. This team has very precise chicken embryology technics.

Assessment of the team's academic reputation and appeal

This team is very well integrated within the priorities of the MNHN and some of the future projects are based on tight collaborations with other teams of the MNHN in the field of paleontology and zootechnology.

This team has an international visibility with very strong collaborations with researchers of different countries that had the opportunity to stay for sabbatical stays, leading to publications. The team leader and members have been invited to 18 national and international conferences as speakers. The team leader is a very efficient leader in terms of successful grant applications. The team has been involved in 3 ANR, (1 as coordinator), 1 AFM project and, last but not least, 3 EU grants for a total of 1.4 million euros for EU grants and 460000€ for national grants, over the evaluated period. New applications are in progress.

Assessment of the team's interaction with the social, economic and cultural environment

Because of the presence of a part-time PUPH in the team and also because of its main research theme, the group has established connections with clinicians and clinical research. They also actively participate to a large dissemination of knowledge on embryology through national associations and various media (television and documentary). One member of the team is a national expert for the Tribunal de Grande Instance, Cour d'Appel and Cour de Cassation.

Assessment of the team's organisation and life

The team being small (only 2 full time researchers, 7 total persons over the period), it is difficult to appreciate this criteria, but placed in the perspective that the team leader will take the head of the unit, a more formal organization will have to be set up in order to take into account his new responsibilities.

Assessment of the team's involvement in training through research

The team is well implanted in the MNHN, participating in some of the missions of the MNHN: all the researchers of the team are involved in teaching but also in the organization of the Master "From DNA to biodiversity: regulations during morphogenesis" and the module "Origin of the Head in Vertebrates: embryological, genetic and evolutionary aspects" of the Ecole Doctorale at the MNHN. They also teach in different Universities and also abroad (Stanford University).

During the time of evaluated period, 2 master students and 5 graduate students have been trained. All of the PhDs (one being awarded a prize : prix Arconati-Visconti of the Chancellerie des Universités de Paris in 2010) have been defended with publications. All these students are currently in post docs, or went back to their clinical duties (one veterinary, one dentist and one clinician). The team has also trained 2 post docs, one having been promoted CNRS CR1 during the evaluated period. There has been a problem to maintain a continuity in the recruitment of PhD students for the last year due to a change of Doctoral school. There is a need to attract more students by establishing a strategy.



Assessment of the five-year plan and strategy

Team 2 proposes a very good project with the clear intention to integrate more the general field of research of the unit. The project is clearly feasible since it is already partially funded with grants already obtained and others being submitted. However, the limited size of the team and the number of research axis axes will impose to continue to develop collaborations. A very good opportunity is the validated recruitment of a Maître de Conférence to strengthen the position of the team in the field of craniofacial development and its integration into the MNHN. On the more technical aspects, the team has already all the required expertise (chicken embryology, mouse molecular genetics) and all the new mouse lines are already on site to start the project.

Conclusion

- Strengths and opportunities:

This team has a unique expertise in the field of craniofacial development and molecular genetics with a special emphasis on Dlx5/6 genes family. It has explored many areas of interest through excellent collaborations, including other functions relevant to clinical research. This team has a clear ability in building and getting funds from EU projects.

The location of this team in the MNHN is a clear opportunity for the development of ongoing projects (ie: craniofacial development and paleontology). This effort is supported by the MNHN since a position for a Maître de Conférence has been validated and will be opened in 2013.

- Weaknesses and threats:

The team leader wants to keep it that way, however, the size of the team is small considering the numbers of research axes proposed. There is a risk of dispersion due to the gene candidate approach of the team.

The team leader has been able to maintain the quality of the work of the team through his very centralized management. However, his new administrative duties as unit director might interfere with the management of the team.

- Recommendations:

In order to prevent dispersion and be able to tackle all the different aspects of the projet, the team has to continue to ensure collaborations. The new administrative role of the team leader as unit director should be an incentive to set up a new team management, relying more on the senior scientists of the team.



Team 3 : Function and mechanisms of thyroid hormone receptors

Name of team leader: Mr Laurent SACHS

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	1
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	3	3	2

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1



- Detailed assessments

Assessment of scientific quality and outputs

This young team, which started in 2007 under the direction of a former scientist from Team 1 joined by another scientist, develops new lines of research aiming at deciphering variations in the 3D organization of the genome during metamorphosis. During the reporting period, the team produced an important paper regarding the chromatin attributes of thyroid hormone receptor (TR) binding sites at selected gene regulatory regions. Most importantly, in order to gain access to the 3 dimensional organization of the genome in relation with TR activity, the team engaged a difficult transition from single gene studies to genome wide approaches, including a state-of-the-art technology called ChIA-PET (Chromatin interaction Analysis with Paired-End Tag sequencing). This transition appears to have been successful and the team is now fully independent of the Singapore laboratory that developed the technique in running high technology research. This very important, innovative and promising methodology (i.e. ChIA-PET), shared by only a few labs in the world, is now run in the lab which is the only one applying it to animals in vivo, and, to our knowledge, is also the first one to use it in the field of TH signalling. The implementation of this methodology is original in this context and the efforts done to establish this technique compensate partly a rather low rate of publications. Nonetheless, high impact publications are expected in the near future. In order to facilitate genome wide studies in *Xenopus tropicalis*, the team has also been actively engaged in re-annotation of the genome and successfully reduced genome fragmentation.

Assessment of the team's academic reputation and appeal

This dynamic young team shows a very high potential and exhibited high enthusiasm. Members of the team have participated in numerous international conferences and have been invited in several instances to present their data. The committee was impressed by the very high complementarity between individual competencies, allowing an efficient partition of tasks within the team. It is anticipated that the international visibility of the team will increase substantially in a near future and this will likely impact also the visibility of the unit in general. The team has been involved in EU contracts, acting as workpackage leader, and is actively involved in the creation and activities of a national network on nuclear receptors. Finally, this team has been responsible for organization of the French nuclear receptors meeting.

Assessment of the team's interaction with the social, economic and cultural environment

This team showed high enthusiasm about fulfilling the different missions devoted to MNHN scientists. Team members have engaged a number of collaborations within MNHN, notably regarding (i) TH dependent metamorphosis regulatory networks in several species, and (ii) sanitary conditions of amphibian colony breeding. In addition, the team produced a cartoon aimed at explaining the research run within a large EU consortium to the general public, and contributes to activities in schools and cultural dissemination in the MNHN.

Assessment of the team's organisation and life

It is difficult to assess the management skills of the team leader for such a small group. However, the high complementarity of team members has been noticed and is certainly an asset. The team skills in bioinformatics are also useful to other groups of the unit.

Assessment of the team's involvement in training through research

Both scientists have responsibilities in the management of Master studies at the MNHN and Paris XI University. A PhD student is currently in the group, and the team shows active mentorship through a number of short term internships. In addition, one team member is responsible for the C2I certificate ("Certificat Informatique et Internet") in the MNHN and is a C2I expert for the Ministry of Education.



Assessment of the five-year plan and strategy

The project is highly innovative and ambitious and the team has all the required competencies for its implementation. State-of-the-art technology and a well planned strategy should allow the generation of original and high value data regarding TR binding to chromatin and the 3D organization of TR dependent genomic regions in the context of metamorphosis. Although challenging, the project appears feasible since all the necessary tools and techniques are available in the group. This very innovative project is likely to generate publications in high impact journals and will be widely recognized by the scientific community.

Conclusion

- Strengths and opportunities:

This team has developed very innovative tools and projects which could, in addition to enhance the international visibility of the team, be very useful for the scientific community and for the whole unit. This may impact the ability of the team and the unit to take leadership in a highly competitive field.

- Weaknesses and threats:

The publication level needs to be increased in the future not to become a potential problem for the team and the unit. The size of this team could also be problematic on a medium-term level if no personnel is recruited. The difficulty to recruit engineers in bioinformatics could also be a weakness on the medium-term.

The difficulty to extract scientific meaning from large amounts of data, as well as the reduced opportunities to secure funding for expensive experiments, could be threats.

- Recommendations:

It would be especially useful to continue the efforts to consolidate the team, by incorporating more Ph.D students and/or post-docs as well as by attracting scientists from other teams and from outside the unit.

In the same line, increasing ties with other groups using genome-wide techniques in Paris would be interesting and could indirectly help increasing team size.



Team 4 : Development and evolution of neurosecretory systems

Name of team leader: Mr Hervé TOSTIVINT

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	1
N2: Permanent EPST or EPIC researchers and similar positions			
N3: Other permanent staff (without research duties)			
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	1
N6: Other contractual staff (without research duties)	1	1	
TOTAL N1 to N6	3	3	2

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1



• Detailed assessments

Assessment of scientific quality and outputs

Assessment as a group is impossible because the team is composed of one single scientist (if it is done so, this will be an individual evaluation). In any case, the principal investigator has done interesting contributions to the field focused on the evolution of neuropeptide gene families in vertebrate. He has notably participated to the elucidation of the origin of three forms of GnRH (Gonadotropin Releasing Hormone) of teleosts; the identification of two new peptides belonging to the family of Urotensin II in teleosts; the identification of the teleost orthologue of Urotensin II-related peptide of tetrapods. Therefore, despite his youngness it presents a robust track record in the field.

- Very young group, recently included in the unit.
- Papers in good journals in the field as first or last author.
- Very small team of only one scientist, still a research team in infancy.
- Very new and innovative subject of high interest for the MNHN and for the unit.
- Necessity of external funding (National and/or International).

Assessment of the team's academic reputation and appeal

- Invitations to international meetings.

Assessment of the team's interaction with the social, economic and cultural environment

- Involvement in teaching, writing articles for educational and popular magazines; writing articles for the teaching online platform of the MNHN; lectures for training secondary school teachers provided by the MNHN.

Assessment of the team's involvement in training through research

- Good involvement and welcome of Masters and PhD (1,5).

Assessment of the five-year plan and strategy

The first part of the project is scientifically highly interesting and new for the MNHN, this should be supported rapidly by grants obtained by the team itself.

The second part of the project, highly interesting because it provides a functional role for the above neuropeptides, is completely dependent of external collaborations. Its feasibility must be appreciated and, if done within the team, supported by recruitments to explore the phenotypes. A more mechanistic approach is recommendend by more lack and/or gain of function experiments. Besides morpholinos (which are the preferred method for embryologists), it would be ideal to use alternative mechanisms of gene expression repression.

The medium-term equilibrium between the two axes of the project must be discussed within the whole unit.



Conclusion

- Strengths and opportunities:

New and attractive subject for the unit and the MNHN.

- Weaknesses and threats:

One-scientist team with very little external fundings.

- Recommendations:

Either increase rapidly the size of the team by being attractive for post-docs and scientists and raising funds, or join another team.



5 • Conduct of the visit

Visit dates:

Start: 29 January 2013, at 8:30

End: 30 January 2013, at 17:30

Visit site:

Institution: MNHN

Address: Muséum National d'Histoire Naturelle, 7 rue Cuvier, 75231 Paris

Conduct or programme of visit :

Day one – 29 January 2013

- 8:30** Welcome & Closed-door Meeting of Visiting Committee with AERES Scientific Advisor
- 9:15** Introduction of Plenary Session: AERES Role & Procedures: AERES Scientific Advisor
- 9:30** General Presentation of UMR-7221 & Discussion
(30' presentation, 30' discussion); Director of the Unit
- 10:30** *Coffee Break*
- 10:45** Presentation of Research Team 1: "Integration by thyroid hormones signalling"
(40' presentation, 35' discussion); Ms Barbara DEMENEIX
- 12:00** Presentation of Research Team 2: "Molecular regulations of morphogenetic processes"
(30' presentation, 30' discussion); Mr Giovanni LEVI
- 13:00** *Lunch (buffet)*
- 14:00** Presentation of Research Team 3: "Function and mechanisms of thyroid hormone receptors"
(30' presentation, 30' discussion); Mr Laurent SACHS
- 15:00** Presentation of Research Team 4: "Development and evolution of neurosecretory systems"
(30' presentation, 30' discussion); Mr Hervé TOSTIVINT
- 16:00** *Coffee Break*
- 16:15** Meetings of Visiting Committee with personnel:
Discussion with engineers, technicians, administrative staff
- 17:15** Meetings of Visiting Committee with personnel:
Discussion with students and post-docs
- 18:15** Meetings of Visiting Committee with personnel:
Discussion with staff scientists (excluding management staff)



Day two - 30 January 2013

- 8:30 Visit of the research facilities
- 9:30 Closed-door meeting of the Visiting Committee (in presence of AERES Scientific Advisor)
- 10:30 *Coffee Break*
- 11:00 Closed-door Discussion with Representatives of the Managing Bodies
- 11:45 Discussion with the Director of the Unit (if necessary)
- 12:30 *Lunch (committee only)*
- 13:30 Closed-door meeting of the Visiting Committee (in presence of AERES Scientific Advisor)
- 17:00 End of the visit

Specific points to be mentioned:

Mr Miguel LOPEZ (Universidad Santiago de Compostella, Spain) contribute to write the report, but unfortunately he was absent at the visit.



6 • Statistics by field: SVE on 10/06/2013

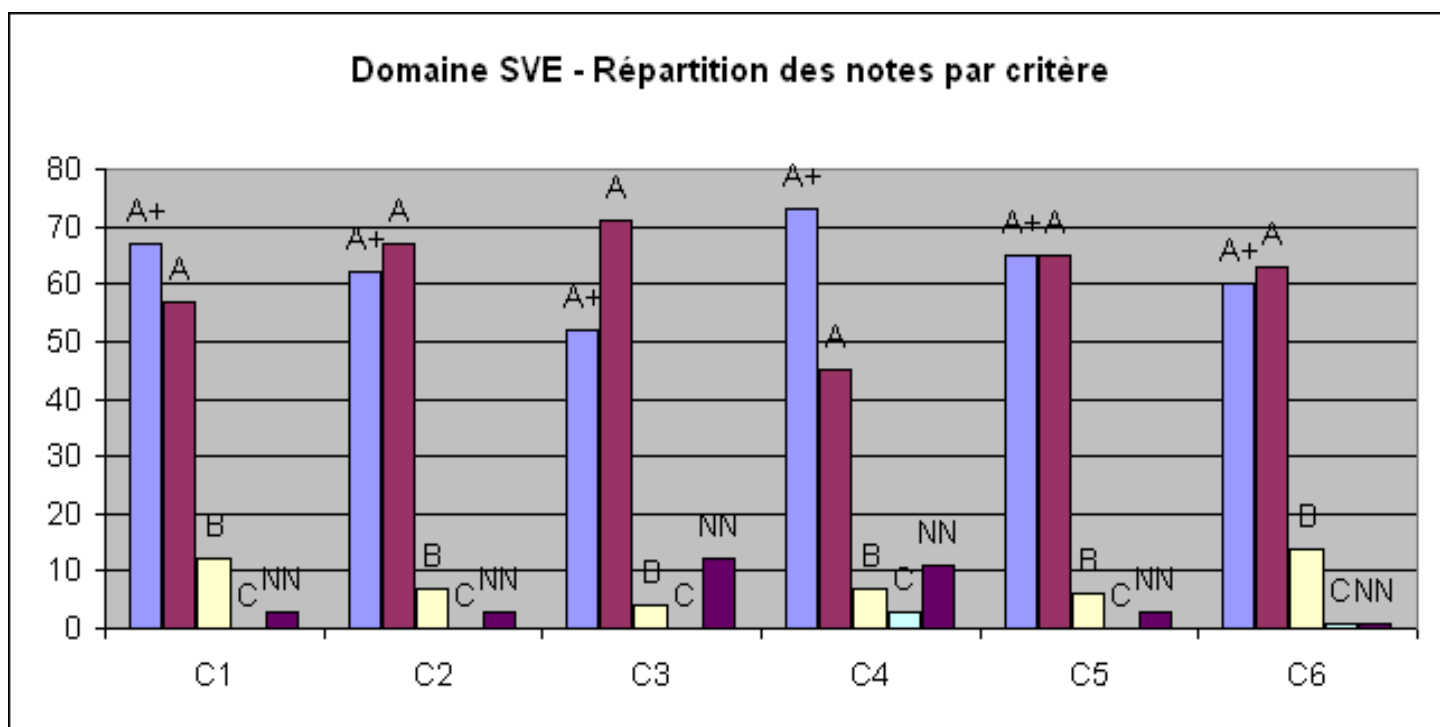
Grades

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	67	62	52	73	65	60
A	57	67	71	45	65	63
B	12	7	4	7	6	14
C	0	0	0	3	0	1
Non Noté	3	3	12	11	3	1

Percentages

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	48%	45%	37%	53%	47%	43%
A	41%	48%	51%	32%	47%	45%
B	9%	5%	3%	5%	4%	10%
C	0%	0%	0%	2%	0%	1%
Non Noté	2%	2%	9%	8%	2%	1%

Histogram





7 • Supervising bodies' general comments



MUSÉUM NATIONAL D'HISTOIRE NATURELLE
DÉPT. RÉGULATIONS DÉVELOPPEMENT ET DIVERSITÉ MOLÉCULAIRE USM 501
CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE
UMR 7221 ÉVOLUTION DES RÉGULATIONS ENDOCRINIENNES



A l'attention du comité de l'AERES

Paris, 23 avril 2013

Objet : Evaluation AERES – UMR 7221 / MNHN

Chers membres du comité,

Nous avons lu avec plaisir les commentaires du rapport d'évaluation de notre unité «UMR 7221 / MNHN - Evolution des Régulations Endocriniennes ».

Nous vous remercions pour le temps consacré à notre évaluation et pour les remarques et suggestions constructives.

Ces conseils vont sûrement faire progresser notre unité dans les années à venir.

Ainsi, nous tenions à vous informer que nous n'avons aucune correction à apporter.

Nous vous prions d'agréer, chers membres du comité, l'expression de nos salutations distinguées.

Giovanni LEVI

Barbara DEMENEIX

Le Directeur général
du Muséum national d'histoire naturelle

Thomas GRENON