Institut de génomique fonctionnelle de Lyon

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Institute of Functional Genomics

From the

CNRS

ENS

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University of Lyon 1

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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

Mai 2010

Research Unit

Name of the research unit: Institute of Functional Genomics

Requested label: UMR CNRS

N° in the case of renewal: UMR 5242

Name of the director: M. Vincent LAUDET

Members of the review committee

Chairperson

Mrs Brigitte GALLIOT, University of Genova, Switzerland

Other committee members

Mrs Miep HELFRICH, University of Abideen, Great-Britain

M. Ilpo HUHTANIEMI, Imperial College London, Great-Britain

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Report

1 • Introduction

- **Date and execution of the visit:**

The committee visited the Institute of Functional Genomics in Lyon (IGFL) on February 8 – 9, 2010. The committee members had received well in advance detailed documents with reports and projects, all in English. On site, the organization of the visit was well prepared, with public presentations and discussions with group leaders, technical and administrative staff, students and postdocs, but also with the four trustees. The committee could take the time to discuss various issues and indeed this visit took place in the best conditions. The committee wishes to congratulate the management of the IGFL for this professional organization.

As complementary documents, the committee asked for the CVs of the PIs.

- **History and geographical localization of the research unit, and brief presentation of its field and scientific activities:**

The IGFL is a very young institute launched in 2007, currently spread out over different locations within and outside the Ecole Normale Superieure (ENS), with a new building planned for late 2011. Therefore it can only be evaluated for what it is : a young growing plant full of vigor, planted in a supportive soil but certainly showing some potential frailties. In fact 4 out of the 10 evaluated PIs that are now part of the IGFL, were already active at the ENS in Lyon in 2005. All group leaders at the IGFL are French and older than 44, all have already reached some or even considerable maturity as PI, having set up their own groups at least 5 years ago. One exception is Laurent Viriot who established his own team at the IGFL in 2008, but before that already spent 11 years as assistant professor. Among these 10 groups, 2 are led by women, a ratio considered as good by the committee. The committee also met two selected junior group leaders, who briefly presented their scientific projects.

The scientific interests at the IGFL all clearly focus on questions related to development and evolution. The scientific activities of the different groups are linked to three main themes :

1) the development and evolution of mineralized tissues, a theme that implicates 6 different groups (Bleicher, Hänni, Jurdic, Laudet, Vanacker, Viriot),

2) the role of nuclear receptors in development and homeostasis, a gene family that is of main interest for 5 groups (Flamant, Jurdic, Laudet, Samarut, Vanacker),

3) the question of evolutionary adaptations, a question addressed by 4 groups (Hänni, Laudet, Viriot, Volff) with approaches as diverse as paleontology, phylogeny, genomics and development.

Several technical platforms were established in the past years to develop and maintain the most appropriate tools for all IGFL teams. These platforms, which are also shared with other institutes in Lyon, are directed by IGFL group leaders: CeCIL (Centre Commun d'Imagerie de Laennec, F. Bleicher), IFR (Institut Fédératif de Lyon, P. Jurdic), PALGENE (C. Hänni), Plateau de Biologie Experimentale de la souris (J-M. Vanacker).

- **Management team:**

The directors of the IGFL are nominated by the trustees further to a proposal made by the IGFL's management board and the laboratory board for 4 years: the former director was nominated president of the ENS in 2008 and had to resign. Vincent LAUDET, who was acting first as deputy director at that time will be the new director up to 2012. Since 2008 Vincent LAUDET has not had the assistence of a deputy director, a situation that was discussed with the

committee (see recommendations). A staff of 3 full-time persons is dedicated to the secretarial and financial work. The management of the institute relies on three distinct boards : 1) a management board that includes all PIs and meets once a month, 2) a laboratory board where all positions in the institute (technical assistants, post-docs, …) are represented ; this board meets 3 times a year, 3) a prospective board that includes directors and professors to discuss 4-5 times a year all issues linked to the development of the unit and to its external interactions.

The governance developed at the IGFL (see below) relies on the combination of the independence of the various PIs and the sharing of resources. The committee was impressed by the excellent organization of this combination.

- **Staff members (on the basis of the application file submitted to the AERES):**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	19	17
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	22	22
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	3	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	16	15
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	10	7
N6: Number of Ph.D. students (Form 2.8 of the report and 2.7 of the project file)	21	21
N7: Number of staff members with a HDR or a similar grade	22	19

The committee received from three groups of employees, i) the researchers, ii) the technical and administrative staff and iii) the post-docs and PhD students, the results of specific surveys organized independently from the management of the IGFL and designed to test the satisfaction of the staff members from each of these categories. Most members expressed their satisfaction to work at the IGFL and their eagerness to move to the new building.

As specific points expressed by the tenured researchers, the committee was glad to learn about their overall satisfaction concerning their autonomy in the scientific projects, their possibility to write grants and to receive appropriate training. However some researchers also expressed difficulties with access to students, to establish sustained interactions within the institute, or to develop a career plan. The committee was surprised to learn that a relatively large number of these researchers expect to become fully independent, i.e. expect to be setting up their own team. Some clarification about the actual constraints that apply to PI positions seems to be required as only a few of these researchers appear ready to apply for competitive international/French group leader positions.

The engineer, technical and administrative staff (ITA) of the IGFL is mostly composed of women (70%) and 1/3 (7/21) are not tenured. As positive points, the ITA staff mentioned the principle of shared duties between the different groups, the « minicolloques » and the new website as sources of valuable information at the IGFL and the ready availability of the IGFL director. The committee was also glad to notice that the organization of the continuing education for the ITA staff is excellent. However, the committee was surprised to learn that staff working on temporary contracts does not see any financial recognition of his/her professional experience, even after several years. This situation provides a clear case of inequality between tenured and non-tenured ITA positions and a major problem for the ITA staff at the IGFL at the moment.

As specific requests, the ITA staff is asking for more feedback on their annual evaluations and more information on possibilities of career advancement, especially for those working on the platforms. There is currently no IT representative on the IFR board but the IT staff does not see a clear need for it as the communication between them and the directors is fully satisfactory. By contrast, the ITA staff would have considered it appropriate to have

had a representative member in the AERES evaluation committee. For the middle-term future, the ITA staff foresees some difficulties with the new organization of the institute, in particular the fact that a number of duties that were previously shared with the Laboratoire de Biologie Moléculaire et Cellulaire (LBMC) will soon become duties of IGFL staff exclusively. This potentially increases their workload substantially and there appears to be a need for recruitment in particular with regards to the management of the informatics and the administration. Indeed, at the administrative level the fact that the IGFL is sponsored by four major trustees with distinct administrative regulations for each of them, makes the daily life rather complicated.

The committee also met enthusiastic post-docs and PhD students, who expressed their satisfaction to get the chance to develop their skills and autonomy in their daily lab life within the different IGFL teams but also through specific training, seminars, journal clubs and international conferences. The committee found that the PhD studies at the IGFL are well organized and the tutorship is satisfactory. As a request from both post-docs and PhD students, more information concerning scientific careers in general and more feedback on their own career plans seem to be needed. Also the selection process of the master students to enter the PhD program does not seem clear to all students.

2 • Overall appreciation on the research unit

- **Overall opinion:**

Overall the research performed at the IGFL was considered as good to excellent, which is a reflection of the high number of publications of each group, the international recognition obtained by some teams and the good level of funding raised in France and in Europe. The committe did feel however that the visibility of the IGFL did not match up with the quality of the research performed. Indeed, the committee noted that the best scientific results, which in some teams correspond to potential major discoveries, were certainly not promoted enough and with some more efforts, might have been better communicated, i.e. in international conferences where broad scientific fields are represented and published in more visible journals. In addition, there was no evidence of promotion of scientific discoveries outside the usual channels (journals and scientific conferences). A recommendation is that the IGFL considers communicating their science (which is eminently suitable for this purpose) with general audiences. This would lead to greater recognition of the importance of their approaches, might lead to better links with clinicians and would help their fundraising efforts. Students and postdocs should be trained in communication of science to wider audiences and they should take an active part in this.

The committee warmly congratulates the past and current directors of the IGFL for having set up in Lyon a completely novel institute devoted to the analysis of the intricate mechanisms that drive animal development and animal evolution. Indeed thanks to their vision and their dynamism, they designed well-thought scientific strategies to convince the four trustees (Ecole Normale Supérieure –ENS-, Centre National de la Recherche Scientifique –CNRS-, Institut National de Recherches Agronomiques –INRA-, Université Claude Bernard de Lyon –UCBL-) to set up the foundations of an institute that has the potential to become an internationally recognized and attractive site for French, European and non-European scientists. To reach that level, the IGFL needs develop in the immediate future the appropriate genomic, bioinformatic and imaging resources and a strong politic of top-level scientific communication.

- **Strengths and opportunities:**

The committee found the three distinct scientific trends of research within the IGFL quite convincing and coherent. There is obviously a large potential for developing synergies among the different teams.

The presence of an active Scientific Advisory Board is an excellent opportunity for the future of the IGFL.

The committee would like to acknowledge the human resources at the IGFL : these are highly motivated to cooperate and develop their scientific activities despite some heterogeneity between the scientists regarding their teaching duties, between the ITA staff regarding their status. This dynamism of the different teams under the lead of their respective PIs is certainly a major strength for the future of the IGFL. The feeling to have the chance to participate in a rather unique adventure is obviously shared by most members of the IGFL and hence promotes a strong enthusiasm.

The level of funding of the institute and of each of the groups is overall satisfactory and reflects well the dynamism of the teams.

The participation of some of the teams within European networks is excellent.

The IGFL is an active member of a number of high quality technological platforms.

The acquisition of a microCT scanner will provide a unique opportunity to take the lead in developmental paleontology and further enhance collaboration and knowledge exchange within and outside the institute.

- **Weaknesses and threats:**

The size of some teams is too small to properly achieve their scientific projects. To maintain or enhance their scientific productivity, these teams need grow and/or focus on a more limited number of projects.

The scientific communication, specially the promotion of the most significant scientific results, is often not pushed to achieve maximal impact within the international community.

The absence of a lecture theatre in the new building will certainly not help scientific communication.

The attractivity of the IGFL for European (non-French) and non-European scientists, specially PhD and post-docs, is currently limited.

Most of the teams are planning to have genomic approaches, however high throughput sequencing facilities are currently not available neither in the Institute, nor in the close vicinity. The development of a genomic Platform appears an urgent need to sustain the whole project.

Also to develop the genomic approach, the Institute that already established close collaborations with groups of experts in bioinformatics, requires a high level bioinformatics facility and should recruit top-scientists in this field. A bioinformatics team is currently lacking at the IGFL.

The move of the IGFL to a new specifically designed building has been delayed for many years, threatening the cohesion of the teams in one Institute. This move, now planned for late 2011, will be a necessary, but difficult transition phase and should not be delayed further.

- **Recommendations to the head of the research unit:**

The question of the nomination of a deputy director is currently pending. The committee suggests to explore the possibility of nominating a deputy director with a strong record in lab management. Given his/her background, this deputy director would thus be in charge of several aspects of the management of the unit, in close collaboration with the director : accounting, equipment, grants, reports …. This would leave more time to the director for all scientific aspects of his unit, including the recruitment of 9 new groups, and for elaborating fundraising strategies where the deputy director could assist him. This deputy director would not need to have the scientific potential to become himself/herself the next director but could provide a continuity between the successive directors.

Developing a genomic platform and making a call for a team in bioinformatics are considered by the committee as priorities. Trustees should help face this necessary development of a genomic Platform and bioinformatics facility. The committee also encourages the director and his team to launch a dynamic fundraising strategy towards private sponsors, more specifically to develop the genomic platform.

The IGFL management should explore all the possibilities to set up mechanims for the recognition of the years of service and their development for all its employees, whatever their employment status.

The committee strongly recommends to establish a clear strategy for the development of the scientific careers : the PIs should be encouraged through the management board and the scientific advisory board to identify in their groups the most promising researchers and to help them establish a career plan that includes international/national mobility.

Concerning the visibility of the institute, the committee recommends to the head of the IGFL to promote in his management board a systematic policy of top-level scientific communication, which might result in a lower number of publications but within more visible journals.

Following on the theme of visibility, the committee did not see much evidence, or concrete plans, to increase visibility of the Institute or of the individual research groups with the general public. The committee would encourage greater emphasis on this. Discussing science with a general audience is also of importance for the training of the younger researchers and this should become a standard part of their education.

- **Data on the work produced :**

(cf. http://www.aeres-evaluation.fr/IMG/pdf/Criteres_Identification_Ensgts-Chercheurs.pdf)

A1: Number of permanent researchers with or without teaching duties (recorded in N1 and N2) who are active in research	38
A2: Number of other researchers (recorded in N3, N4 and N5) who are active in research	23
A3: Ratio of members who are active in research among permanent researchers [(A1)/(N1 + N2)]	0.97
A4: Number of HDR granted during the past 4 years	1
A5: Number of PhD granted during the past 4 years A6: Any other relevant item in the field	12

3 • Specific comments on the research unit

- **Appreciation on the results:**

The director and the teams of the IGFL (104 people) are highly motivated to develop an International Institute in functional genomics, focusing on the molecular mechanisms linking development and evolution. The scientific productivity, including publications, oral presentations and PhD defenses, is high and of good to excellent quality. Over the past 5 years (2005 – 2009) the scientists of the IGFL published 241 peer-reviewed articles (about 48 papers /year) ; depending on the year 14% to 38% of these papers were published in journals with impact factor>6, which is a good rate. Over the same period, 12 students have defended their PhD and all of them have published their results in peer-reviewed journals.

The research on mineralized tissues provides excellent basis for future synergy between the different teams within and outside the IGFL. The research on nuclear receptors provides results with obvious biomedical interests. The approaches to tackle the question of evolutionary adaptations were launched more recently, but already provided results based on innovative strategies. Solid and efficient partnerships were established within the Lyon scientific community, through high-quality technological platforms and University teaching.

- **Appreciation on the impact, the attractiveness of the research unit and of the quality of its links with international, national and local partners:**

The IGFL is a very young institute (only 3 full years of activity) and the committee is confident that its impact and attractiveness will increase in the coming years, especially once the new building is opened. Over the 2005-2009 period, the IGFL scientists were invited to present their results in 35 conferences outside of France, meaning that on average, 7/10 teams were invited each year. The communication strategy should certainly be considered as a priority by all PIs of the IGFL in the coming years, specially when excellent scientific results deserve the best visibility.

In the coming years, the IGFL will prove its ability to recruit top-level young scientists through the recruitment of new groups (up to 9). The current IGFL teams are all members of national networks and several of them are involved in european networks. Their respective level of funding is good. Beside the platforms that are shared with other institutes of the Lyon scientific community, the PALGENE platform constitutes a potentially valuable resource to the French research community. Finally several IGFL teams have signed industrial contracts with private companies.

- **Appreciation on the strategy, governance and life of the research unit:**

Despite the lack of a deputy director since 2008, which, in this stage of intense development of the IGFL, represents an overload of duties for the director and might prevent a secure continuity with the next director (in 2012 or 2016), the governance over the past four years was highly efficient, well adapted to the size and the dynamism of the unit. In addition, during the visit the committee could very well perceive two very positive features of the management in this institute: first the clear independence of each PI to run his/her group at the scientific, financial and human resources levels and second the well organized daily sharing of numerous resources betweeen the different groups. This combination of team independence and resource sharing, which is the voluntary hallmark of the current director, seems quite efficient and obviously promotes positive interactions between the members of the institute.

Most of the external communication (seminars, meetings) was so far organized jointly with the laboratories based at the Ecole Normale Supérieure ; in the future events organized by the IGFL itself might help make visible its scientific specificity.

- **Appreciation on the project:**

The project of the two successive directors of the IGFL is to build up in France a highly dynamic multi-sponsored organization, formed ultimately (after the recruitment of 9 new team leaders) of 18 independent teams, which would give to each PI the possibility to develop independently his/her line of research, integrated within the different scientific trends of the institute. Each PI would have the possibility to hire several postdocs via National and International Grants.

However the committee wants to point out that some of the teams currently established are rather small and therefore need to be reinforced and more focused in their projects. Also the committee wants to insist on the risk that in the absence of substantial continuous funding the institute might become a constellation of small teams that could have difficulties to become visible at the international level. In conclusion, the major efforts produced to set up this innovative and original institute deserve full consideration, much scientific interest and curiosity, and major support for the coming years that will be decisive.

4 • Appreciation team by team

Team 1: Odontoblasts and dental tissue regeneration

Team leader: Françoise BLEICHER

- **Staff members (on the basis of the application file submitted to the AERES):**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	4	5
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	2
N7: Number of staff members with a HDR or a similar grade	5	5

- **Appreciation on the results:**

This team included 12 people in the past period. Only a quarter of the team members (1 CR1 CNRS, 1 engineer (IE) and 1 technician) are fully dedicated to research activities, the other members of the team have 50% or less research activity, as the rest of their time is dedicated to clinical and teaching duties. This group is focused on odontoblast physiopathology. This domain of research covers only a part of the field of dental research. Very few groups are working on this topic, making the area of research original and relevant.

Their research is very much appreciated by colleagues working on the tooth field and this is illustrated by the quality of publications of the group. The group published 23 articles from 2005 to 2009 (4.6 papers/year), not only in dental specialised journals, but also in journals with a broader scientific interest such as Matrix, J. Immunology, J. Biol. Chem. etc…. In 16 of these articles members of the group had the first or last authorship, whereas 7 articles resulted from collaborations. Taking into account the number of scientifically active people in the group (12), each group member contributed to 2 papers every 5 years on average. Accumulating the IF of the 23 articles (64.353) we get an IF of 2.78/per article, that is a very good number for research groups working in the dental field.

Members of the group participated actively in international and national scientific meetings (TMD meetings, IADR, Research-Industry meetings etc), and authors of books edited by Springer. Many members of the group are reviewers of numerous scientific journals, and experts in evaluation committees.

Finally the majority of the group members have academic, clinical and heavy teaching responsibilities.

- **Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners:**

Several members of the group were invited to international conferences and symposia, and to give lectures at Universities including outside France.

A problem for this group is the difficulty they meet to recruit post-docs and PhD students, not only from abroad but also from France.

This team showed some ability to raise funds from private companies and to successfully apply for competitive public funding (Région Rhone-Alpes, ESPRI, CIBLE etc…). They are participating in scientific and industrial clusters, international (COST action) or national scientific networks, and created collaborations with several foreign partners (China, Italy, Germany and UK). The group created solid national collaborations.

- **Appreciation on the strategy, governance and life of the team:**

This team will include 11 people for the period 2010-2014 but this number does not really reflect the research potential as 3 scientists (1 CR1 CNRS, 1 engineer (IE) and 1 technician) only are fully dedicated ; 4 members have 50% research activities, the rest of their time being dedicated to teaching and clinical duties. A new member will join the team with 30% research activity (70% dedicated to clinic and teaching). The other 3 members are a PhD dental student, a dentist research student based on one-year contract with possibility of extension and one postdoctoral student.

The group is organized in such a way that 4 different research axes could develop. One first axis focuses on the study of the immune system in the dentin/pulp complex. This research is solid, and the future directions clear. A second axis is focusing in the relationship of nerves with odontoblast and the transmission of pain. This is an original research that is of a general scientific interest. A third axis focuses on molecular mechanisms involved in pathogenesis (carious lesions etc), a research area that is promising. Finally an axis on clinical applications is cited. This axis of research is not so clear, and there is not much information about the way it will be developed in the future.

The communication between the group members to share ideas and solve daily problems, appears satisfactory. The group joined the Institute very recently, and the PIs of the groups focusing their research on hard tissues did not develop yet close interactions. It is clear that such type of interactions would definitively help this group to further develop. This could be achieved by sharing PhD students (common projects), common applications for research grants etc. The external communication (press releases in local, national and international media) has to be monitored by the director of the Institute.

- **Appreciation on the project:**

The existing projects are original, solid, well designed, relevant and realisable on a short, medium, and long-term. This group has acquired through the years the know-how, so the feasibility of the proposed projects on the medium and long-term is high.

The information of the existence of a resource allocation policy is not yet clear, it is obvious that the group has to compete for soft money from the various funding bodies and companies.

- **Conclusion:**

  - Overall appreciation:

Very positive.

  - Strengths:

The strengths are the originality of the projects, the unique know-how, the quality of work, the transparency of the scientific directions. The opportunities for this team are the new scientific environment provided by the IGFL, including the access to the various technical platforms, the potential for new collaborations within the IGFL with the

teams interested in the biology of mineralized tissues, and the funding opportunities that have increased by being part of the Institute.

— Weaknesses and threats:

- Difficulty in attracting PhD students or postdocs.
- The clinical research is not sufficiently worked out and would require more manpower.
- The number of projects (4) is too ambitious for the number of researchers in the group when considering their other duties (clinical and teaching).
- The current lack of clear collaborations with groups of the Institute working on similar topics (as bone research etc). This should and could easily be improved over the coming years.
- The retirement of several members of the team during the 2011-2014 period.

— Recommendations :

- The committee suggests to limit the research activities to two (instead of 4). The strongest and most promising axes are clearly the physiolopathology of the odontoblast (relation with immune system), and the neuronal/odontoblast interaction (involving cilia, Ca etc). The other axes should develop only if specific funds are available.
- Common studentships should be developed with other groups of the Institute to build on the existing expertise and make best use of funds and facilities.
- Similarly joint grant applications should be made with other groups within the Institute to focus on joint strengths and establish synergies.
- For clinical studies, money should be raised from pharmaceutical companies, Hospital fund etc.

Team 2: Functional genomics of reproduction

Team leader : M. Philippe DURAND

- **Staff members:**

	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1
N7: Number of staff members with a HDR or a similar grade	4

- **Appreciation on the results:**

This team is composed of 4 full time researchers (2 DR-INRA and 2 CR-CNRS), 2 researchers with medical teaching duties, 1 postdoc (INRA), 1 PhD student and 1 technician works on spermatogenesis. Their aim is to better understand the links between post-transcriptional regulation and differentiation using BTG family. The role of microRNAs in the spermatogenic process is investigated. Most of the intratesticular regulation factors are produced in other organs. During the past years, the PI has developed two systems of co-cultures enabling to study the regulations of the mitotic and meiotic phases of rat spermatogenesis as an alternative to KO strategy. Their results showing that FSH and testosterone, via the Sertoli cells, have a positive effect on meiotic division and the expression of specific genes in round spermatids are interesting and certainly important as those on the limitation by the levels of cyclin B1 and Cdk1 and the activity of the MPF complexes on the G2/M transition of both meiotic divisions. Their original culture system also was used in clinical research, focusing on the detection of changes in gene expression in human Sertoli cells in the context of human infertilities. Thanks to this approach, this team could validate the use of clusterin as a marker of differentiation of Sertoli cells in rats and humans. Their original culture system can be used to evaluate the effects and the mechanisms of action of environmental toxicants on spermatogenesis and carcinogenesis.

Since 2005, this group has published well with 25 articles (5 papers/year) in respected international journals with 1.4 < IF < 6.4. Out of these 25 papers, 8 were signed by members of the group as 1st or last author. One thesis was defended, one is under the way.

- **Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners:**

This group has been reasonably successful in attracting PhD students and postdoc (1 thesis presented in the current contract, 1 PhD and 1 postdoc under the way) and has been successful in attracting fundings from national sources. They have international and national collaborations and in particular their visibility in the national community is good.

- **Appreciation on the strategy, governance and life of the team:**

This team is quite isolated in the thematic of the unit. In the general introduction, no interactions with other groups were described and nothing was written on the future of this scientific axis. The PI will retire in a few years during the course of the next contract period, therefore he did not present a new project. The future of the members of this group has not been considered so far.

- **Appreciation on the project:**

There is no project.

- **Conclusion:**

Good scientific level for this work designed to highlight the mechanisms regulating the disorders of spermatogenesis, thanks to an original assay developed by the PI in the past. This work, which has obvious clinical implications, will obviously stop with the retirement of the PI.

Team 3 : Neurodevelopment

Team leader: M. Frédéric FLAMANT

- **Staff members (on the basis of the application file submitted to the AERES):**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	2
N7: Number of staff members with a HDR or a similar grade	2	2

- **Appreciation on the results:**

This team is focused on the study of mammalian brain development. In previous years one focus was on the role of the transcription factor Otx2 for retinal and cerebellar development but with the departure of the scientist mostly involved in this question, this topic is not pursued further. A second focus, which remains at the core of the group's interest, is the role of thyroid hormone receptors (TR) in mammalian brain development. Thyroid hormones (TH) have long been known to be crucial for brain development and function (with TH deficiency leading to cretinism and other deficiencies), but their mode of action are still not well understood. The pleiotropic role of thyroid hormones has made it difficult to dissect, which of its effects on brain development are due to direct action on the nervous system versus indirect action, e.g. on general metabolism. Therefore the development of conditional TR knockout mice (using Cre-loxP, tamoxifen inducible constructs and a dominant-negative allele) in this team, which allows to interfere with TR signalling in specified neural cell types, represents a significant methodological advance. Indeed this sophisticated tool allows to elucidate the direct effects of TR in various neural cell types. Transgenic mice expressing Cre in 8 different cerebellar cell types have already been constructed and are currently analyzed. For the characterization of the complex phenotypes of TR-deficient mice, the team has built up an extensive collaborative network.

The research findings of the present team have resulted in a significant number of publications (17 since 2005), 11 of them in high impact journals (IF > 5) such as the Journal of Neuroscience, Neuron, EMBO Reports, and Pharmacological Reviews. However, many of these papers were done in collaboration with other groups so the group should make efforts to increasingly publish their findings in higher impact journals in the future.

- **Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners:**

The findings of this team have attracted considerable interest, resulting in a number of invitations to speak at international conferences. In addition, the research was also presented in posters at several international conferences. The team leader was able to secure funding for his research through both French and EU grants and he coordinated the ANR-funded SWITCH program for four research groups. As mentioned above, he has already built up an extensive network of national and international collaborators to characterize the phenotypes of TR-deficient mice and plans to further extend this network in the next few years.

While the research project so far represents basic science, it has important medical implications and may in the longer term lead to translational projects and interactions with more clinically oriented research groups. Furthermore, the mouse models generated and characterized in this group can serve as important tools for testing TR-modulating drugs and may lead to interaction with companies developing such drugs in the future.

- **Appreciation on the strategy, governance and life of the team:**

This team is not large (8 people) but all members are fully dedicated to research (4 full time researchers, 2 postdocs, 1 PhD student, 1 undergraduate). In contrast to some other groups at the IGFL, the work of the Flamant team is very much focussed on one topic, i.e. TR effects on neural development and function. Given the complexity of TR effects, this focusing on one research topic is probably a wise strategy and will allow a thorough characterization of phenotypes, which otherwise would not be possible.

In order to allow a more in depth characterization of the TR deficient mice several new and challenging technical approaches (including purification of mRNA from a single cell type; knockdown on brain slices in vitro; RNA-Seq; ChIP-SEq) will be established in this lab. Also the expertise of a new team member in behavioral and neuroanatomical studies will significantly broaden the scope of techniques available to analyze these mice. Finally, the team leader is actively seeking new collaborations to elucidate other phenotypic aspects, which are beyond the expertise and capacity of his lab.

- **Appreciation on the project:**

One part of the project is dedicated to the detailed characterization of various strains of TR deficient mice, with defects in various neural cell types. This is a natural extension of previous work of the group and will provide important information on the specific role of TR signaling in particular neural cell types. A second part of the project will investigate the role of TR in cerebellar Purkinje cells in more detail. This will require establishment of new techniques (such as purification of mRNA from a single cell type and knockdown on brain slices in vitro) and is thus more risky. The methods to be employed have, however, already been succesfully used in other labs and should be adaptable for the proposed project. Given the central role of Purkinje cells in cerebellar development and function, this part of the project most likely will result in important novel insights into TR action on the cerebellum. A final part of the project proposes to characterize TH target genes in different neural cell types and elucidate differences between TRα1 and TRß1 targets in the mammalian brain using high throughput sequencing (RNA-Seq and ChIP-Seq) both in vitro and in vivo. While technically and bioinformatically challenging, these approaches if successful will greatly enhance our understanding of TH action in the brain and pave the way for treating diseases involving TH misregulation. The close contact with other teams in the IGFL, which also plan to use high throughput sequencing, and the proposed establishment of a next generation sequencing facility in Lyon will greatly facilitate this part of the project.

Taken together, the project is well thought out and on the one hand builds on existing strengths and resources of the group (TR deficient mice), while on the other hand reaching out to embrace new technologies to address important unresolved questions on TR effects in the brain.

- **Conclusion and recommendations:**

The achievements of this team in the last few years are remarkable and form the foundation of a project, which will significantly advance our understanding of how TH affects development and function of the mammalian brain. A strength of the team is its commitment to one complex research topic, the availability of important resources (TR deficient mice) and its embedding into a network of international collaborators. The establishment of new techniques, the interaction with other IGFL groups on next generation sequencing, and the potential of using a new platform for next generation sequencing in Lyon provide important opportunities for the team.

The team itself identified as a weakness that it is the only neurobiological research team in the area, but given the extensive network of collaborators and possibilities to interact locally with other groups on methodological aspects and regarding nuclear receptors this is not a major drawback. While the recent publication record was also relatively weak, the proposed research shows great potential for higher impact publications in the future. Potential threats include the increasing difficulties to obtain funding as well as the risks inherent in establishing new methodologies in the lab.

Team : Paleogenetics and molecular evolution

Team leader : Catherine HÄNNI

- **Staff members (on the basis of the application file submitted to the AERES):**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	2
N4 Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0.8	0.8
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	3
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results:**

This team has a good level of publications at both quantitative and qualitative levels : 23 publications, 11 of them being signed by members of the group as 1st or last authors. Most of these publications are published in top 25% journals in the category of evolutionary biology and genetics, and 8 of them in journals with large audiences (Trends in Biotechnology, PNAS, Current Biology, Nature, PLoS One). The group is also doing well with the criteria of the thesis defenses: 2 thesis defenses in 2007, 3 thesis in preparation.

- **Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners:**

The teams received several funds mainly from the National Research Agency (ANR) including the prestigious ANR Blanche. The team has a good collaborative network at both national and international levels, including collaborations with experts in population genetics and evolutionary genetics as well as a theoretician in population genetics. As the best example of international collaboration, the committee would like to highlight the Krause et al paper published in Nature in 2007 (collaboration with the Paabo's group who is one of the world leaders in this field).

As to the recruitment potential, the team proved to be able to recruit good-level scientists as for example the newcomer member who performed doctoral and post-doctoral training in two top-level labs in phylogeny.

- **Appreciation on the strategy, governance and life of the team:**

In 2009 this team was composed of 9 members (3 scientists, 1 engineer, 1 post-doc, 3 PhD students, 1 undergraduate), all fully dedicated to research except one member who is in charge of teaching duties. The team has been instrumental in the early development of an important and rare technology which focuses on the recovery and analysis of ancient DNA. The group leader clearly established herself as the French leader in paleogenetics.

Following this line, she set up an open platform for the analysis of ancient DNA, named PALGENE, which is supported by the CNRS. Palgene appears well designed and managed, and constitutes a valuable resource to the research community.

However, the team has limitations in the field of modelling and population genetics that has repercussions on the project. While the molecular methods being employed by the team were reasonably up to date – given the local availability of new sequencing technology – it was clear that the methods of data analysis were not. Most analysis seemed to be 'ad-hoc interpretation' rather than being systematic or model-based. It was noted that the group had produced at least 2 papers where systematic / model-based data analysis methods had been used. However, it was evident from the talk and from the "questions/answers session" that the group was lacking expertise in this field and that this has to be quickly addressed.

- **Appreciation on the project:**

The project (both in the booklet and in the PI presentation) was not sufficiently defined. For instance, one of the question addresses by the PI is the potential role of adaptation in genome evolution using paleogenetic. But the strategies developed to answer the question were not clearly evidenced. However, it is recognized that ancient DNA research is very cross-disciplinary and so usually requires extensive collaboration.

The team really needs the help of, or needs to recruit a population geneticists / computer simulation modeler, and perhaps a theoretical evolutionary biologists to give the required support.

- **Conclusion and recommendations:**

Several positive points come from the evaluation :

1) The group has a fairly good publication record and a good number of the publications are in high-ranking journals.

2) The PI supervised 5 students in the last four years (which is above the average for PIs in the institute).

3) The PI has obtained several grants.

4) The group has high international visibility and is generally recognized at the best, and best known, in France.

5) There appear to be good interactions with the other institute groups (particularly a good synergy with the Laudet group, and a potential one with the Viriot group).

6) The Palgen Platform appears well-designed and managed and constitutes a valuable resource to the research community.

Therefore the presence of this group is acknowledged as very important for the IGFL and for its future development.

However, the project was not clearly defined. Therefore the committee recommends :

1) To rework the project: to better explain what the questions are and how the PI will answer them in an integrated manner.

2) To collaborate with population geneticists / computer simulation modeler, and perhaps a theoretical evolutionary biologists, to bring the required support.

3) To work towards enhancing team communication.

Team : Cell biology and bone physiopathology

Team leader: Pierre JURDIC

- **Staff members (on the basis of the application file submitted to the AERES):**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	2
N7: Number of staff members with a HDR or a similar grade	2	2

- **Appreciation on the results:**

This team (10 people over the past period : 3 scientists, 1 engineer, 1 technician, 2 post-docs, 2 PhD students, 1 undergaduate) is working in the area of osteoclast biology studying a number of specialised features of these bone resorbing cells. They have particular expertise in the study of cytoskeletal structures, such as podosomes and their role in bone resorption, in the formation of the sealing zone and in the interaction of the cells and putative receptors with calcium phosphate in bone mineral. The team has also an interest in the study of osteoclast differentiation and were involved in the first reports of osteoclast formation from dendritic cells. Additionally, the team are interested in adaptor molecules such as DAP12 and their role in osteoclast function and have been studying the role of semaphorins in bone physiology (osteoblasts and osteoclasts) thereby developing expertise in bone histo-morphometry that can be applied elsewhere and as a service.

The work is of high scientific quality as indicated by a good number of publications, 30 since 2005 (i.e. 6 per year) and 13/30 were signed by members of the group as first and/or last authors. These papers were most often published in high impact factor journals, including the best specialist journals, such as Journal of Bone and Mineral Research, but also Blood and good cell biology journals such as Journal of Cell Science and EMBO J. This is excellent for a group that works very much in a niche area. Clearly they have managed to broaden the interest for their work on bone cells to a wider audience.

The PhD students and postdocs have all contributed to the publications and have frequently been first author (13 papers). The group leader has however often given way to others on senior authorship and this is something that could be improved. He collaborates extensively and with excellent groups, but needs to make sure he is more often visibly the lead of the work.

From the 4 topics currently under study the work on podosomes and the work on osteoclast differentiation is the strongest. The group has already integrated in an European network on podosome studies T3Net, is well connected in this field and has published well in this area. The work on transdifferentiation of dendritic cells to osteoclasts is very novel and has refined the existing paradigm that osteoclasts are solely monocyte-derived. This work could have major implications for the understanding of bone loss in inflammatory conditions, especially rheumatoid arthritis, but others may follow, possibly including (but not mentioned so far) periodontal disease.

It is this area of osteoclast differentiation that also offers the best potential for translational research and for interaction with pharma through targeted new anti-resorptive approaches in such inflammation-related bone diseases.

This was not mentioned in the SWOT analysis, but is a clear opportunity for the future. An associated weakness though is that this area has by now probably been picked up by other groups and undoubtedly by pharma and the group has to be careful that they are not overtaken by concerted efforts in this field from larger groups.

- **Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners:**

The group is well known in the bone field and is well connected within Europe and further afield with several senior scientists having studied with the group over the years during sabatticals. The group has also managed to attract excellent PhD students and postdocs that have trained in top labs in the field, thereby further extending their collaborations internationally. The committee was surprised to see that the team leader did not list any invited talks at international conferences from himself, although work by the group has been orally presented at several important conferences in the field. The committee wonders whether the group has a sufficiently high profile commensurate with the quality of its research. From the funding awarded to the group, it is clear that they are rated highly within France. From the invitation to join the T3Net, it is clear the group is rated within Europe. Further recognition in the form of invited plenary talks at conferences would be appropriate and should be sought. The PhD students studying in the group have presented at national and international meetings, published and generally appear to have done well.

- **Appreciation on the strategy, governance and life of the team:**

The group appears to be well balanced with several experienced members working together with younger members of the team on joint projects. The group has extensive technical expertise in the area of osteoclast biology and is extending this now into bioinformatics, trying to unravel the gene expression pathways that lead to osteoclast differentiation. They are in a perfect position to do this work and can benefit from the expertise available within the Institute. The communication between the team members appears good, they are able to communicate well in English and the communication with others members in the Institute is good. Collaborations between the different groups that work on mineralised tissues should be established further, but already there are shared facilities with the group of Viriot and a major item of equipment, a new microCT scanner will hopefully further enhance collaboration and knowledge exchange. The group leader is director of the Institut Fédératif de Recherches (IFR), thereby ensuring availability of research facilities, an important role that benefits the whole of the Institute and research groups throughout Lyon. Members of the group do not have a large teaching load, other than involvement in postgraduate research supervision.

- **Appreciation on the project:**

The work proposed for the coming 4 years looks sound. The work on osteoclast differentiation building on the extensive gene expression studies already carried out is very attractive. This could yield important new data on potentially new genes in this pathway, or might unravel new roles for known genes and this could lead to strong publications. Here the committee thinks the group has an edge as no-one else will have performed these analyses so far and will have compared the various osteoclast subtypes they have analysed. The group is already well ahead with specific differentially expressed genes selected. The committee would encourage close scrutiny by the commercialisation department (based at ENS?, CNRS?, University of Lyon?) to protect any possible commercial applications, which could definitely arise from this work. The group should also engage with strong bioinformatics teams, something that would benefit the Institute as a whole.

So far the group has contributed majorly to the work on osteoclast differentiation, but has not taken the lead. It will be important that the plans for the coming 4 years position the present team as leaders in this field. From the discussions during the visit it became clear that indeed the team intends to make the work on osteoclast differentiation the major focus of the group and that they are finishing off some papers on Dap12 and on Semaphorins and will not continue in those areas. This is a good move : in order to capitalise on their leading position they should indeed focus on 2 main topics. The work on podosomes will continue with the team as partner in an EU-funded consortium. An international PhD has been recruited to this project and this work again could be leading in the bone field. Overall, the committee feels the group could do well in the structure proposed for the new Institute. The links with the other groups working on mineralised tissues could provide new angles. There is far too little collaboration in general between dental research and bone research and this offers great opportunities for the IGFL. In addition, the collaboration between immunologists and bone biologists is a productive one and Dr. Jurdic is well placed and well connected in the field of osteoimmunology.

- **Conclusion and recommendations:**

Overall, the work of this team is of a high quality and published in excellent journals. Nevertheless, it has not resulted in sufficient international prominence of the group, despite the fact that the group is extremely well respected by those working in the same area (osteoclast biology, osteoimmunology). This is something that could be improved.

To capitalise on the potential for translation of the osteoclast differentiation work the group should start discussions and liaison with potential funders in this area. This might be facilitated by the Institute Director or other sponsors since the team does not have much expertise in clinical work and is not as yet connected with rheumatologists and has found these links difficult to establish.

Strengths : excellent research, leading position in a new area, well connected internationally, attractive team for young scientists.

Opportunities : develop a new area of osteoclast biology/osteoimmunology with possibilities for clinical translation, opportunities to build on existing expertise in bone histomorphometry and develop new international links through participation in the EUMODIC network.

Weaknesses : group does not seek enough international exposure through participation and plenary lectures in international meetings and by writing reviews in their research area; funding at present restricted to funding for laboratory studies, no funding to do translational research and no concrete plans on how to do and fund this type of work.

Risks : other, larger, groups may capitalise on the dendritic cell work, which is now published; as big pharma is moving away from R&D for new anti-resorptive treatments, it might be more difficult to find funding for the translational studies, the group will have to make the case very strongly and capitalise on their data on osteoclast heterogeneity.

Team : Molecular zoology

Team leader : Vincent LAUDET

- **Staff members (on the basis of the application file submitted to the AERES):**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	3	3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	3	3
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	4
N7: Number of staff members with a HDR or a similar grade	2	2

- **Appreciation on the results:**

This team, which is one of the largest at the IGFL (19 members over the past period, will be reduced to 11), is an internationally recognized group, historically working on the evolution of the sequence and function of nuclear

receptors. Since 2005 this group published 69 papers (13.8 papers/year) either as collaborators (31 papers) or as first and/or last authors (38 papers). Several high impact articles were published on nuclear receptors in first and last positions (Current Biology, PLoS Genetics, PNAS, Mol. Biol. Evol.). In addition, the team has diversified its interests to include developmental studies in zebrafish and an original study of the molecular basis for the evolution/adaptation of tooth patterns and ruggae in rodents. The zebrafish work has led to more minor publications, while the tooth/ruggae work is exciting and starting to yield interesting results, in part published, thanks to a good collaboration with the excellent Institute for Evolutionary Sciences of Montpellier (ISEM). Several PhD students and Postdocs were trained during the period.

- **Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners:**

This group and its work are internationally recognized and visible. They are able to attract students and post-docs, both from abroad and from France. Some of the foreign post-docs have won permanent researcher positions through their work in the group. The group is well funded from national (ANR, INCA) and European (EU FP6 NoE) sources. Longterm collaborators and co-authors include D. Moras (IGBMC, Illkirch, Structural biology) and C. and B. Thisse (Univ. Virginia, USA; zebrafish), L. and N. Holland (Scripps, San Diego, USA, Amphioxus).

- **Appreciation on the strategy, governance and life of the team:**

The team is young and well organized with weekly group meetings in English. The PI has heavy teaching and administrative duties linked to his position as institute head, but this does not seem to negatively affect the atmosphere or productivity of the group. Two other group members are assistant professors. The PI has been implicated in this organization of the AERES and was a member of the study section in Developmental Biology at CNRS (section 26). The PI has a very positive attitude towards tenured staff in the group, who are encouraged to leave the group with their own projects and direct collaborators and establish new research groups. Two CNRS members did this during the past period and another two are about to leave the team to establish their own groups.

- **Appreciation on the project:**

The proposed project has three parts in continuation with the work carried out in the previous period, but has been refocused in light of the departure of two scientists involved in the nuclear receptor projects. As a result, the importance of this "historic" part will continue but become more minor in the group's strategy. By contrast, the part on rodent evolution will be developed. The zebrafish part will remain stable. The committee strongly supports the rodent evolution project, which is original, exciting and reasonably risky. This part of the project will greatly benefit from the presence of the complementary team of Laurent Viriot in the institute, in addition to the already established collaboration with ISEM. Also, one of the proposed new teams of the institute is computationally modeling tooth development. The proposed zebrafish work has not reached critical mass but involves important technological developments. It is seen as less original. It could be reduced to strengthen the rodent project.

- **Conclusion and recommendations:**

The overall appreciation of this group is excellent. The team has managed to keep very original, productive and diversified lines of research over the years, to train students/post-docs and foster several spin off groups. The PI has managed through adequate delegation to efficiently head a high-level, internationally recognized, and well funded team in spite of heavy teaching and administrative duties. The interactions with the Viriot team and the ISEM on rodent evolution appear particularly promising. The zebrafish work, which lacks critical mass, may cause a lack of focus and could be reduced. The scientists and senior engineer working on fish would certainly benefit from a shift to the rodent project.

Team : Oncogenesis and development

Team leader: Jacques SAMARUT

- **Staff members (on the basis of the application file submitted to the AERES):**

	Past	Future
E6 N1: Number of researchers with teaching duties (Form 2.1 of the application file)	6	5
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	5	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3	2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	5	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	5	5
N7: Number of staff members with a HDR or a similar grade	5	2

- **Appreciation on the results:**

This team belongs to the world leaders in the study of thyroid hormone action with their unique knockout mouse models. They have also done important work in the field of chicken embryonic stem cells. Their newest project on the role of androgen receptor in prostate cancer has good potential but has not yet delivered important research results. Their overall publication record is laudable (26 publications since 2005 – 5.2 per year – with 13/26 signed as 1st and/or last authors), with numerous publications in top special journals (e.g. Molecular Endocrinology, Journal of Biological Chemistry), although the highest IF publications are missing from recent years.

- **Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners:**

There was no report on prices and distinctions, but the reputation of the group is very high amongst scientists working in the field of thyroid research, and the group leader is a frequent speaker in international scientific congresses. Most of the group members are French, but there are also some foreign graduate students in the group. English is used in the scientific communication of the team. The group has been very successful in recruiting grants both nationally and as co-applicant from European Union, and is consequently a member of several European research networks. The group's attempts to emphasize the translational and clinical aspects of their work are laudable.

- **Appreciation on the strategy, governance and life of the team:**

The unit is now one of the biggest in IGFL (24 members over the past period, will be reduced to 14 in 2011). It is recognized that two of its current members are in the process of establishing their own independent groups. However these plans appear not to be fully defined. Also part of the research will be carried in a geographically distinct location in Lyon Sud, which poses a challenge for coherence of the group. The proposed new research relies heavily on the group's established track record on unique animal models in the study of thyroid hormone function. The STORM project (selective thyroid receptor modulators) is interesting and potentially very important. The androgen receptor and prostate project is also very topical and up-to-date, but because the group has no track record in the field it remains to be seen how well they will be able to establish themselves in a new competitive topic. Entering this new field can be considered a calculated risk. Abandoning the chicken embryonic stem cell projects serves well the purpose of better focus.

- **Appreciation on the project:**

The group has excellent track record, an it plans to continue partly on its field of established strength (thyroid research). The new plans represent a calculated risk in the androgen receptor/prostate project. Streamlining of the future reasearch occurs in the form of discontinuation of the stem cell research, which will be continued by two senior collaborators in their prospected new independent groups.

- **Conclusion and recommendations:**

Overall this is an excellent group that has impressive track record and clear scientific plans on what they should do and what is expected from them. The future plans have good focus but also represent an entry into a new field (prostate). The choice is well founded but includes some risks.

As to the gouvernance of this team, the committee encourages the PI to better discuss with the most promising scientists of his group their career plans, to help them face the conditions to establish themselves as independent scientists.

Title of the team : "Physiopathology of orphan nuclear receptors"

Name of the team or project leader : Jean-Marc VANACKER

- **Staff members (on the basis of the application file submitted to the AERES):**

	Past	Future
E7 N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	2
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results:**

In 2009, this team was composed of 5.5 people (1 full time researcher, 2 postdoctoral fellows – 1 left in June-, 1 PhD student, 1 master student and 1 technical assistant). In 2010 it will be reinforce by 1 full time researcher.

The team studies several aspects of the functions of the orphan nuclear receptor ERRα in pathophysiologies related to estrogen or androgen signalling, namely bone homeostasis and breast/prostate cancers. The research activity of this group is original, and the questions addressed are relevant. This topic has great development potential of biological and medical interests. The publication record of the team is globally good with 12 papers since 2005, 8 of them being published by the team itself (first and/or last authors). These papers are published in international peer reviewed journals of good quality (Nucleic Acids Research, Journal of Biological Chemistry, Developmental Biology). The ongoing international collaborations have been fruitful, providing several publications. One PhD thesis was recently defended, and PhD students and postdoc do publish their data. However, none of the original papers reaches high impact journals.

As further addressed below (see project assessment), the committee would recommend to focus the team on the in depth study of the most promising aspects of the project.

- **Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners:**

The group has developed several local, national and international collaborations, and has been successful in raising competitive fundings in collaboration with national partners. The committee has also noted good opportunity to collaborate with other teams at IGFL, especially to pursue in depth study of bone pathophysiology.

Although the group has recently recruited one full time researcher, and has maintained an average ratio of 1 full researcher, 1 postdoc, 1 PhD student, 1 engineer, the committee feels that the team lacks international recruitment and visibility. Visibility and attractiveness would certainly be improved by increasing the impact of publications. The policy of the team regarding participation to international meetings in the field is unclear, but this is certainly to be encouraged.

- **Appreciation on the strategy, governance and life of the team:**

The committee thinks that the present size of the team is below critical mass. This should be partially solved with the recent recruitment of one full time researcher. The committee did not have the opportunity to discuss the policy of the team regarding group meetings and journal clubs, but participation in such activities, preferentially in English to train students, is certainly encouraged. As mentioned above, the team has interesting opportunities to interact with groups within IGFL.

The committee notes that none of the team member has teaching duties whereas the team leader is the director of the animal facility at the ENS Lyon (Plateau de Biologie Experimentale de la souris), which represents an important duty and substantial involvement although well-limited in time.

- **Appreciation on the project:**

The various aspects of the projects are based on relevant and interesting published or preliminary data. The various axes of research proposed are original, aimed at i) understanding the functions of ERRα in organs that are sex hormone-dependent (bone, breast and prostate) and ii) studying if and how ERRα could be used as a therapeutic target in the future. In this respect, the whole project is coherent and interesting. The in vivo (mouse models), cellular and molecular methods proposed to solve the questions are very classic but appropriate, and the team and collaborators have the appropriate expertise to develop the proposed project.

However, the committee has some concerns about the number of axes that are open. Taking into account the small size of the group, the committee thinks that it will be extremely difficult to develop all the interesting aspects of the project, sufficiently in depth to produce publications in highly visible journals.

The committee believes that it would be wiser to focus the team efforts on some promising aspects of the project, to consolidate the existing data, and to study fewer questions in more details. In addition to the recent recruitment of a second full time researcher, the team should be reinforced by further recruitment of PhD students and postdoc, which would provide the possibility of in depth studies focusing on selected questions, rather than adding more questions and scattering the team task force.

- **Conclusion and recommendations:**

The overall appreciation of the committee is positive, the work of the team is of reasonable quality, the project is original and very promising, although too broad. The team would benefit from increasing its international visibility, through focusing on the most promising aspects of the project, and through higher impact publications.

– Strength and opportunities lie in :

- the originality of the project.

- the potential for development around mechanism of action and targets of ERRα, and for future clinical development of ERRα as a therapeutic target.

- the expertise in the nuclear receptor field.

- the appropriate insertion into the IGFL scientific environment where synergies on studies involving the mineralized tissue could be developed.

- a recent recruitment.

— Weaknesses and threat are seen in :

- too broad research project given the size of the team.

- no paper of high impact.

- a lack of international attractiveness and limited visibility.

Team : Evo-devo of vertebrate dentition

Team leader : Laurent VIRIOT

- **Staff members (on the basis of the application file submitted to the AERES):**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	1
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results:**

The team has settled in the IGFL in September 2008. Their originality is to use both field palaeontology and developmental biology to understand the mechanisms that control tooth and dentition morphological changes during the course of evolution. Their previous research focused on the evolution of dentition in muroid rodents. In particular, the Viriot's team analysed the role of the EDA pathway in mouse dentition and used the tooth microwear pattern to study the evolution of mastication. Their publication record is good with 17 publications since 2005, including book chapters, 11 as last author, with several recent papers in high impact journals (PNAS) or journals with broad audience (PLoS One).

- **Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners:**

Thanks to the unique competence Laurent Viriot developed over the years and the originality of his work, he could set up many stable national and international collaborations and he managed to raise funds in France and in the

States too. His collaborations include groups within the IGFL, in particular the Vincent Laudet's group, with whom he shares projects and funding.

- **Appreciation on the strategy, governance and life of the team:**

The team leader is heavily involved in teaching and his team is just starting to grow, with collaborators that just joined. Therefore it is too early to evaluate the team's organization and the quality of the governance.

- **Appreciation on the project:**

The team leader proposes to extend his research projects to the evolution of dentition in all vertebrates, using selected extant species as well as the fossil record. He will also perform functional studies in model species (mouse, zebrafish, crocodile). He will focus on:

1) morphogenesis and evolution of molar teeth in rodents,

2) Tooth diversity in Cypriniform fish and

3) Mechanisms of tooth ever-replacement.

The project is original and highly relevant. It is also very wide, ranging from field palaeontology to functional studies in three different model species.

- **Conclusion and recommendations:**

The committee was very much impressed by the originality and the high rationale underlying the work performed by this small team in tooth evolution, one of the main scientific topics of the IGFL. Its strength lies in its unique, internationally recognized competence in comparative dental anatomy, X-ray 3D imaging and morphometry.

The committee strongly recommends that the group increases in size in order to be able to perform their very relevant and ambitious projects in the best conditions. It is also essential for the projects of this team that the IGFL acquires a microCT scanner, a piece of equipment that may be shared by several groups within the unit.

Title of the team : "Vertebrate evolutionary genomics"

Name of the team or project leader : Jean-Nicolas VOLFF

- **Staff members (on the basis of the application file submitted to the AERES):**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0.5	0.5
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	2
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results:**

The Pl moved recently from Germany to establish de novo the team at the IGFL (2007). The team is small, composed of 6 people in June 2009 (2 scientists with teaching duties, 0.5 engineer, 1 post-doc, 1 PhD student, 1 undergraduate student). This team carries a research on functional genomics in teleost fish to decipher the evolutionary mechanisms that drive biodiversity in vertebrates. They focus on several criteria that are potentially involved in genomic variability and are accessible through genomics : gene and genomic duplications, transposable elements, sex-determining genes and pigmentation genes. This line of research is highly relevant to the remit of the institute. The publication record is good for a relatively small group although the PI should occasionally aim for higher impact journals : 27 publications since 2005 (5.4 per year with IF<6) in a field that is highly productive, 18 of them being signed by the PI or members of his group as 1st or last authors. Over the same period the group leader has signed 4 reviews, for two of them he is the unique author and these are well cited (Heredity 2005, Bioessays 2006). As chief editor of a book series (Genome Dynamics), he has also 5 edited books and is in the editorial board of 5 journals.

- **Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners:**

Jean-Nicolas Volff, who spent 12 years in Germany and established there as an independent group leader in 2001, developed over the years a good network of European collaborators. The team has currently collaborations with very well recognized teams in the Europe. He also established a network of collaborations in France and within the IGFL.

The capacity of the PI to raise national grants is fully satisfactory, as examples he is the coordinator of an « ANR Blanche » network in France and he is a member of the trout genome sequence consortium in Europe.

- **Appreciation on the strategy, governance and life of the team:**

The team is small and young at the IGFL. The two senior members of this team have actually heavy teaching duties. Therefore there is an evidence of rationalization of project number to maintain focus and reach higher impact journals. Also the recruitment of a specialist bio informatician (who could be shared with an other IGL team) would significantly support the in depth development of this team. The strategies implemented by the group complement other work going on in other units within institute.

- **Appreciation on the project:**

Work on sex chromosomes is likely to be a productive long-term project. Membership of trout genome sequence consortium is likely to enhance bioinformatics expertise and lead to further long-term projects. Both sex chromosome and transposon projects have degrees of originality. Transposon project is higher risk, more speculative, and a more competitive area of research, but can be justified and is potentially highly rewarding. The sex chromosome research is novel but more secure.

- **Conclusion:**

The team is a small and young unit at the IGFL but with good funding and a good publication record.

— Strengths lie in:

- good publication record.
- managable number of projects.
- a combination of reliable, and more speculative projects.
- good evolutionary genomics basis.

— Weaknesses:

- small size of the group.

— Recommendations are :

- increase the size of the team!
- aim for higher-ranking journals.
- hile a good balance of secure and speculative, and of novel and mainstream projects is evident, the sex chromosome research should remain the main focus.

Note de l'unité	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	**A**	**A**	**A+**	**A+**

Nom de l'équipe : *ODONTOBLASTS AND DENTAL TISSUE REGENERATION*

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	*A*	*B*	*A*	*A*

Nom de l'équipe : *FUNCTIONAL GENOMICS OF REPRODUCTION*

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
non noté	*A*	*B*	*A*	*non noté*

Nom de l'équipe : *NEURODEVELOPMENT*

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	*A*	*A*	*A*	*A*

Nom de l'équipe : *PALEOGENETICS AND MOLECULAR EVOLUTION*

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	*A*	*A*	*A*	*B*

Nom de l'équipe : *CELL BIOLOGY AND BONE PHYSIOPATHOLOGY*

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	*A*	*A*	*A*	*A*

Nom de l'équipe : *MOLECULAR ZOOLOGY*

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	*A+*	*A+*	*A+*	*A+*

Nom de l'équipe : *ONCOGENESIS AND DEVELOPMENT*

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	*A+*	*A+*	*B*	*A*

Nom de l'équipe : *PHYSIOPATHOLOGY OF ORPHAN NUCLEAR RECEPTORS*

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	*A*	*B*	*A*	*B*

Nom de l'équipe : *EVO-DEVO OF VERTEBRATE DENTITION*

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	*A+*	*non noté*	*A+*	*A+*

Nom de l'équipe : *VERTEBRATE EVOLUTIONARY GENOMICS*

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	*A+*	*A*	*A*	*A*

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Le Directeur général

à

Monsieur Pierre Glorieux
Directeur de la section
des Unités de recherche
AERES
20, rue de Vivienne
75002 – PARIS

Lyon, le 20 mai 2010

Monsieur le Directeur,

Je vous remercie de l'envoi du rapport d'évaluation de l'Institut de Génomique Fonctionnelle de Lyon IGFL UMR 5242. Le rapport d'évaluation représente un outil précieux pour le pilotage et le positionnement de l'unité. Le Comité a formulé quelques recommandations qui feront l'objet de toute l'attention de l'ENS de Lyon et de l'UMR 5242.

L'ENS de Lyon se félicite de l'évaluation très positive ; le comité souligne le travail réalisé par le Directeur actuel et le Directeur précédent qui a permis la création d'un institut attractif au niveau national et européen. Le recrutement de neuf équipes supplémentaires confortera le positionnement de l'IGFL au niveau international et contribuera à renforcer les grands axes de recherche de l'IGFL.

Cette UMR contribue fortement au dynamisme de notre établissement et des tutelles partenaires (CNRS, INRA et UCB). Le fort soutien de l'ensemble des tutelles est un élément indispensable pour permettre l'équipement du bâtiment destiné à accueillir l'IGFL et pour développer des approches de génomique, bioinformatique et d'imagerie.

Je vous invite à trouver, ci-jointe, la réponse du directeur du laboratoire Vincent Laudet.

Je vous remercie ainsi que les évaluateurs pour la qualité de leurs travaux et vous prie d'agréer, Monsieur le Directeur, l'expression de ma sincère considération.

Olivier FARON

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Réponse de l'unité Institut génomique fonctionnelle de Lyon – UMR 5242.

Directeur : Vincent Laudet

Commentaires et demandes argumentées de modifications

1 . Introduction

No specific comments. We thank the visiting committee for their overall, very positive evaluation of the laboratory. We will carefully consider their suggestions in order to implement them.

2 . Overall appreciation on the research unit

In the section **Strengths and Opportunities**, seventh paragraph. Report : « *The acquisition of a microCT scanner will provide a unique opportunity to take the lead in developmental paleontology and further enhance collaborations and knowledge exchange within and outside the institute*. »

This project has unfortunately been blocked by one of our trustees, the CNRS. In fact, the cost of this equipment is ca. 400 k€. In July 2009, we obtained IBISA labelling funding of 200 k€ for the IFR 128's AniRA platform. We asked to the CNRS for the supplementary 200 k€ required to acquire this equipment in the 2010 laboratory budget (*équipement mi-lourd*). After obtaining a positive review by the Life science institute of the CNRS (INSB) our proposal was turned down on the last referring by the CNRS. This negative decision will strongly impair the IGFL's mineralized tissue research axis whose achievements and project were very positively considered by the AERES committee.

In a very similar topic, we thanks the committee for having pointed out that the lack of a genomic platform in house (specially for massive sequencing) would be detrimental for the development of the IGFL. We are currently searching the financial support for setting up such a platform and this is done through the application for the budget of the scientific equipment of the whole building. To date this budget, estimated at 8 million Euros is not yet secured and this is of course a worry for a building that will open at the end of 2012.

In the section **Weaknesses** we would like to comment on the question of the size of the groups. We agree with the committee that the size of some groups is too small, the reason for this being mainly historical since most of the groups were recently created. The last established teams (Volff and Viriot) were created in 2007 and 2008 respectively. We are engaged in a systematic policy of encouraging and supporting these newly established groups and we have been reasonably successful recently with the Viriot group who for the first 18 month at the IGFL comprised only 1-2 persons. The situation has not sufficiently improved for the Volff group which is lacking a staff scientist fully engaged in experimental work. We are pursuing our efforts in that matter by asking for the creation of a CR2 position at INRA. Other slightly older groups (e.g. Vanacker) are also in the process of increasing their critical mass. Finally, we would like to point out that (*i*) this policy should be done without undermining the established groups that also may need help over specific periods; (*ii*) our plan to attract 9 new groups to occupy the new

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building could be severely impaired if the trustees do not make a very significant effort in terms of creating new positions for the IGFL. There is absolutely no chance of attracting talented group leaders without a strongly attractive policy, and having adequate personnel resources working in the groups is obviously a major component of such a policy.

4 . Appreciation team by team

Overall, we would like to comment on the fact that the team by team reports are quite heterogeneous in their presentation, contents and spirit. It would have been desirable to have a more standardized format.

The report suggests on a number of occasions that group leaders reduce the amount of specific topics they are developing within their teams. We would like to make the general comment that the ANR system for financing research in France is a very strong factor pushing in this direction. ANR grants are most often obtained through collaborative research with 2-3 other groups. A network of 3 groups for 3 years can reasonably obtain 700 to 800 000 Euros, that is ca. 90 000 Euros per year. If such a program contains a post-doc salary (45 000 Euros/year), there remains approx. 45 000 Euros per annum for bench fees. This represents the cost of a maximum of 3 persons working at the bench. It follows that a group of *ca.* 10 persons would need at least 3 or 4 such contracts to have a chance to be financially secure. QED.

Team 1 : Françoise Bleicher

The team would like to thank the Committee Members for their encouragements and very positive comments on our past research and project. We fully agree with their recommendations and we will focus our projects on the two main axes that are highlighted by the Committee. The strategy of joint grant applications with other groups within IGFL is already underway as a 2010 ANR grant was applied for in collaboration with Vincent Laudet's group.

Team 2 : Philippe Durand

First we would like to thank the committee for its appreciation. However, besides the briefness of the report, we are quite surprised that the report only refers to data on the intra-testicular regulation of spermatogenesis, as these data were published during the year 2004 i.e. before the creation of the IGFL, and thus, were not presented in our team's "Activity Report". In contrast, there is no mention of the eight papers that we have published during the years 2005-2009, on the topics that we present in our written report, and that have been presented, for most of them, in our oral presentation. Moreover it is written in the committee's report that "*Their original culture system also was used in clinical research, focusing on the detection of changes in gene expression in human Sertoli cells in the context of human infertilities. Thanks to this approach, this team could validate the use of clusterin as a marker of differentiation of Sertoli cells in rats and humans*." Actually all these above results were obtained using *in vivo* approaches, and not our culture systems.

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We also would like to comment on one sentence, in the section "**Appreciation of the strategy**". The report mentions that "*The team is quite isolated in the thematic of the unit*". We don't think this is the case. In fact the team of Jean-Nicolas Volff is also working in the field of reproduction and the teams working on nuclear receptors are also close to the research done in Philippe Durand's team. For example the team of Vincent Laudet is active in the field of endocrine disruptors, very close to the aspects of toxicology worked in Philippe Durand team. Finally ,the overall question of cell differentiation is also worked on in other contexts by Pierre Jurdic's and Françoise Bleicher's teams.

Team 4 : Catherine Hänni

In the section "**Appreciation of the strategy**" the report alluded to the lack of a massive sequencing platform in house. We would like to emphasize that such a platform is planned to be part of the scientific equipment of the new building and that we are presently searching for the funds that will be necessary to establish it. We fully agree with the fact that the scientific program proposed by the team would be impossible to do without having such a platform in house.

We would like to clarify the status of the National Platform for Paleogenetics, Palgene. This is a project driven by the CNRS and the Ecole Normale Superieure de Lyon who provided funds, space and the positions for it to be established close to the unique skills of Catherine Hänni's team, who have pioneering experience in this field. The platform has been operational for some time. The resource is thus clearly a major asset for the competitiveness and the visibility of the team. Note that the platform is fully open to both the national and international communities that are interested by paleogenetic and paleogenomic studies and want to carry out their research in the best possible conditions. Also, it is important to note about Palgene that, as indicated in the written report and mentioned by the IGFL's director during his talk, after having been incubated by the IGFL it will be an independent structure in the next Quadriennal period (starting January 2011). A specific file was send to the CNRS to propose Palgene as an independant "UMS" for the next Quadriennal. This file contains all the different projects that have been already performed in Palgene as well as those currently carried out.

Finally, we take the point raised by the reviewers that the group is lacking expertise in modelling and population genetics even if the committee raised the fact that the team "*has a good collaborative network*" in these fields. The departure of a lecturer (Maitre de conference) from the team provides a vacant position. The head of ENS de Lyon has decided to re-allocate this position to Catherine Hänni's team and this will provide us with an excellent opportunity to recruit a scientist competent in these approaches.

Team 5 : Pierre Jurdic

In the section **Appreciation on the results**; paragraphe 3. We would like to comment the following sentence «*The group leader has however often given way to others on senior authorship and this is something that could be improved. He collaborates extensively and with excellent groups, but needs to make sure he is*

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more often visibly the lead of the work". Indeed, it has to be understood that the French system is quite different and unique. The PI has in his group two senior scientists with permanent positions (CR1 CNRS and CR1 INSERM). They are each in charge of a specific program (cytoskeleton organisation and osteoimmunology, respectively). They are really in charge of the day-to-day advancement of the team's projects since the PI is very busy with other tasks (e.g. management of the IFR128 – the PI is its director). These senior scientists are also evaluated every two years by their respective trustees and they are expected (due to their positions) to publish as last authors since they are in charge of projects (the CR1 INSERM has already been told that she was not publishing enough as a last author!). In this system there is then a direct conflict between senior scientists and PI that both should sign as last author! The PI personally considers that it is fair that people deeply involved in the advancement of scientific projects are rewarded by a last author position. Most of the people in the field will know anyway that the work has been produced in the PI's laboratory since he usually keeps the corresponding author position to indicate that the work is coming from his group. In addition we would like to point out that this comment was not done for other group leaders for which it could have been equally relevant and was even found as a positive point in some case (see Vincent Laudet's team).

In the section **Appreciation on the project**; paragraphe 2. The sentence « *So far the group has contributed majorly to the work on osteoclast differentiation, but has not taken the lead.*" It is true that we are not leaders in the field of osteoclast differentiation. However, after the PI's visit last September to several leaders of the field in the US, we believe this should change. We also want to stress that our main paper on osteoclast podosomes has been cited more than 120 times and the Blood paper on DC transdifferentiation into osteoclasts is now reaching over 80 citations.....

Team 6 : Vincent Laudet

In the section **Appreciation of the results** . We would like to comment on an inconsistency. The journal *Plos Genetics* is cited, correctly, as a high impact journal but two lines after it is stated that « *The zebrafish work has led to more minor publications* ». In fact a recent paper of the group on zebrafish has been published in *Plos Genetics*…

In the section **Appreciation of the project** the report suggests that « *The proposed zebrafish work has not reached critical mass but involves important technological developments. It is seen as less original. It could be reduced to strengthen the rodent project*". In addition in the section **Conclusions and recommendations** the report also suggests that "*The zebrafish work, which lacks critical mass, may cause a lack of focus and could be reduced. The scientists and senior engineer working on fish would certainly benefit from a shift to the rodent project*". We would like to answer that, as mentioned above the zebrafish work has in fact generated 10 papers, including several in excellent journals such as *Plos Genetics*, *Molecular Endocrinology* or *Developmental Cell*. In addition, we should emphasize that more than 50% of our current research grants concern the zebrafish work, including the part dealing with endocrine disruptors. Reducing this

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part of our research would have a major impact on the competitiveness of the team. We nevertheless appreciate the criticism that this part is lacking focus and we will work on this aspect in the future to improve the coherence of our research on this model organism.

Team 8 : Jean-Marc Vanacker

Concerning the PI's position as a director of the ENS's animal facility (PBES), it should be noted that this accounts for a 10% commitment (for a two year period) for the benefit of the whole community and that this reflects the PI's expertise in the field of animal-based experimentation, rather than scattering of his activities.

Comment on the section **Appreciation on the results**. The team has published 13 papers since 2005 with a global IF of over 54 (4.5 per paper in average; no IF being available for PlosOne to date), for 9 of these papers the PI is last author (global IF: 38). Publications were in *Nucleic Acids Res*, *J Biol Chem* (2), *Dev Biol*, *Trends Endocrol Metab*. Although the PI clearly acknowledges the lack of very high IF papers, the qualification "*reasonable quality*" given by the jury to the publication file maybe underrated, given the PI has undergone two moves (from Lyon to Montpellier in 2004, from Montpellier to Lyon in 2008) within 5 years.

We would also like to emphasize that the team is actually focussed on TWO axes: studying of (*i)* ERRa in bone and (*ii)* ERRa in cancer, and not several scattered projects. This impression of scattering may have been given to the committee by the fact that team members were nominally identified on sub-aspects of the two axes during the oral presentation. It should be noted that this approach (studying bone and hormone-dependent cancer as the same time, in the same team) has been deemed as "*original, coherent and interesting*" in the committee's written report. In terms of funding each of the two axes represents roughly 50% of the money raised by the team. For all these reasons, it does not seem to make any sense to discard one of the two axes. Furthermore the team settled in the IGFL two years ago and has recruited new team members ever since, and current (March 2010) comprises 6 persons (2 permanent full time researchers, 1 post-doc, 1 ITA, 2 students; see application form) which is within the IGFL's average (4 other teams have less or an equal number of persons). During the oral presentation the PI clearly pointed out that the team has to be reinforced in terms of personnel, a process which is undergoing since grant applications, that ask for salaries for temporary positions, are under consideration.

Team 9 : Laurent Viriot

We thank the committee for its positive evaluation. We would like to mention that we have already and efficiently tackled the small size of the group. An assistant professor (Maitre de Conference) position from the ENS de Lyon has been provided to the group and will be recruited shortly. An ATER available within the IGFL will also be allocated to this group. In addition a post-doc obtained in an ANR has recently joined the group as well as a PhD student with an « allocation couplée » from the ENS de Lyon. Finally, very recently, one of the group's post-docs has been well-positioned for a recruitment as a CR2 CNRS (section 29).

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Team 10 : Jean-Nicolas Volff

On the section **Appreciation of the strategy**, the report insists on the small size of the group and on the need for « *the recruitment of a specialist bio informatician (who could be shared with an other IGFL team) would significantly support the in depth development of this team*". We would like to emphasize that the team has already a bioinformatics engineer (devoted to 50% to the team). What the group requires (amongst other things) is a permanent researcher and a research technician for bench work. The IGFL has already asked twice for the creation of a research associate (CR2) position at INRA in the field of sex determination in fish, but unfortunately this request, as not yet been fulfilled. Such a position will again be requested of INRA in 2010. In addition, the direction of the IGFL is considering appointing an INRA technician from Philippe Durand's team (as this latter team is not renewed in the upcoming contract period) to Jean-Nicolas Volff's team.

In the section **Appreciation on the project**. We would like to comment on the sentence « *Transposon project is higher risk, more speculative, and a more competitive area of research, but can be justified and is potentially highly rewarding*". Indeed the team has a long-term internationally recognized expertise in this field of research, especially in the context of fish genomics, as can be seen from the publication list. This significantly reduces the risks of the proposed research.

More generally, the evaluation of this team's research came across as being relatively superficial. It is a bit pitiful to see a lack of scientific input and relatively vague recommendations in this section of the report.

Vincent Laudet

30 mars 2010