IBDML - Institut de biologie du développement de Marseille - Luminy

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Institute of Developmental Biology of Marseille Luminy

From the

Université d'Aix-Marseille 2

CNRS

January 2011

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Le Président de l'AERES

Didier Houssin

Section des unités de recherche

Le Directeur

Pierre Glorieux

January 2011

Research Unit

Name of the research unit: Institute of Developmental Biology of Marseille Luminy

Requested label: UMR CNRS

N° in the case of renewal

Name of the director: Ms Geneviève ROUGON

Members of the review committee

Committee chairman

Mr Alain VINCENT, Center for Developmental Biology, Toulouse, France

Other committee members

Mr James CASTELLI-GAIR HOMBRÍA, CSIC/Universidad Pablo de Olavide, Sevilla, Spain

Mr Daniel CHOURROUT, Sars International Centre for Marine Molecular Biology, Bergen, Norway

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Observers

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University, School and Research Organization representatives

Mr Pierre CHIAPETTA, University of Aix-Marseille 2

Mr Bernard POULAIN, CNRS

Report

1 • Introduction

- Date and execution of the visit

The visit occurred on January 19th-21st, 2011. The overall organization of the visit was very satisfactory and the director and her assistants should be praised for that. The time initially reserved for interviewing the director and vice-director was certainly too short, but, thanks to the availability of Genveviève Rougon troughout the rest of the visit, most, if not all important aspects of the unit's life could be discussed. The written information provided was adequate, and the print-out of the director and each team's presentations was a very useful complement. The presentation of the Director and discussion with the technical staff occurred in front of the entire committee, whereas, for the the discussions with the PhD/postdocs and with staff scientists, the committee split into two groups. Only the internal administrators and the vice-director of IBDML attended the presentation of the Director. In contrast, all team members did attend the presentation of their leader. Following each presentation, the discussion was split in two parts: first, a 10 minutes discussion in the presence of all team members, followed by another 10 minutes with the team leader(s) only.

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

IBDML was created in January 2006 as a mixed Unit between the CNRS and Université de la Méditerranée, by merging three CNRS and one INSERM pre-existing units with common research interests. The objective was to share intellectual resources, open-access facilities and management to promote interdisciplinary research in Developmental Biology and Neuroscience, using various vertebrate and invertebrate models. Since its creation, the IBDML was headed by Geneviève Rougon, former director of the Federative Institute IFR138. The IBDML is located on the University campus, in a building that contains other research units, and has the particularity of being 3 parts : University, CNRS and INSERM. Thanks to the efforts of the Director and the support from the University and CNRS, the relevant laboratory surfaces of the CNRS/University building were refurbished and one team from the previous INSERM unit could be relocated in the CNRS building. IBDML presently hosts 18 teams, representing 230 members. Since its creation, the IBDML has recruited 6 new teams, mostly with support from ATIPE-CNRS. Two "internal" groups have been recognised as teams. One team has been closed and 5 emigrated: Two joined the INMED INSERM unit, Marseille; one joined the ESPCI, Paris; one left to Melbourne, Australia and one left to CRBM, Montpellier. Of note, two teams were seeded by young investigators issued from IBDML, one at INSERM Timone, Marseille and the other at ENS, Paris. Following the retirement of M. Semeriva, the team that he headed has not been retained by IBDML and will join TAGC, INSERM Marseille. IBDML concentrates a large part of its efforts on a few major themes (Cell and tissue organisation and dynamics / neurogenesis, brain organisation and neuro-pathologies/ gene network regulation and evolution). Brain organogenesis and plasticity is a strong transversal axis. The main model organisms are Drosophila and mouse. A few teams use chicken and Xenopus. The ascidian model will not be maintained. A new team will introduce the nematode model in 2011.

- Management team

The laboratory is managed by the Director, assisted by three administrative assistants, in charge of infrastructure, finance and informatics and communication. The Director also consults the group leaders (team leader's board) and the Institute Personnel board on all management matters (general laboratory policy, priorities for staff recruitment, laboratory budget, purchase of large equipments). Then, required decisions are subjected to approval by the "Comité de laboratoire". The director also takes advice from an external committee (Scientific Advisory Board) on scientific matters. The criteria and decision process leading to recruitment of a new team seem to have been fluctuating. Dedicated team leaders bear scientific reponsabilities for technological platforms and facilities.

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	15	11
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	51	46
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	59	26
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	57	55
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	16	
N6: Number of Ph.D. students (Form 2.7 of the application file)	40	
N7: Number of staff members with a HDR or a similar grade	41	39

2 • Overall appreciation on the research unit

• Summary

IBDML groups a large number of teams working on various animal models (Drosophila, chicken, mouse Xenopus, and in the past, ascidians). While neurobiology is certainly a strong transversal theme, there is no strict common theme, apart from reaching for excellence, and therefore a wide variety of projects is currently developped. The laboratory plays a major local role, since it gathers most of the forces in the field of developmental biology in the Marseille area, and gives the campus a strong visibility at the national and international levels. Despite its recent history (decision of creation 2004, effective in 2006), IBDML gives the feeling of a strong cohesion between all teams, through the organisation of the seminar series, establishment of common services and platforms and innovative in-house collaborations. IBDML has also been very efficient in generating collaborations with other units/disciplines on campus. The overall quality of the research is very high, with several outstanding groups. The committee therefore formulates an extremely positive opinion on the activities of IBDML. The creation of IBDML which was built on the acquired experience and achievements of several pre-existing units can be considered as a success both in terms of scientific achievements and of management. Ongoing programs and collaborations with physicists constitute a real strength. The congruence of developmental biology, physiology and evolution aspects in studying the ontogeny, physiology and dysfunctioning of the nervous system, creates the conditions of further increasing the excellence and international visibility of IBDML. Because the present director will leave in two years, appropriate procedures have to be set up to make sure that scientific excellence and maintenance of the necessary thematic diversity will continue to be major determinants in modelling the IBDML.

• Strengths and opportunities :

- The success of the merging of several pre-existing research units into a coherent and efficient assembly of teams working on fundamental biological questions, using appropriate animal models. The essential role played by Geneviève Rougon, current director, in securing this success, deserves to be praised.
- a very high overall quality of the research done at IBDML, with several outstanding groups.
- the presence of a large proportion of young group leaders, among which some have already acquired a strong to very strong international visibility.
- a very good internal cohesion, with a general feeling of the personnel that they contribute to the IBDML reputation.
- the solidity of the training of the PhD students and involvement of IBDML members in teaching, including training on the imaging platform.
- the state of the art imaging platform, run in concert with the CIML; the quality of the mouse husbandry, which is complementary to the main mouse facility at CIML, and of the Drosophila facility, owing to the dedication of several young team leaders.
- the establishment of solid, fruitful interactions with other units on campus (see above), udeniably increasing the attractiveness of IBDML (see for example the recent implementation of a nematode team).
- the abilility of most IBDML teams to attract funding for their research, despite the fact that financing of fundamental research by ANR becomes more and more difficult to obtain. Many projects are supported by International programmes and one team has obtained a pretigious ERC award for young investigators.
- the prospect of additional support from University for teaching and further renovation of the building.

- Weaknesses and threats :

- The lack of sufficiently clear procedures for the recruitment of new groups. The absence of foreigners and women among the newly recruited teams. The limited number of young IBDML investigators starting their own team outside Marseille.

- The recent departure of two teams with expertise in computational biology. The potential difficulty in attracting a computational biology/modelling team despite the needs which have been expressed by the director.

- Some heterogeneity in the number of students/post-docs per team and the potential negative impact of a no-student situation on the future of a team.

- The difficulty of some young teams with excellent research projects to publish primary research papers in a reasonable time frame, calling for a mentoring program.

- The recent departure of several University Professors, resulting in an overloading of the last-recruited professor with teaching duties.

- An increasing deficit in training opportunities for the technical staff. The limited access to English and Animal Experimentation training sessions is counterproductive in a European level laboratory.

- Whereas IBDML members have strongly invested in teaching and training of PhD students, several professors or assistant professors have recently left or will soon leave IBDML, in part because of the retirement process. The expected hiring of a new Developmental Biology professor is essential for maintaining the IBDML success in attracting the best PhD students.

- Recommendations to the head of the research unit :

- The committee strongly supports the initiative taken by the actual Director to set up an external search committee in charge of selecting the best possible future director. The next director should be in charge of the elaboration of the strategic plan for IBDML for the next contract. The success of the selection procedure has therefore a strategic importance. In case no external candidacy is satisfactory, the procedure for the designation of an internal director needs to be anticipated.

- For the next recruitments, the IBDML should adopt clear and well-explained recruitment procedures, based on both quality, and adjustment of the new or emerging groups to the IBDML research topics and strategy.

- The committee supports the reconduction into IBDML for the next 5-years period of all, but two teams for which a re-examination of their situation in two years could be useful. In one case (Development and pathologies of neuromuscular circuits), there could be a re-evaluation of the scientific production and projects relative to the team composition. For the other team (Morphogenesis of epithelial cells), there could be a re-evaluation of the situation of its team leader; the CNRS should adopt a policy and give its scientific delegate the adequate support required for maintaining a productive team in a very competitive environment while he exercises at the same time highly demanding scientific responsabilities at the national level.

- Production results

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	13
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	45
A3: Ratio of members who are active in research among staff members [(A1 + A2)/(N1 + N2)]	0.88
A4: Number of HDR granted during the past 4 years	12
A5: Number of PhD granted during the past 4 years	55

3 • Specific comments

- Appreciation on the results

With a total working force of close to 230 members, the IBDML constitutes a major French research force in Cellular and Developmental Biology and Neuroscience, with clear relevance to bio-medicine through the development of mouse models for human pathologies. Molecular and genetic studies in Drosophila and mouse, coupled with state-of the art imaging technology, have led to major discoveries on the gene networks and signalling cues controlling the dynamics of cell shape changes and tissue cohesion, axon growth in normal conditions and response to nerve injury, and the organisation and elongation of muscle fibres and the cardiac tube. Other high impact research includes a digital formalisation of a chordate development and anatomy. Globally, the research performed at IBDML is of very high standard. A significant number of the primary articles have been published in leading journals (IF>16) and in the order of 120 publications have been published in highly recognised journals (IF>6), including articles issued from collaborations. Several groups have reached an outstanding level of publication. Another young team has been invited to write comments or reviews in Cell and Nature, attesting of its international visibility. The two teams created during the last 4 years from pre-existing groups, have increased their publication level, with new original projects. Nevertheless there remains some heterogeneity in quality among the teams, with some teams showing a productivity that could be increased, and two of them raising serious interrogations.

The IBDML has developed strong partnerships with other laboratories on campus, including via sharing technological platforms. One particularly relevant example is the development of high resolution computed tomography (micro-CT) with CPPM. The team of Biomolecular chemistry, which involves chemists and pharmacologists has developed multidisciplinary projects and secured research collaborations with local start-up companies, some of which have been funded by previous and current IBDML members. Collaborations with local and external biotechnology companies are developed in several other teams, leading to joint publications. The IBDML actively contributes to international programs. IBDML teams have contributed to and/or are partners of EU Marie Curie networks, EU-FP6 and FP7, COST and HFSP programs.

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

The very high quality of some teams is reflected by their invitations to international meetings and symposia. Several team leaders or members were awarded national scientific prizes and distinctions. T. lecuit has become editor of a major jounal in the field. IBDML members have been actively involved in the organisation of several international Neurobiology and Developmental Biology meetings.

The attractiveness and ability of IBDML to recruit high level young team leaders is attested by the number of applications received, following each call, and the awarding of competitive grants, including ATIPE, HFSP and one ERC grant to the newly recruited teams. The selection of teams working on various model systems does not affect the coherence of the laboratory and offers the possibility for fruitful collaborations on campus. The confrontation of several models and linked experimental approaches is seen as an essential element of the performance, dynamism and visibility of the laboratory. Work performed at the IBDML shows promising trans-disciplinary aspects, with a strong interface with physics.

The flow of PhD students is very good. Most students registered at IBDML obtained their PhD within four years. A significant fraction of students have joined industry after completion of their PhD. 9 students have, however, left the lab without a first-authored publication, which is quite a high number. Although a publication may happen later, this situation should be limited to exceptional cases. The number of post-docs has significanly increased, in part due to the financial support of many teams by ANR grants. A number of foreign post-docs are supported by European fellowships. The recruitement of post-docs suffers from the lack of competiveness of offered financial support, a general problem in France, that is not specific to IBDML. More than half of the permanent research and teaching staff has an HDR.

Funding of the IBDML teams is, in general very satisfactory, with many teams supported by ANR grants. All young teams have been well supported by starting grants. It might become more difficult for some of them to maintain the same level of financing, past this period, and mentoring on this aspect is recommended. The heterogeneity in the capacity of the groups to raise external grants is somewhat buffered by the redistribution of 20% of the total team's funding, but it can only be a temporary solution.

The publication level is very satisfactory with around 60 publications per year, about 40% of them in journals with an impact factor >6, which is very high. 60% of total publications are with an IBDML member as first or last author. There is some heterogeneity, however, among teams, both in terms of the total number of publications, the fraction of those which are signed as first or corresponding author, and the contribution of students. The apparent choice of some young teams not to publish their data, except in high ranking journals, presents some risk. Again, mentoring by senior scientists, as proposed by the director, could prove essential to avoid unproductive situations.

- Appreciation on the management and life of the research unit

Globally, all members of the committee were very pleased with the quality of the research unit organisation and management. It congratulates all staff members and especially Geneviève Rougon, for her intensive and successful work at the head of IBDML since its creation. Discussions with personnel representatives have revealed consensual positive views regarding the scientific atmosphere and the general daily life at IBDML. Although significant renovation of the building and relocating of several groups has been done during the last four-year period, the building architecture remains a temporary constraint limiting day to day scientific exchanges. This could be improved by the further refurbishment of lab space, and dedication of space to common rooms.

It was noted that the atmosphere of the laboratory was very good. Technical staff, PhD students/postdocs or staff scientists were globally satisfied with the organisation of the laboratory, the scientific animation, including biennial scientific retreats, and the opportunities to follow training courses and attend conferences. In particular PhD students and postdocs considered that they would get good professional opportunities following their stay in the laboratory. Internal communication was judged appropriate, although some disparities among teams were brought to the attention of the committee members. Specific complains concerned the limited access to English training sessions offered by CNRS. This recent difficulty is considered as detrimental to scientific communication inside and outside the unit especially now that IBDML is attracting higher numbers of foreign scientists. Limited access to the Animal Experimentation training sessions is also problematic. Another difficult problem is ACMO and the low number of First aid workers. Considering the size of the unit (numbers of members and square meters), this question deserves strong attention and appropriate solutions from the Délégation Régionale du CNRS, University and the IBDML director. The technical staff also expressed the needs for a closer follow-up of their carreers. A unit of this size would benefit from the presence of a "secrétaire général" to help the Unit director, in particular for this aspect of the unit management.

The laboratory has adopted a financial policy including a 20% charge on all teams' contracts, except salaries, which covers common equipment and serves to maintain a low-cost usage of all services. This offers the possibility of a selective help to facilitate the start of junior groups and seems to work very well. It also establishes a strong solidarity between groups, which is particularly beneficial to a large and diverse institute such as IBDML, at a time when fundamental research is becoming more difficult to fund. It also protects the teams that encounter a transient decrease in their external support, although the rules make clear that it cannot work beyond a reasonable period of time. Past the team selection process, emergence of projects and risk taking is essentially directly supported by the teams. As noted above, mentoring of young team leaders could possibly help avoiding dangerous, no grant or no student situations.

The technological platforms and services are operational, perform adequately and have not reached saturation. The IBDML imaging platform is very well equipped with the last generation confocal microsocopes and was instrumental in the pioneering studies performed at IBDML on tissue dynamics. It has received the Ibisa label and signed a partnership agreement with the Nikon company for technological training and development. An additional qualified technician is nevertheless necessary for full operability of this platform which is a trademark of IBDML. Maintenance of the informatics network and software is of the quality expected to ensure the conservation of rapidly expanding, precious data. The IBDML mouse facility has been reorganised by a young team leader in charge. There is no problem of limited capacity for the hosting of mice, thanks to a strict scientific and financial policy. A central service is available at CIML for generating the KI and KO, cryogeny and high throughput screening of phenotypic anomalies. For practical reasons, one IBDML member works full time at the CIML mouse facility. The fly kitchen and facilities have also been reorganised and modernised by a young team leader and are fully operational.

The involvement of the laboratory in teaching activities is excellent. It implicates not only the university assistant professors and professors, but also CNRS and INSERM researchers, some of them being involved in teaching or organisation of higher education on campus and outside. Several team leaders have expressed a desire of creating a European PhD program and the committee considers that it would re-enforce the IBDML attractiveness.

- Appreciation on the scientific strategy and the project

The strategic aim of the creation of IBDML was to gather a critical mass in the field of developmental biology and neurobiology in order to improve the national and international visibility and attractiveness of the pre-existing units with three main scientific objectives : Increase the fundamental, basic knowledge of developmental and neurobiological processes; Develop translational research; Offer innovative teaching programs. It is fair to say that the first objective has been largely fufilled. New initiatives need to be taken to promote the development of translational research as well as interdisciplinary teaching and PhD student training. The recent designation of PF Lenne, a physicist involved in trans-disciplinary teaching, as vice-director of IBDML is a strong, positive sign directed towards both the University and CNRS, and IBDML members. The successful integration of the L. Kerkerian-Legoff team is a positive asset for re-enforcing the contribution of translational grants to IBDML and collaborations with medical teams.

During the past 4-years period, there has been a significant turn-over with 6 new teams, 5 team departures and two closings, one due to retirement of the team leader. Two young scientists from IBDML have started their own team outside the unit. The recruitement policy constitutes a major level for modeling the future of an Institute of this size and ambition. The possibility for a permanent scientist to start a new team at IBDML, if stemming from a pre-existing team, is a matter of debate and possibly, frustration among scientists with HDR. The committee suggests that the procedures for selection of new teams be clearly explained to all members of IBDML. The advice from an external SAB is seen as very positive in these conditions. The relative weakness in computational biology and modeling could be of some concern with the departure of two systems biology-oriented teams. The director and vice-director are fully conscious of this potential problem. Increasing the collaborations with another, on campus, INSERM unit can only be part of the solution. The departure of an assistant professor and near retirement of a professor need to be considered. Active support from the University and CNRS is needed to maintain the traditionally strong teaching component of IBDML. This could be the occasion to broaden transversal interdisciplinary teaching and to fill in the existing gap in French science between biology and physics or mathematics. Finally, it is recommended to find a solution for maintaining and following up the library of HQNBA-scaffold drugs developed by the leader of the Biomolecular chemistry team, following his retirement.

On the short-term, it is essential to complete the new director recruitment process. A too long transition period can be a source of difficulty.

On the medium-term, the recruitment of new teams should be the occasion to reinforce systems biology in the unit. Strong attention must also be given to the future of the team headed by the current unit director, since one very productive young member is ready to leave and to start a new team in a Medical Institute.

In conclusion, the committee was impressed with the quality of the science at IBDML and warmly congratulates the current director. The new director will have many trump cards to play and confirm IBDML as an excellent European research unit in developmental biology and neurobiology.

4 • Appreciation team by team

E1: Signals in vertebrate embryogenesis

Team leader: Mr Laurent KODJABACHIAN

- Staff members

	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)	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 engineers, technicians and administrative staff without a tenured position (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	1	1

- Appreciation on the results

The Kodjabachian group uses functional genomics in Xenopus embryos to study how signalling pathways control differentiation and morphogenesis in vertebrates. Work of the last 4 years has led to 3 major achievements, each of them representing a significant advance in the field. The team has 1) re-evaluated the contributions of BMP and FGF signalling in Xenopus neural induction and proposed a unifying model to explain this phenomenon across all vertebrates. 2) showed that distinct Nodal ligands sequentially control mesendoderm induction and gastrulation movements in Xenopus. 3) studied signalling and regulatory pathways involved in the specification of mucociliary epithelia, both in Xenopus ectoderm and in regenerated human airway tissue (the latter in collaboration with a group in Sophia-Antipolis). Specifically, they have identified the conserved function of the BMP pathway in mucous versus ciliated cell specification, and of the microRNA miR-449 in differentiation of multiciliated cells via regulation of the Delta/Notch pathway. These projects led in the last five years to three publications in both generalist and excellent specialized journals. A publication on the last project on mucociliary epithelia is being revised for a high impact journal.

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

This young and very small group has already a good international notoriety in the Xenopus community as well as in the field of vertebrate neural induction. Even though the group is currently very small, the recent work, when published, should broaden its international notoriety and help attracting PhD students and post-docs. The PI has established a close and fruitful collaboration with a group in Sophia-Antipolis working on human airway epithelia.

- Appreciation on the scientific strategy and the project

In the next four years members of the group will concentrate their efforts on understanding how mucociliary epithelia are built, function and regenerate, using the Xenopus epidermis as main model system. They will undertake a comprehensive characterization of the cell types and of the architecture of the mature mucociliary epithelium during development and regeneration using a combination of lineage tracing, marker gene expression and analysis of cell morphology. They will investigate the function of major signalling pathways in mucociliary epithelium development. They will also investigate the control of multiciliogenesis by microRNAs and by the Delta/Notch pathway.

- Conclusion:

— Summary

This is a small and dynamic group with a very good past scientific activity and promising projects on the formation and homeostasis of multiciliated epithelia.

— Strengths and opportunities

The PI has demonstrated his capacity to produce high impact data in a very competitive field. He has established key collaborations allowing him to increase the relevance of his findings for human physiopathology. The group had a recent opportunity to attract one or two experienced permanent scientists and a post-doctoral fellow. This addition to the group should significantly increase the manpower.

— Weaknesses and threats

The group is currently very small considering the width of the project and the competitivity of the multiciliogenesis field. In addition, there is a risk that the recent evolution in the group's scientific interests will slow down its international recognition in the next few years. The funding for the next four years is still low and thus the viability of the group highly depends on pending applications.

— Recommendations

Considering the competition in the field, it is essential to increase the size of the group and to stay focused on specific questions.

Team 2: Hox and chromatin-mediated control of development

Team leader: Mr Yacine GRABA

- Staff members

	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)	4	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	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 engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	
N7: Number of staff members with a HDR or a similar grade	2	2

- Appreciation on the results

This team has a long-standing interest in the structure/function of Drosophila Hox proteins and Hox protein motifs that arose at different time points during metazoan evolution. The work recently carried out by the team uncovered several unexpected aspects of regulation of Hox protein activity via peptide motifs and deserved the publication of one paper in a high standard journal and two reviews in very visible journals. Many observations remain to be published. The competence and tools in the team are steadily enhanced (BiFC techniques, recent article in BMC Biology, 2011, as an example). Another research theme of the last four years was chromatin. While there is no apparent connecting thread, characterisation of the antagonistic roles of the chromatin modifiers HAT and DRp3 HDAC, on the one side and the chromatin associated proteins Reptin and Pontin, on the other, has led to publications in high standard journals.

The publication record of the team in this period has been very satisfactory with 7 primary papers. Five of these were done in collaboration with other groups and the team members were the main executors of the work in 4 of these publications. Undeniably, the team is known and well visible in the Hox field, as testified by regularly invited reviews.

Three PhD students successfully defended their thesis in this period, representing a very good number given the size of the team. Of some concern, however, one of these PhD students has left the lab without first-authored publications.

The present international collaborations are based on a European COST Network. While a productive collaboration with a team in Switzerland is coming to an end, a new, promising, collaboration with a crystallography unit on campus has started.

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

This very well funded team has very good visibility in the scientific community, in a fluctuating spotlight of international research with several invitations of the team leaders to international meetings and several links to other labs in France and a participation to a European COST. The team provides an attractive scientific environment and has had no problems to recruit excellent young scientists. Two experienced CNRS investigators (CR1) have joined the team during the last ten years. Because of the refocusing of the Hox project, there is some risk that the unique expertise on chromatin structure carried by one of them could get lost. The second one is ready to spin off, a good sign of the team's vitality.

- Appreciation on the scientific strategy and the project

For the 4 next years the group will focus on questions about the specificity and diversity of Hox protein function, rather than the hardcore chromatin questions. The team leader seems fully conscious of the need to adapt to severe competition and has decided to focus on what the team is most efficient at. There, the team is pinpointing and studying important but thus far weakly characterized protein domains. How deeply structural features of Hox proteins will be addressed is unclear in the report. Furthermore, the biological readout of the role of either post-translational modifications of Hox proteins or Hox-specific peptides is also unclear. The search for new co-factors is favoured over the tissue-specific interactions with collaborators, in the proposed genome-wide analyses of Hox protein requirement.

- Conclusion

— Summary

The scientific production of this group is very good. The research projects are original and relevant. The human skill of the group is very good. The project is very well funded.

— Strengths and opportunities

The project is very well funded for the next four years. The development of a strong collaboration with a crystallography group in Marseille will provide the necessary expertise to get deeper into Hox proteins structure. The COST networking gives an international dimension to the team.

— Weaknesses and threats

Y. Graba and J. Pradel have been successfully working together as co-team leaders for many years and the synergistic interactions within the group were very fruitful. Now that J. Pradel has retired, there is some concern that the chromatin background of the team gets lost at a time when the analysis of epigenetic regulation has become a major aspect of transcriptional regulation. Another concern is the anticipated departure of an experienced researcher with a permanent position (although in itself a positive point). Interactions with other groups at IBDML are less evident than it was in the past.

— Recommendations

Refocusing of the team on Hox proteins creates the conditions for new discoveries. To continue publishing in high impact journals, as the team leaders have done in the past, a reflection on finding very central questions and perhaps more provoking ideas might be necessary to be fully competitive in this research field. Research on cellular and developmental aspects of Hox proteins should not be totally dismissed and could be given more consideration.

E3: Morphogenesis of epithelial cells

Team leader: Mr André LE BIVIC

- Staff members

	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)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	6	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	
N7: Number of staff members with a HDR or a similar grade	1	2

- Appreciation on the results

This team studies fundamental issues of cell biology focussing on the mechanisms controlling cell polarity. Their entry point is Crumbs-3 for which, using biochemical approaches, the group has isolated new interacting proteins. This has given rise to a number of publications in collaboration with other groups. The research of this group is relevant because the role of the Crumbs 3 complex is important during epithelial polarity and integrity.

The recent publication output of the group is weak. Although the team publishes in respected specialized international journals, most research publications (11 out of 12) are collaborations with other groups, where the team is either represented only by the team leader (7 of 11), or the team members appear in intermediate positions of a long list of authors. A historical search of the group's publications record shows that the number of publications where team members appear as leading authors has decreased since the 2003/2007 period. This worrying trend has increased in the 2006/2010 period when only a leading research paper on Human Molecular Genetics was published. This is paralleled by the decreasing number of conferences and invited lectures in prominent forums. This situation reflects the fact that the team leader declined international invitations since 2006, since he started a CNRS Life Sciences executive position.

2 PhD theses have been defended in the period, which is a satisfactory number.

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

The team shows a good ability to recruit post-docs. The team is integrated in a European consortium that allowed it to recruit a post-doc and a PhD student. The team was also able to recruit a post-doc through a Marie Curie reintegration grant. This team shows a good rate of fund raising, from several sources including ARC, ANR, FRM and Vaincre la mucoviscidose. The group profits from being part of a European consortium from 2004 to 2011.There is, however, a serious concern about the lack of secured funding after 2011.

- Appreciation on the scientific strategy and the project

The project is interesting but could be more ambitious. It relies on questions and technologies that represent mainly a continuation of the past projects, without enough risk-taking. There are some exceptions to this, however, like the super-resolution analysis in Drosophila imaginal discs, in collaboration with the Lenne group and the FRAP/FLIP analysis.

- Conclusion

— Summary

This good team used to be more successful in publishing. However, in the past years its work has lost impact in the field. Although the team could identify some interesting questions to address, there is a lack of ambition in the major objectives. There is an urgent need to reinforce the team with a senior scientist that could run it when the team leader is involved in scientific administrative issues.

— Strengths and opportunities

The know-how of the group in the cell polarity field allows some risk-taking approaches, such as a FRAP/FLIP analysis of the mobility of Crumbs 3 (Crb) complex members in human epithelial cells lines and the high resolution microscopy analysis of Crb in Drosophila imaginal discs in collaboration with other groups at IBDML. It should lead to new insights into the trafficking of CRB. The relocation of the group to the 7th floor will be beneficial to intra-IBDML collaborative projects.

— Weaknesses and threats

The team seems to be losing scientific impetus, with a decreasing number of publications where the team members appear as leading authors. It is certainly relevant that this trend correlates with the involvement of the team leader in the CNRS Life Sciences executive team, which implies significant additional work and time spent in Paris. The decreased publication output is likely to affect the future funding of the group. If this was the case, it is unclear if the group will be able to regain its past achievement levels.

— Recommendations

It is likely that the group's decrease in scientific output could be caused by frequent intermittent absence of the team leader from his laboratory. For this reason, if the PI does not decide to rapidly change his personal situation to spend more time in the lab, we recommend that the team be reinforced with a permanent scientist capable of supervising the day-to-day work of the group.

E4: Principles of cell organization and tissue mechanics

Team leader: Mr Thomas LECUIT

- Staff members

	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)	4	4
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)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	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	3	3

- Appreciation on the results

The research of this group is extremely relevant, original and very solid experimentally. The group leader has initiated the field of tissue morphogenesis at the cell biological level. He is also one of the first to address this at the biophysical level. This is very relevant because the right level of analysis to understand morphogenesis is the cellular level and the right approach, the biophysical one. By making it a successful approach, this team has opened a new avenue of research.

The impact of research performed in T. Lecuit's team is very high. The team has clearly a strong leading position in the field. This is reflected in the publication record: in the last 5 years, a total of 13 publications, among which 3 articles published in Nature and reviews in top journals.

Many conferences and invited lectures in very prominent forums: 39 conferences and 23 invited lectures; 4 PhD theses supervised.

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

The young team leader has been awarded several prizes and distinctions: CNRS Bronze medal, Prix Paoletti CNRS, Price Lacassagne from College de France. EMBO member, etc

From its performance in the publication record it is clear that this team is very successful in recruiting the best collaborators.

Excellent rate of fund raising: HFSP, ANR (2x), FRM.

The team has an excellent participation to international scientific networks: coordination of an HFSP grant. From the performance of the team, it is clear that it is very well managed and that young members are well supervised.

- Appreciation on the scientific strategy and the project

The projects of the team are excellent and innovative. Beside the logical continuation of its current research, the team will also explore new areas with high potential, such as the analysis of mechanical properties in growing tissues such as imaginal discs.

- Conclusion :

— Summary

This is an excellent group. The french granting system should make sure to support this group to its maximal possibilities and provide resources to allow him to continue like this.

— Strengths and opportunities

The project is very well funded for the next four years. The work of this team on the physics of cell and tissue shape and dynamics would benefit from a stronger biochemistry. The committee therefore considers very positively the prospect of the team to strengthen its biochemistry side, in order to get even more mechanistic insight at the molecular level.

— Weaknesses and threats

None

— Recommendations

The committee considers that efforts in the international exposure of IBDML (at the level of the institute) would help this already excellent team to get even better postdoctoral collaborators. This team would also be one of those that would benefit most from an international PhD program to be set at the Institute level.

E5 : Cell Physics

Team leader : Mr Pierre-François LENNE

- Staff members

	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)	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)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

The team has a long-standing interest in membrane dynamics using optical/modeling approaches. Its work initially focused on the analysis of the role of lipid-dependent microdomains and cytoskeletal-based meshwork in plasma membrane compartmentalization. Prior to the translocation of the lab from the Fresnel Institute to the IBDML in 2009, the team changed its focus to the role of cell adhesion and cell mechanics in tissue morphogenesis. In collaboration with the group of Thomas Lecuit, they explored the role of actomyosin networks in the cellular rearrangements triggering blastoderm elongation during Drosophila gastrulation.

The publication record of the team in this period is of outstanding quality with 11 primary publications in excellent journals (Nature, Nature Cell Biology,EMBO J) as well as 11 collaborative publications. The quality of the outputs is also appreciated by the successful defence of 2 PhD theses during this period.

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

This well-funded team has very high visibility with several invitations to international conferences and symposia in the 2006-2010 period, and the award of the Feulgen prize of the Society of Histochemistry to PFL. The team had no problem in recruting young scientists and post-docs and was highly successful in raising significant funds (ANR, HFSP, PACA) in the past. The team is also scientifically well connected through collaborations within the institute and beyond and has several contacts with industry. The team is also strongly involved in teaching activities and the organization of local, national and international meetings.

- Appreciation on the scientific strategy and the project

In the coming years, the team will focus its projects on cell adhesion and cell mechanics in tissue morphogenesis. They will continue using Drosophila embyros as an in vivo assay system, but will also extend their analysis to epithelial structures in other systems/organisms in order to elucidate the common principles by which cell adhesion and mechanics control tissue morphogenesis in development. The excellent funding of the group in the past years (and the expected funding in future years) will allow them to further develop these challenging projects.

- Conclusion :

— Summary

In summary, this is a very strong and active research group with several outstanding scientific achievements in the past four years. The expertise of the team in (bio) physics will be extremely beneficial to other biology-centred labs in the IBDML as it provides complementary expertise in analysing the physical basis of biological processes.

— Strengths and opportunities

The project developed is highly original and benefits from the high expertise of the team and its high international visibility and attractivity. The development of challenging in vivo high resolution imaging technologies offer opportunities of local interactions and international collaborations.

— Weaknesses and threats

There are no weaknesses and threats recognizable at the moment.

— Recommendations

There is no necessity to give specific recommendations on the research projects of this team. In the future, it might be beneficial to develop a biological profile, which would be clearly distinguishable from the ongoing and highly visible activities of the Lecuit lab.

E6: Genetic control of heart development

Team leader: Mr Robert G. KELLY

- Staff members

	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)	4	4
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	3	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 engineers, technicians and administrative staff without a tenured position (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	3	3

- Appreciation on the results

The Kelly lab studies the second heart field (SHF) in the mouse, a population of cardiac progenitors that contributes myocardial progenitors required during heart elongation and growth. Understanding the genetic control of heart development and organogenesis is very important from a clinical point of view as subtle changes in this process can lead to congenital heart defects. Dr. Kelly was among the first researchers to identify this unique cardiac population in 2001. Since then, his group has charaterized key transcription factors that regulate SHF development (e.g., Tbx1, Tbx3 and Hes1). In addition the group studies craniofacial muscle development and the development of the cardiac conduction system. The group publishes very well, with 6 publications as first and last authors in respected jounals (3 in Circulation Research) several reviews on the link between heart and craniofacial muscle development, and an invited review, an editorial and 2 collaborative papers in Circulation Research during the period evaluated. In addition, the group collaborates with many other groups. In sum, this team is well known and respected in the heart field. The past and present international collaborations and funding are based on two European FP6 and FP7 consortiums.

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

As stated above, the impact and attractivness of this very well funded team is very high. The team leader had many invitations to international meetings. The team seems to provide an attractive and pleasant scientific environment and has had no problems to recruit excellent young scientists. Three experienced investigators have joined the team during the last five years.

- Appreciation on the scientific strategy and the project

The focus for the next years is to look at novel regulators of the subpulmonary myocardium and coronary vasculature. In collaboration with an external lab in Marseille, they wish to study A-P patterning of the heart (RA signaling). Further work will be devoted to understand the role of Tbx1 in conferring robustness of myogenesis in head muscle progenitors. Finally, they aim to learn the dynamic cell behavior of SHF cells and their contribution to the conduction system. All these research directions are likely to yield important insights on the development of the heart. Nevertheless, although very speculative, it is not certain that these directions will yield major breakthroughs in the field, a goal that this team is capable to achieve.

- Conclusion :

— Summary

The scientific production, contribution and recognition of this team are very good. The research projects are relevant but mostly a direct continuation of the ongoing projects. The technical and theoretical skills of the group members seem very good. The projects are well funded.

— Strengths and opportunities

This team is very much respected in the field of heart development. It is well connected and well funded. The development of many collaborations will provide other necessary expertises. The Committee did not find major threats from competitors working on similar questions.

— Weaknesses and threats

The team has been very focused on the understanding of SHF niche in the mouse in term of deciphering genetic and cellular mechanisms. Although a clear focus is usually a plus, as reflected by the genetic tools in hands, the lab could take some more high-risk/high-gain projects that may yield new breakthroughs – such as the identification of the second heart field.

— Recommendations

As written above, this team has been doing a very good work in the last five years in term of publications, recognition and collaborations. The only recommendation is perhaps to broaden the scope of questions asked, with willing to take more risks.

E7: Molecular mechanisms underlying mesenchymal cell differentiation

Team leader: Mr Laurent FASANO

- Staff members

	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)	2	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)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	
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	3	3

- Appreciation on the results

During the last five years this group has been studying the function of the mouse TSHZ3 transcription factor during development and in the regenerating muscle. Using in vivo analysis of Tshz3 mouse mutant phenotype as well as in vitro experiments, the group has found that Tshz3 is necessary for smooth muscle differentiation in the ureter and that its inactivation in mice results in hydronephros. In a two-hybrid screen for Tshz3 interactors they identified the Sox9 transcription factor as a Tshz3 partner in this process. They have also found an involvement of Tshz3 in the central control of the respiratory rhythm and in myoblast differentiation during muscle regeneration. These findings led to the publication of 5 original research reports in good specialized journals and one review. Of concern, several of the PhDs completed during the period did not yet give rise to publications with the students as first authors.

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

The PI has obtained ANR funding in 2009 for his project on the transcriptional control of smooth muscle formation, and has established key national and international collaborations for both the fundamental aspects and clinical aspects of this project. Nevertheless, the attractiveness and international recognition of the group could be improved.

- Appreciation on the scientific strategy and the project

This group has a scientifically and clinically relevant project: the genetic control of smooth muscle formation in the ureter. This project builds on previous results on mouse Tshz3 function and concerns the functional study of Tshz3 and Sox factors in the transcriptional network required for ureteric smooth muscle development. The group will use conditional and inducible mutants for Tshz3 and Sox9, as well as compound mutants for these two genes. They want to identify candidate target genes by expression profiling, test them in their mouse models and, for the most promising, search for mutations in inherited human diseases of the kidney and urinary tract.

In addition to this main project, the group has a couple of additional projects concerning Tshz3 function in the brain. They propose to identify Tshz3 target genes in different neuronal populations including the red nucleus in the brainstem and the cerebral cortex, using conditional mutants, laser microdissection and microarray profiling.

The main project is scientifically very interesting and well designed. It benefits from the availability of suitable animal models produced by the group or obtained through collaborations. The additional projects appear less defined and may constitute a significant risk of dispersion.

- Conclusion :

— Summary

This group has a very good past scientific activity and a scientifically and clinically relevant project, which should allow higher international visibility and attractiveness to be reached, if the team does not disperse its efforts in too many side projects.

— Strengths and opportunities

The group benefits from the presence of several scientists with tenured positions. The PI has succeeded in obtaining good funding for the main project on the genetic control of smooth muscle formation in the ureter, and has established good collaborations and attracted a postdoc (starting January 2012) in his group.

— Weaknesses and threats

Potential weaknesses are the small size of the team and a tendency to disperse their efforts in a variety of side projects. In particular, there is no post-doc so far in the group and three former PhD students have now left the lab.

— Recommendations

The group should focus their efforts on the main project about smooth muscle formation in order to improve their international recognition and their attractiveness.

E8: Molecular Control of Neurogenesis

Team leader: Mr H. CREMER

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	-	-
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)	5	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	
N7: Number of staff members with a HDR or a similar grade	3	3

- Appreciation on the results

This team has established a highly dynamic and internationally competitive research program, having made interesting discoveries in highly competitive areas. The group investigates the molecular regulation of adult neurogenesis in the mouse brain. They focus in particular on the ongoing generation of neuronal precursors from the forebrain subventricular zone that migrate to the olfactory bulb (OB) via the rostral migratory stream (RMS) and integrate as GABAergic, dopamine, or glutamate interneurons. A particular strength the group has developed over the past years concerns the use of cell isolation and gene expression analyses of neuronal subpopulations. Over the reviewing period, they showed that chemokine signalling is essential for the migration of forebrain interneurons, that the bHLH transcription factor NeuroD1 is an efficient inducer of terminal neuronal differentiation and that the proteoglycan Agrin is necessary for synaptogenesis of new neurons.

The team has published 15 papers in total, of which 9 original papers and 1 review in which the group leader appeared as first or senior authors. Several of these papers appeared in highly cited journals (J. Neuroscience, PNAS, J. Cell Science, Curr. Opinion Neurobiology). This is a very good record. Four PhD projects have been terminated over the past years under the full or partial supervision of H. Cremer. Two PhD students are currently working in the group.

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

The PI has built a highly dynamic group with an excellent national and international visibility. This is supported by the invitation of H. Cremer to several national and international conferences, the serving as an evaluator for national and international funding agencies. In addition to 3 tenured collaborators from CNRS (2 CR1 and 1 IR), H. Cremer has also been able to recruit international post-doc and students, funded through ANR, EU, and INSERM Young Investigator grants.

The overall funding of the lab is excellent, including 2 grants from ANR, the award of 'Equipe Labelisée' from FRM, two major EU networks, the Network of Excellence "NeuroNE" and the Initial Training Network "Axregen", most of which will run until 2014.

This clearly testifies of the international visibility and scientific impact of the Cremer's research group.

- Appreciation on the scientific strategy and the project

The team projects are original and hold great promise. The technological developments are cutting edge. The identification of factors regulating the migration and integration of adult-generated neurons will be followed up and taken to the functional level. Moreover, this work will be extended to the analysis of miRNA. In particular, during the presentation it became clear that the group has obtained a wealth of highly interesting data that should lead to high profile publications, likely increasing the impact of the work of this group to the highest level in the near future. In this respect, methodological expertise can have a real impact. It is notewhorthy that the group has found that the postnatal neurogenic system in the mouse forebrain can be functionally manipulated by in vivo electroporation. This approach might also allow in the medium-term the development of new therapeutic strategies.

- Conclusion :

— Summary

This is a very good team which has already taken steps to expand its work from brain anatomy and genetics to cell biology and physiology.

— Strengths and opportunities

The group is well funded by national and international agencies, and integrated in European networks.

— Weaknesses and threats

The committee does not foresee any particular problem for this team.

— Recommendations

An obvious challenge for the next years will be to further increase the impact of publications to the highest levels. All the premises indicate that this will be the case.

E9: Neural stem cell plasticity in Drosophila

Team leader: Mr Cédric MAURANGE

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)		
N7: Number of staff members with a HDR or a similar grade		

- Appreciation on the results

C. Maurange is a newly appointed group leader with a track record of publications in high impact journals. He has been awarded a CNRS-ATIP grant to establish a junior group (at the IBDML since July 2009). The focus of his work is the molecular cues associated with neurogenesis during larval development of Drosophila. Although of recent arrival the group already recruited one post-doc and one PhD student.

Previous research initiated during Dr Maurange's post-doctoral period, allowed him to decipher the molecular mechanisms regulating the number of neural progeny generated during Drosophila development. He has unravelled the central role of sequential transcription factor activity to endow neuroblast progeny with specific neural fate potential. Since the arrival of the team leader at IBDML, his main effort has been devoted to complete a project initiated during his post-doc. The main finding of this project is that the steroid hormone ecdysone controls the proliferation/differentiation balance of the neuroepithelium thus regulating the number of neural stem cells generated during larval development.

The proposed projects are very interesting, keeping in line with the group leader's expertise. The main objectives of his proposed research are: i) identification of new temporal transcription factors involved in neurogenesis during post-embryonic development, ii) study of the nuclear architecture and epigenetic regulation in neuroblasts, iii) identification of mis-regulated proliferation programs in cancer neuroblasts. These objectives deal with areas of great research interest but also highly competitive.

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

This is a new group; therefore we cannot judge most of the issues in this section.

However, in the short period since the group arrived at IBDML, it has been able to raise sufficient funds for research:

- CNRS-ATIP grant
- 1post-doc (AXA research fund, ATIP CNRS) + 1 PhD student
- ARC: 3-year post-doc salary.

- Appreciation on the scientific strategy and the project

The proposed project is very ambitious, but given the successful track record of the team leader, the committee can be optimistic that he will continue to contribute major advances to the field. However, the size of the team seems to be still too small to adequately respond to future challenges.

The group leader is now recruiting personnel for his team. A very good postdoc coming from the plant field has recently joined the group and will bring her strong molecular biology experience.

The group's contribution to teaching activity is modest. This is positive at this stage in the team leader's career, since it allows the group leader to attract University students without devoting excessive time to preparing lectures, which would interfere with the set up of the laboratory.

- Conclusion :

— Summary

This is a good, very promising group but efforts should be made to keep projects focused.

— Strengths and opportunities

Projects are well supported by ongoing grants. There is a strong potential for further scientific development. The last subproject (1.3) uses a nice experimental model where known elements of the existing neuroblast gene regulatory network can be further analysed without having to rely on the possible finding of new elements in the system.

— Weaknesses and threats

Of the three subprojects, the first two, using transcriptomic analysis of neuroblasts, seem less well defined. The chosen strategy could be a risky one, given that the success of these subprojects relies entirely in data that may or may not turn up from the analysis.

— Recommendations

The group is operating in a very competitive field of research and all efforts should be made to strengthen the group with young scientists in order to reach critical mass.

E10: Development and pathologies of neuromuscular circuits

Team leader: Ms Françoise HELMBACHER

- Staff members

	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)	3	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	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 engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	
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	1	

- Appreciation on the results

This team, established in 2005, is working on the development and pathology of the neuromuscular system in vertebrates. The team leader has found, during her postdoc, a regulatory mechanism controling neuronal cell fate involving a crosstalk between GDNF/Ret and ephrinA/EphA4 signaling pathways. This work was published in Neuron in 2006 in which the PI is a co-corresponding author. Since then, the lab has generated new genetic tools, such as the PEA3 and ETV4-GFP mouse lines, which are now validated in several projects. More recently the group had found a gene, FAT1, which is thought to be involved in neuromuscular pathologies in human. A manuscript summarizing this set of study on FAT1 and FSHD is currently under revision in Nature. This research direction is novel, interesting and very much clinically relevant. It is expected that the PI is planning to pursue this project further. The major problem of this team is the lack of bona fide publications from its activity of the past five years, beside one collaborative work with two other teams in IBDML.

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

Although the lab is very well funded it consists of only three members, which is not a good sign at this phase of the PI career. As written above, due to the lack of a clear research niche and publications, this lab is not well recognized, and this directly impacts its attractivness. On the other hand, the PI seems to be very good in her ability to raise money, and to maintain collaborations. In addition, the group most recent work on FAT1 and FSHD is an important breakthrough in the field of muscle and neuromuscular diseases. This project, combined with the genetic tools that were already established could change the path of this group and yield very important insights.

- Appreciation on the scientific strategy and the project

It is clear that the lab should focus on the neuromuscular pathologies, as planned. The objective would be to study how FAT1 and its molecular partners affect neuromuscular development during embryogenesis and adulthood and how alterations of this signaling mechanism may lead to FSHD in human. The new genetic tools, which have been generated or obtained, should help the team to explore the pathogenesis of this disease in mice.

The PI established collaboration with N. Levy to study the human aspect of this disease (via integration in the French FSHD network). Although this would probably be the major research effort of this team, it is imperative that several ongoing projects, for example the work in chick embryos on the specification of PEA3 motor neuron pools by Neuregulin/ErbB2 signaling (the PhD work of a student in the lab) be completed and published within the next two years. Additional projects with the Etv4-GFP mice should also be published in the next year.

- Conclusion :

— Summary

F. Helmbacher is presently in a delicate stage of her career. On one hand, ongoing work could lead to breakthrough discoveries in the field of neuromuscular disorders and open up novel and exciting research directions – with high clinical relevance. On the other hand, the lack of a single publication from the team's main projects within the last five years is alarming.

— Strengths and opportunities

The publication of the FAT1 – FSHD paper in a high-impact journal could contribute to a higher recognition of the team.

— Weaknesses and threats

The small size of the team and the difficulties of the PI to establish a vital and live research group despite the good funding situation that the team has experienced is of major concern.

— Recommendations

The rapid publication of additional articles is critical for the continuation of funding, attractiveness of the group, and its short term viability. The committee suggests that the activity of this team to be re-assessed in two years.

E11: Specification of heterogeneity of the somatic sensory nervous system

Team leader : Mr Aziz MOQRICH

- Staff members

	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)	3	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	3	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)		
N7: Number of staff members with a HDR or a similar grade	1	3

- Appreciation on the results

This group was recently formed at IBDML (2006). The projects build on the demonstrated expertise of the team leader in investigating the functional relevance of the highly heterogeneous population of nociceptive neurons. During the four past years, one aspect of the projects was aimed at understanding the molecular mechanisms that control establishment of primary nociceptive neuron diversity. This work identified Met/Runx crosstalk as a key event in the molecular logic of primary sensory neuronal diversification and ascertained a novel role of HGF-Met signaling in cell fate determination. This work led to one publication in a high standard journal. They also reported a novel finding that involves neurotrophin signalling in controlling the finely tuned terminal differentiation and branching of cutaneous afferent fibres. For the next four years, the group's main project will be centered on the characterization and functional analysis of nociceptive neuron subpopulations with the ambitious aim to understand the functional significance of sensory neuron diversity in vivo. Based on a microarray strategy, they identified novel genes expressed in discrete subpopulations of sensory neurons. Central to the current and future research is to engineer sophisticated and highly versatile transgenic mouse models aimed to analyze the in vivo function of newly identified genes. Two already generated mouse lines offer very promising tools for future studies.

The group has produced two publications in peer-reviewed journals during the period under review, a collaborative publication and an invited review. This is a very good score if taking into account that the team leader invested a lot in the conception of a fully renovated and equipped mouse facility. The generation of transgenic mice is time consuming and there is no doubt that several aspects of ongoing projects are likely to be completed and submitted for publication in the near future. This is a very promising start.

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

The team leader got an excellent national and international visibility based on his excellent track record in the sensory biology field. He has been invited to speak at several international meetings; he is frequently invited as external speaker in France and abroad. Although recently created, his group is well established with 4 permanent researchers and is very attractive for young co-workers (3 post-doc and PhD students). One PhD student successfully defended his thesis in the assessed period, which is a very good output. The team has been extremely successful at getting funding, being awarded 6 substantial grants including two ANR and a highly prestigious ERC-Starting grant. Strong and well established collaborations with national and international sensory physiologists are in place.

- Appreciation on the scientific strategy and the project

The team leader has proven that he can design an ambitious and original research proposal focused on studying the functional significance of the discrete sub-populations of nociceptive neurons to unravel the molecular mechanisms that control establishment of this diversity during developmental of sensory ganglia. The work is characterized by a focused and logical approach that takes excellent advantage of the mouse animal model and which studies important aspects of pain sensation. The research done is of excellent quality. All the lines of research are well planned for mid-term and long-term success. Very good starting grants are in place. Potential for exciting new findings in perception of pain is apparent. Some completed PhDs during the period did not yet give rise to publications with the students as first authors. If prolonged, this situation could become detrimental to the team.

- Conclusion :

— Summary

This is an excellent and focused team dealing with one of the most interesting biological questions in the sensory biology field. It is to be expected that future work in his lab will consolidate his position as a world expert in his field.

— Strengths and opportunities

A wealth of highly significant data have been generated that will likely lead to high impact publications in the near future and attract further funding. The team leader already forms a central part of IBDML contributing strong genetic approaches to analyze exciting problems in neuroscience.

— Weaknesses and threats

There are no obvious weaknesses and threats recognizable at the moment.

— Recommendations

There is no necessity to give specific recommendations on the research projects of this team.

E12: Live Imaging of cell interactions in the normal and diseased brain

Team leader: Ms Geneviève ROUGON

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	3	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	2	
N6: Number of Ph.D. students (Form 2.7 of the application file)	7	
N7: Number of staff members with a HDR or a similar grade	3	2

- Appreciation on the results

This team has a long-standing interest in the patterning of axons and blood vessels during embryogenesis and in nervous system diseases. Besides deciphering the role of class 3 Semaphorins and VEGFR2 in attractive versus repulsive axonal responses and that of alternatively spliced isoforms of NCAM, the team also set up two in vivo imaging modalities with two scales of spatial resolution, X-ray micro computed tomography (CT) and 2-photon (2P) microscopy, to visualize nerve and blood vessels in mouse models of pathologies. The team had therefore a pioneering involvement both in imaging in vivo and the imaging facility of the Institute.

The publication record of the team in this period is of outstanding quality with 16 primary publications in good to excellent journals (Neuron, PNAS, Plos Biology) as well as 11 collaborative publications. The quality of the outputs is also appreciated by the successful defence of 5 PhD theses during this period.

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

This well-funded team has very high visibility with several invitations of unit members to international conferences and symposia and three national awards in the 2006-2010 period. The team had no problem to recruit young scientists and post-docs and was highly successful in raising significant funds (ARC, FRC, INCA AFM and ANR) in the past and for the next period. The team also has a robust network of international collaborations, including participation to an international FP6 training network, and national collaborations (including within the IBDML) and developed interaction with industrial partners. Unit's members are strongly involved in teaching and formation activities, in organizing local and national meetings and in the administration of research, both at the local (including directorship of the Institute) and national levels.

- Appreciation on the scientific strategy and the project

In the coming years, the team will focus their projects on the further development of 2P and X-Ray multicolor imaging allowing to precisely analyze the dynamics of cell interactions in different models requiring live imaging technologies. The dynamics of neuronal, vascular and inflammatory responses will be, for instance, characterized in models of spinal cord injury and gliobastoma. Consequences of molecular manipulation as with VEGF or anti-VEGF antibodies will be evaluated and chronically followed by these in vivo imaging strategies. The excellent financing of the group allows to further develop these challenging projects.

- Conclusion :

— Summary

In summary, this is a very active and well-funded group presenting an outstanding series of achievements in the past four years. The likely departure of team members working on the role of semaphorin 3 in axon guidance will lead to the re-focusing of the team on the further development of 2P and X-Ray multicolor imaging for which it played a pionneering role and its applications in several highly relevant models.

— Strengths and opportunities

The project developed is highly original and benefits from the high expertise of the team and its high international visibility and attractiveness. The development of challenging in vivo imaging technologies offer opportunities for local interactions and international collaborations.

— Weaknesses and threats

The double task of Geneviève Rougon both as director of the Institute and team leader could have in some way weakened the team management. However, this did not substantially perturb fund raising and scientific production in the last period.

— Recommendations

There is no necessity to give specific recommendations on the research projects of this team which was recognised as one of the most productive groups in the IBDML and is pivotal in the imaging development in the institute.

E13: Stem cell and brain repair

Team leader: Ms Pascale DURBEC

- Staff members

	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	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 engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	3
N7: Number of staff members with a HDR or a similar grade	3	2

- Appreciation on the results

The main interest of this team is in the control of neural stem cell division, commitment and migration during development and in the adult brain with a focus on mechanisms of myelin repair. One topic concerns the role of the orientation of stem cell division in regulating the balance between self-renewal and cell differentiation. The other topic, that represents the future main goal of the team, focuses on migration and differentiation potential of adult stem/progenitor cells under pathological conditions. Work from this team has brought strong support to the view that manipulation of adult neurogenesis can stimulate stem/progenitor cell mobilization in animal models of demyelination. The group has produced 7 publications in good to excellent journals during the period under review, as well as 6 collaborative publications.

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

Members of the team report 6 invitations and oral presentations to national and international congresses. The team has a solid involvement in the training of PhD students and is also involved in teaching at the master level (7 PhD students during the past 4 years, 3 are still in the group). One foreign PhD student was part of a Research Training Network funded by the European community. The team was very successful in raising funds during the past period (national and EC financial sources). It also has a robust network of collaborations (also within the IBDML) and developed interaction with an industrial partner which has the potential to lead to applications in myelin diseases.

- Appreciation on the scientific strategy and the project

The current and future projects are mainly devoted to the characterization of cellular mechanisms and factors involved in the regulation of progenitor recruitment and differentiation into myelin forming cells. Gene expression profile of progenitors derived from sub-ventricular zone of healthy adult mice has been compared to that of EAE mice as a model of multiple sclerosis. Candidate genes are under study. The identification of factors involved in angiogenesis and recent observation that new vessels developed at the sites of demyelinated lesions lead the team to work also on cross talks between neural progenitors and blood vessels during the mobilization of stem/progenitor cells. The team is also developing imaging approaches to monitor the development of demyelinated lesions and the subsequent remyelination process. In parallel, behavioral tests are developed to score recovery in diseased mice. Finally, in collaboration with an industrial partner, compounds are tested for their ability to promote myelin repair both in vitro and in vivo. This interaction with a biopharmaceutical company allowed raising funds for the next year (ANR-Biotech). The research of this group will undoubtedly make important contributions to the general understanding of remyelination in animal models of multiple sclerosis.

- Conclusion :

— Summary

This group has strong and acknowledged expertise in the field of neurogenesis and animal models of MS and made very interesting and original observations leading to a very good scientific production. This is a dynamic group that addresses fundamental biological questions with far reaching implications.

— Strengths and opportunities

The project developed is very original and benefits from the high expertise and international visibility of the team in this field.

— Weaknesses and threats

The departure of a research scientist establishing his own group in Paris results in the closure of a previously productive line of research (control of stem cell division). Although this could be viewed as a short-term risk, it is a good opportunity for the scientific refocusing of the team on projects devoted to progenitor recruitment and differentiation into myelin forming cells.

— Recommendations

There are no specific recommendations on the research projects of this team. Additional funding will be mandatory after 2011.

E14: Cellular Interactions, Neurodegeneration and Neuroplasticity

Team leader: Ms Lydia KERKERIAN-LE GOFF

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	4	3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	6	6
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)	1.3	1.3
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
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	7	6

- Appreciation on the results

This team has a long-standing interest in the study of neurodegenerative diseases affecting the basal ganglia system with a special emphasis on Parkinson's disease (PD). Along this line, the group characterized some aspects of the anatomo-functional organization and neuroplasticity of the basal ganglia network, and the mechanisms of actions of deep brain stimulation of the subthalamic nucleus and metabotropic glutamate receptors in the alleviation of PD. This large team also developed a second axis of research on serotonin function and its involvement in adult neurogenesis in the context of mood disorders. The competence and tools in the team are steadily enhanced with the recruitment of new permanent researchers in this period (in vivo and in vitro electrophysiology). The publication record of the team in this period is very satisfactory with 25 primary publications in good to very good journals of the field as well as 14 collaborative publications. Previously unknown and unexpected interactions between DBS and L-DOPA therapy in models of Parkinson disease led to one recent publication in a very good journal in the Neuroscience field. The quality of the outputs is also appreciated by the successful defence of 10 PhD theses during this period, all of these leading to publications.

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

This team has a very good visibility in the field of basal ganglia and Parkinson disease as attested by the numerous invitations of team members to international conferences and symposia. Members of the team were awarded 4 national prizes and distinctions in the period from 2006 to 2010. The team provides an attractive scientific environment and has recruited excellent permanent young scientists and PhD students but has more difficulty to attract foreign post-doc fellows. The group was and is well funded, being a partner in several ANR projects in the past four years and one being still running. The team also has a robust network of international and national collaborations (including within the IBDML) and developed interactions with an industrial partner for a specific miniaturized stimulation device that led to a patent.

- Appreciation on the scientific strategy and the project

For the coming years, the team will develop an ambitious project and refocus all their strengths on one main axis of research: the pathophysiology, pathogenesis and treatment of BG-related movement disorders such as Parkinson's disease and L-DOPA induced dyskinesia. New questions will be addressed and for these, the team will develop new, up-to-date technologies or refine recently acquired skills (ANR funding).

The major axis will investigate the imbalance between striatonigral and striatopallidal neurons in models of PD, reorganization of synaptic connectivity between these neurons and cholinergic interneurons by dual transneuronal viral (rabies) labelling and the functional role of these interneurons in the basal ganglia network in normal and PD model as studied by optogenetics approach in vivo and on brain slices. The project should clearly bring new and highly relevant data in the field. The tracing strategy fully benefits from the high quality of the IBDML imaging platform.

- Conclusion :

— Summary

In summary, this is a very active group presenting a very good series of achievements in the past four years and a good funding for their projects. The large size of the team creates some thematic dispersion but the proposed project will contribute to some refocusing. The questions addressed by the team are original, relevant and adequately based on their previous achievements and expertise, including the risky but highly relevant development of new technologies. An important issue of the team must be to increase the publication level (impact not number). The strategy of refocusing and technological development should help to achieve this objective.

— Strengths and opportunities

The developed project is original and benefits from the recent recruitment of two dedicated young CNRS investigators. The composition and expertise of the team support international visibility and international collaboration are well established. Connections and collaborations with other groups at IBDML have increased substantially.

— Weaknesses and threats

The competition in the field is very high, meaning that technologic developments must be rapidly efficient (see recommendation).

— Recommendations

The following specific recommendations should be taken into account. Optogenetic is a demanding and challenging technology on which an important but also competitive part of the project is based. Gain from high expertise existing in several labs in Europe and overseas should help to speed up the developing process. In the transneuronal tracing labelling method, the use of defective rabies virus should be considered.

E15: Evolution and Development of Morphology and Behavior

Team leaders: Mr Nicolas GOMPEL/Mr Benjamin PRUD'HOMME

- Staff members

	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)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	3	4
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	3
N7: Number of staff members with a HDR or a similar grade	2	2

- Appreciation on the results

This rather young and ambitious evo-devo team works on several well chosen cases of lineage-specific evolution of morphological and behavioral traits, with very broad questions central to the field. These include (1) the evolution of the insect body plan, using the helmet wing-derived appendage of Membracids, (2) the evolution of male-specific pigmentation of the wing between several Drosophila species, (3) the so-called muscle of Lawrence assumed to play a role in sexual courtship.

Thus far, the scientific production has not really taken off but the novelty of the projects and results described in the report (a high impact paper is under revision) suggests that it is only a matter of time. The PIs are highly conscious of the need to publish relatively high in the near future, and there are reasons to be optimistic when one reads the details of the report.

Compared to average teams in the evo-devo field, that one has the advantage of (and technical competence needed for) exploiting genetically tractable model systems. This permits to quickly transform observations into mechanisms.

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

The team is relatively large, considering its young age, and attractive to students and young scientists. International collaborations exist for at least two of the three projects, although their importance is difficult to measure based on the report. However, it makes no doubt that both team leaders are well integrated in the evo-devo international community. Team leaders have succeeded in attracting important international funding for the evaluated period. Finding new financial resources for the next period is more than urgent and the publication of results in high impact journals is absolutely crucial to this purpose.

- Appreciation on the scientific strategy and the project

Overall, the project is highly interesting and original in the field. The third case studied in the project, on the muscle of Lawrence and its relation to the courtship, appears more speculative than the two others. It will be important to adequately adjust the time and level of effort for each case study. Perhaps new cases will have to be explored, in order to possibly generalize their findings on lineage-specific evolution. One general question was whether cases of intraspecific variation could be identified and exploited, as novelties could be far easier to analyse at the genome level.

- Conclusion :

— Summary

The three sub-projects addressed by the team are interesting, original and altogether form a coherent research activity. The results obtained in each of them are excellent and should give rise shortly to the high impact publications that the group needs to prolong its level of funding.

— Strengths and opportunities

The group is ambitious but has the intellectual and technical abilities to reach its goals and become a major player in the evo-devo field.

— Weaknesses and threats

High level of risk inherent to the level of ambition and competition in the field.

— Recommendations

Bring as quickly as possible the major findings of the group to publication.

E16: RTK signalling: from mouse development and pathologies to new molecular therapies

Team leader: Mr Flavio MAINA

- Staff members

	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)	7	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	2	
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	
N7: Number of staff members with a HDR or a similar grade	3	3

- Appreciation on the results

This team focuses on the involvement of receptor tyrosine kinase (RTK)-mediated signaling in cell survival, migration, differentiation, proliferation and axonal outgrowth during mouse development. More recently, the team has begun to investigate how deregulation of RTK-mediated signaling pathway may underlie neuro-degeneration and cancer. Their approach includes mouse genetics, pharmacology, chemistry, computer modeling, and drug discovery. Specifically, their research has been focusing on the role of the HGF/Met system in mediating signaling pathways in neuronal cells; on the identification of new chemical agents targeting Met signaling and function in cancer cells; on the search for novel signaling pathways triggered by RTKs in embryonic and cancer cells. To support this very ambitious and vast project, the PI has been able to attract substantial funding in the last years, covering the period of the review (for ex. the PI was awarded the prestigious Prix Fondation Bettencourt Schueller, a 'labelisation' from FRM, and grants from INCa, ARC, AFM, etc.). Also, two patent applications have been filed stemming from some results of potentially valuable translational impact. Nonetheless, a major drawback of such a dispersion of effort has been that it has negatively impacted on the number and quality of publications where the PI appears as the last and/or the corresponding author (5 publications, the last of which in 2008, 3 of which in good impact factor journals such as Development, JBC, and Hepatology). The PI is well aware of this issue, and several papers have been submitted or are currently under revision. The committee urges that publication of such studies should be given highest priority, also in order to secure a publication to former PhD students.

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

Of note are several invitations of unit members to international conferences and symposia and one national prize awarded to the team leader in the 2006-2010 period. The team has difficulty to recruit PhD students since no PhD theses are currently supervised by team members.

While funding was very good for the past 2006-2010 period, funding for the period 2011-2015 seems, so far, limited and a favorable outcome of applications to competitive foundations or agencies with pending decisions is crucial. There are collaborations with other teams of the IBDML and foreign partners from Italy, Spain, USA and Germany. However, the overall international visibility and attractiveness of this group has been limited, likely due to a certain lack of focus and high impact publications during the last period.

- Appreciation on the scientific strategy and the project

Given the above constraints, the team has decided to focus in the immediate future on the involvement of RTK signaling in cancer. The team will perform an unbiased in vivo forward genetic screen to identify novel genes involved in breast cancer. To this aim, conditional Sleeping Beauty transposase expression will be used to mobilize a transposon in the tissue of choice leading to mice carrying distinct genetic insertions and multiple tumours. To identify RTK-enhancers of tumorigenesis, a similar screening will be carried out in an RTK-sensitized genetic background with oncogenic Met (Rosa26-LacZ-Met) or ErbB2 (MMTV-ErbB2) transgenic mice. The committee feels that this project is highly risky. If successful, it could lead to important advances, though, if not successful, could affect the long-term viability of the group. It is at this point difficult to predict the outcome of such studies, due to lack of preliminary results. The committee feels that such an appreciation should be left at this point to the judgment of the PI.

- Conclusion:

— Summary

Altogether, this rather small group presents a very good series of achievements in the past four years but large parts still remain to be published.

— Strengths and opportunities

As for the future project, the committee appreciates that the PI is aware of the need of focus. In this respect, the choice to center his research mainly on the cancer project with a translational potential could be justified.

— Weaknesses and threats

It is unclear at the moment, mainly from the lack of preliminary results, whether the genetic screening for novel genes involved in breast cancer will lead to sufficiently significant scientific advance. As noted above, should this project not be successful, the committee would like to convey the feeling that the long-term viability of the group could be affected.

— Recommendations

The committee feels that an immediate priority of this team should be to capitalize on the last years' efforts and publish in the next two years a number of studies that are already in the pipeline. Such a strategy will provide the necessary background to apply successfully for funding and increase the visibility of the team.

E17: Immune response and development in Drosophila

Team leader: Mr Julien ROYET

- Staff members

	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)	3	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	0
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	2	2
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	3	3

- Appreciation on the results

The team has been created at IBDML in September 2005 and initially funded by "Fondation pour la Recherche Médicale" (FRM) (2005-2008 extended to 2010). It now includes 3 researchers with CNRS permanent positions and one assistant professor. This team uses Drosophila as a model to study molecular, and more recently, cellular aspects of the control of innate immune responses. The initial focus of the team was on the identification and characterisation of PGRPs. It resulted in 3 primary articles and 2 reviews including one in Nature Reviews in Microbiology. A second aspect, the (limited) role of circulating haemocytes in the immune "surveillance" led to one publication if a high-ranking journal. A third aspect, now the focus of the team concerns the gut microbial interactions (see projects). This question is becoming of prime importance in the field, as outlined by a recent primer published by the team in Nature Immunology. A side project, originating from the characterisation of bicistronic PGRP-(PMI) transcripts, led the team to study mitochondria remodelling and envisage links with immune defence (EMBO reports, in press).

The publication record of the team in this period has been extremely good with 4 primary papers + 2 in press. 5 of these were done in collaboration with other groups and J. Royet was the corresponding author. Undeniably, this young team is already well known. Two PhD students successfully defended their thesis in this period, while two other are in progress. It seems the group has some difficulty to attract excellent, foreign post-docs and would benefit from an international PhD program.

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

This well funded team (Label Equipe FRM) has very good visibility in the scientific community, in an increasingly competitive and sophisticated field of research. Several invitations of the team leader to international meetings. Several links to other labs in France. The team has had no problems to recruit excellent young permanent scientists. One talended young CNRS collaborator has obtained an "ANR Jeunes Chercheurs". Due to the team leader very active contribution to teaching, the team is in a position to attract excellent PhD students. The low success in attracting foreign post-docs is likely to be a general problem. Information on international collaborations and partners was missing.

- Appreciation on the scientific strategy and the project

For the coming years, the team is very well funded (ANR and AFM), allowing the development of an ambitious new program of studying the Drosophila commensal flora. This is particularly relevant, since it opens the possibility of extending parallels between Drosophila and human innate immunity to the selection and role of the gut flora and the mechanisms of gut tolerance. Financing of the team allows it to test further the possible mitochondrial metabolism/immunity connections, a prospect of true novel discoveries. If unsatisfactory, it will be necessary to decide in time whether resources need to be re-allocated to the main gut/microbia program. The shift towards more cellular biology fully benefits from the high quality of the IBDML imaging platform.

- Conclusion:

— Summary

This is a very active and energetic young group. Its research focuses on studying innate immune mechanisms, using the power of Drosophila genetics and genomics. As a recent development, the lab is shifting from the study of the systemic to the local (gut epithelium) immune response. This could be a risky choice, considering the level of competition in the field but several back-up projects are at hand, based on recent original and published observations of the team. Further improvement of this team is anticipated if the team leader can be discharged from some of his actual teaching duties.

— Strengths and opportunities

The project developed is original and benefits from the recent recruitment of dedicated young CNRS investigators. The composition and expertise of the team may offer opportunities for international collaboration.

— Weaknesses and threats

The competition in the field is fierce, including in Europe, lowering the prospects of strong international funding and capacity to attract the best foreign post-docs.

— Recommendations

There is no necessity to give specific recommendations on the research projects of this team which was recognised as one of the most promising in the IBDML. It is expected that its projects will be a hallmark contribution to the overall scientific profile of the institute.

E18: Polarity and binary decisions in the embryonic nervous system

Team leader: Mr Vincent BERTRAND

- Staff members

N1: Number of researchers with teaching duties (Form 2.1 of the application file)	
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	
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 engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	
N6: Number of Ph.D. students (Form 2.7 of the application file)	
N7: Number of staff members with a HDR or a similar grade	1

- Appreciation on the scientific strategy and the project.

This is a new team (2011). The results of the team leader during his postdoc are very relevant and original. The approaches are genetic analysis and localization studies during asymmetric division. This represents the state of the art techniques to study Wnt signaling during development in C. elegans. In addition, the recovery of mutants by deep sequencing was very impressive and represents a major advance in the field.

The team leader has obtained an ATIP AVENIR grant in order to join the institute. This success suggests that, in the future, he will be efficient in raising funds to support his work.

The project is relevant: analysis of the Wnt gradient and Wnt signal transduction during asymmetric division. It seems feasible. It is rather ambitious. Two main questions: how does the Wnt gradient look like? How does beta-catenin independent TCF transcriptional control happens at the molecular level? He has already some interesting insights and assays to tackle this question.

- Conclusion:

This seems like a promising group. The project is excellent and has a strong potential for the future. The analysis of the cell biology of the generation of morphogen gradient is attracting a lot of attention in recent times. Similarly, the possibility of beta-catenin independent TCF transcriptional activity will be a hit in the Wnt field. The team leader masters a number of state of the art molecular techniques which give him a differential, strategic advantage. He should check in early stages the relevance of the gradient distributions of Wnt for the asymmetric division. If this turns out to be irrelevant, the relevance of the gradient for other systems in the worm will need to be assessed.

Title: Biomolecular chemistry team

Team leader: Mr Jean-Louis KRAUS

- Staff members

	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)	1	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	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 engineers, technicians and administrative staff without a tenured position (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	0	

This team occupies a specific slot at IBDML, due to its unique expertise in drug design. This has led to many collaborations in the neurogenerative diseases and cancer fields, including one very active with another IBDML team.

The publication record of the team in this period is of excellent quality with about 20 publications in specialised primary journals, most of which are signed by JL Kraus as senior author. The quality of the output is also appreciated by the successful defence of several PhD theses during this period. The team's research is supported by both academic grants (ANR, Canceropôle) and contracts with biotech companies, one of which was co-founded by JL Kraus.

The large number of studies initiated or pursued over the past five years has been conducted through multidisciplinary collaborations with academics and biotech start-ups. One recurrent theme was the development of the multi-target drug concept, that is, drugs targeting several signaling pathways. The project continuation for the next two years focuses on the concept of dual drug for glioblastoma. The committee recommends that ongoing collaborations with IBDML teams be materialized with publications and/or patents and a solution be taken for the library of small molecules that are under development

The team leader, 66 years old, has been a very active team leader and teaching professor for many years. The committee unanimously congratulates the team leader for his successful research activity at IBDML, carried out along important teaching duties, and praises his overall academic career. The committee wishes him good luck with his new projects as biotech start-up partner.

Title: Chordate embryogenesis

Team leader: Mr Patrick LEMAIRE

- Staff members

	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	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	6	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	2	
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	1	0

Note: 2 post-docs, 1 student, one fixed term contract software developer and 1 tenured scientist (PL) will move to the CRBM in Montpellier on Jan. 2011, and are thus not counted as future staff at IBDML. The team will survive 1 year at IBDML, during which time the 3 members still at IBDML will relocate to other teams/institutes.

- Appreciation on the results

The team leader and part of his team recently moved to Montpellier (CRBM) after 16 years at IBDML.

The team applies modern genomic approaches to developmental biology. It has found a niche in the study of chordate embryogenesis. By successfully unraveling key cascades controlling early Ciona development, it has become a reference group in the field at the international level.

During the last period, the team made an intense effort to establish Ciona tools allowing systematic annotation of cis-regulatory elements and integration of expression data acquired in normal conditions or upon loss of function of Transcription Factors (ANISEED), with the aim to describe gene regulatory networks. This methodological effort appears somewhat complicated by the rapid evolution of tunicate genomes compared to those of other chordates, which multiplies the comparisons required between pairs of closely related genomes, currently being sequenced or to be sequenced. The methodological investment is important, and should in the end be very useful for the relatively small, but very active, community of ascidian biologists.

The impact of research performed in this team is very high. The team has clearly a strong position in the field. This is reflected in the publication record: in the last 5 years, a total of 18 publications, with 9 primary articles signed by the team as first/last authors, among which 4 in Current Biology, 2 Development, one PLoS Biology one Genome Research, as well as reviews in very good journals.

Along the same line, many conferences and invited lectures at international meetings; One meeting organised; 5 PhD theses supervised.

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

The team is a good mixture of permanent researchers, students and post-docs. The team leader is obviously able to attract excellent group members. Several outstanding junior scientists who are now independent researchers in France have been trained in the team. From the performance of the team, it is clear that it is well managed.

The team has an excellent rate of fund raising: ANR (2x) as coordinator, and several other national and European grants (FP6, FP7) as partner as well as a good web of European collaborations.

The team has created a number of resources that have given great visibility to the Marseille Luminy campus and IBDML. It also has a large number of collaborations where it shows leadership.

- Appreciation on the scientific strategy and the project

The project is very ambitious, system-biology oriented and uses state of the art technologies to answer fundamental evolutionary and developmental questions. The working hypotheses appear very general, with tunicates being the favored model organism. Their further elaboration should ultimately provide answers of importance for our understanding of both developmental and evolutionary mechanisms. On one hand, there is always the risk that the team, which is highly involved in the development of tools, may be confronted to very strong external competition for ambitions extending beyond the particular model organism. On the other, the publication and student training records of the team are very good, much higher than average. The considerable methodological investments of recent years now begin to pay off and should lead to high impact publications during the next period.

- Conclusion :

— Summary

The team has undertaken major efforts to raise genome analysis in tunicates to a level suitable to decipher developmental regulatory gene networks. The strategy for the coming years will benefit from further elaboration, with more specific questions based on the actual resource building. Choices may have to be made, depending on whether the main focus and force is in developmental mechanisms or evolutionary biology at the systems level.

— Strengths and opportunities

The research is ambitious and the model organism particularly adequate for fine embryological observations. The team and team leader are highly recognised. The current investments by the group and new scientific environment (CRBM) may create the momentum for moving towards evolutionary biology at the systems level, and in the long term, re-enforce the impact of Ciona in the Evo-Devo field.

— Weaknesses and threats

The chordate group to which the model organism belongs appears to be rather derived due to specialisation towards a divergent life style compared to vertebrates. The tools available for functional analysis are not as potent as in some other model organisms, vertebrates or invertebrates. Therefore, the scientific cost/benefit ratio of the strategy for one team on such a model system may be questioned, in particular for a team whose historical strength is on developmental biology.

— Recommendations

There is no necessity to give specific recommendations on the research projects of this team, which was recognised as one of the most productive groups of IBDML.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
IBDML - INSTITUT DE BIOLOGIE DU DÉVELOPPEMENT DE MARSEILLE-LUMINY	**A+**	**A+**	**A+**	**A+**	**A+**
POLARISATION ET DÉCISIONS BINAIRES DE DESTINS CELLULAIRES DANS LE SYSTÉME NERVEUX EMBRYONNAIRE DE C. ELEGANS [ROUGON-BERTRAND]	Non noté	Non noté	Non noté	Non noté	Non noté
CONTRÔLE MOLÉCULAIRE DE LA NEUROGENÈSE [ROUGON-CREMER]	A	A	Non noté	A+	A

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
CELLULES SOUCHES ET RÉPARATION DU CERVEAU [ROUGON-DURBEC]	A	A	Non noté	A+	A
MÉCANISMES MOLÉCULAIRES SOUS-JACENTS À LA DIFFÉRENCIATION DES CELLULES MÉSENCHYMATEUSES [ROUGON-FASANO]	A	A	Non noté	A	A
EVOLUTION ET DÉVELOPPEMENT DE LA MORPHOLOGIE ET DU COMPORTEMENT [ROUGON-GOMPEL-PRUDIOMME]	A+	A+	Non noté	A+	A+
CONTROL DU DÉVELOPPMENT MÉDIÉ PAR LES HOX ET LA CHROMATINE [ROUGON-GRABA]	A+	A	Non noté	A	A
DEVELOPPEMENT ET NEUROPATHOLOGIE DES CIRCUITS NEUROMUSCULAIRES [ROUGON-HELMBACHER]	B	B	Non noté	A	B
CONTRÔLE GÉNÉTIQUE DU DÉVELOPPEMENT CARDIAQUE [ROUGON-KELLY]	A+	A	Non noté	A	A
INTERACTIONS CELLULAIRES, DÉGÉNÉRESCENCE ET PLASTICITÉ NEURONALE [ROUGON-KERKERIAN]	A	A+	Non noté	A	A
SIGNALISATION AU COURS DU DÉVELOPPEMENT CHEZ LES VERTÉBRÉS [ROUGON-KODJABACHIAN]	A+	A	Non noté	A+	A+
MORPHOGENÈSE DES CELLULES ÉPITHÉLIALES [ROUGON-LE BIVIC]	A	B	Non noté	B	A
PRINCIPES D'ORGANISATION CELULLAIRES ET MÉCANIQUE TISSULAIRE [ROUGON-LECUIT]	A+	A+	Non noté	A+	A+
EMBRYOGENÈSE CHEZ LES CHORDÉS [ROUGON-LEMAIRE]	A+	A+	Non noté	A+	A+
PHYSIQUE CELLULAIRE [ROUGON-LENNE]	A+	A+	Non noté	A+	A+
SIGNALISATION RTK: DU DÉVELOPPEMENT ET DES PATHOLOGIES DE LA SOURIS AUX NOUVELLES THÉRAPIES CELLULAIRES [ROUGON-MAINA]	A	A	Non noté	B	A
PLASTICITÉ DES CELLULES SOUCHES NEURONALES CHEZ LA DROSOPHILE [ROUGON-MAURANGE]	Non noté	A+	Non noté	A+	A+
SPÉCIFICATION DE L'HÉTÉROGÉNÉITÉ DU SYSTÉME NERVEUX SENSORIEL SOMATIQUE [ROUGON-MOQRICH]	A	A+	Non noté	A+	A+
IMAGERIE IN VIVO DES INTERACTIONS CELLULAIRES DANS LE CERVEAU NORMAL ET PATHOLOGIQUE . [ROUGON-ROUGON]	A+	A+	Non noté	A+	A+
RÉPONSE IMMUNITAIRE ET DÉVELOPPEMENT CHEZ LA DROSOPHILE [ROUGON-ROYET]	A+	A+	Non noté	A+	A+

C1 Qualité scientifique et production

C2 Rayonnement et attractivité, intégration dans l'environnement

C3 Gouvernance et vie du laboratoire

C4 Stratégie et projet scientifique

Statistiques de notes globales par domaines scientifiques

(État au 06/05/2011)

Sciences du Vivant et Environnement

Note globale	SVE1_LS1_LS2	SVE1_LS3	SVE1_LS4	SVE1_LS5	SVE1_LS6	SVE1_LS7	SVE2 _LS3 *	SVE2_LS8 *	SVE2_LS9 *	Total
A+	7	3	1	4	7	6		2		30
A	27	1	13	20	21	26	2	12	23	145
B	6	1	6	2	8	23	3	3	6	58
C	1					4				5
Non noté	1									1
Total	**42**	**5**	**20**	**26**	**36**	**59**	**5**	**17**	**29**	**239**
A+	16,7%	60,0%	5,0%	15,4%	19,4%	10,2%		11,8%		12,6%
A	64,3%	20,0%	65,0%	76,9%	58,3%	44,1%	40,0%	70,6%	79,3%	60,7%
B	14,3%	20,0%	30,0%	7,7%	22,2%	39,0%	60,0%	17,6%	20,7%	24,3%
C	2,4%					6,8%				2,1%
Non noté	2,4%									0,4%
Total	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

*** les résultats SVE2 ne sont pas définitifs au 06/05/2011.**

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

• SVE1 Biologie, santé
- **SVE1_LS1 Biologie moléculaire, Biologie structurale, Biochimie**
- **SVE1_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes**
- **SVE1_LS3 Biologie cellulaire, Biologie du développement animal**
- **SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie**
- **SVE1_LS5 Neurosciences**
- **SVE1_LS6 Immunologie, Infectiologie**
- **SVE1_LS7 Recherche clinique, Santé publique**

• SVE2 Ecologie, environnement
- **SVE2_LS8 Evolution, Ecologie, Biologie de l'environnement**
- **SVE2_LS9 Sciences et technologies du vivant, Biotechnologie**
- **SVE2_LS3 Biologie cellulaire, Biologie du développement végétal**

UNIVERSITÉ DE LA MÉDITERRANÉE
AIX-MARSEILLE II

Objet : Réponse au rapport d'évaluation - **S2UR120001638 - IBDML - Institut de Biologie du Développement de Marseille-Luminy - 0131843H** - de l'unité IBDML - Institut de Biologie du Développement de Marseille-Luminy

Observations d'Aix-Marseille Université

- **General comments:**

1) Attention will be given to the evolution of two teams. We propose specifically that performance and projects of these teams be reviewed at a 2-year mid-term of the quadrennial by the IBDML external scientific advisory board. We would like to stress that the heavy administrative tasks that the head of one of them (André Le Bivic Morphogenesis of epithelial cells), carries out at the national level for the benefit of the entire scientific community, are a large distraction from pursuing competitive and innovative research.

2) We do agree with the AERES committee that the lack of publication of some post-docs and PhD students in some of the teams at the end of their stay is a serious concern (see also below a specific response of the Graba's group on this matter). Monitoring of the students'projects and their evolution in more frequent meetings between the tutors and the internal « suivi de thèse » committees should improve the situation.

3) Some concern was raised about our procedures to recruit new teams. « *The lack of sufficiently clear procedures for the recruitment of new groups* ». We feel that our procedures could be modified but are clearly defined in our « internal functioning charter ». Briefly, we launch international open calls to which internal and external candidates can answer. A short list is established by the "group leader committee" on the basis of excellence of the project, its feasibility at IBDML and the ability of the applicant to raise his/her own funding (ATIP/AVENIR, ERC etc...) whereas an advice is requested from our external scientific advisory board. It is clear that the mobility clause associated to these starting grants does not favor internal candidates. Our procedure however helps to maintain turn over of the teams, a feature appreciated by the committee, and should also encourage « *our young investigators to start their own team outside Marseille* » (as recommended by the committee). « *The absence of foreigners and women among the newly recruited teams* » this situation could only be corrected by introducing « quotas »in our procedure, something we do not presently favor. By contrast, we do agree that the future calls can include specific scientific topics in view to « *adjust the new or emerging groups to the IBDML research topics and strategy* ».

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4) "*Another difficult problem is ACMO and the low number of First aid workers. Considering the size of the unit (numbers of members and square meters), this question deserves strong attention and appropriate solutions from the Délégation Régionale du CNRS, University and the IBDML director* ». We want to clarify the fact that the CNRS and University agencies as well as ourselves pay great attention to health and security issues and that the last visit by an external "ad hoc" committee did not pointed out major problems. We do have now the requested number of first aid workers and three ACMOs covering all the risk specificities and continued presence as well as a specific financial line allocated to safety. We believe that this recommendation had been issued following an individual request from one of our agent willing to be assigned with a full time ACMO position. His request was considered inappropriate by ourselves and the CNRS as a single person cannot cover all the requested competences.

Team 2: Hox and chromatin-mediated control of development :

Team leader: **M. Yacine GRABA**

(a)- The AERES report states that « *The publication record of the team in this period has been very satisfactory with **5** primary papers* ». The number of primary papers of the team at the time of the visit of the AERES committee was **7** as mentioned in an updated list of publications provided to the AERES committee. This list included 2 articles accepted for publication in "PNAS" and "BMC Biology" in December 2010 (see. **Ref 1**- Bruno Hudry, Séverine Viala, Yacine Graba and Samir Merabet (2011). Visualisation of protein interactions in living Drosophila embryos by the bimolecular fluorescence complementation assay. ***BMC Biology***. Jan 28;9:5.

Ref 2- Mehdi Saadaoui, Samir Merabet, Isma Litim-Mecheri, Elise Arbeille, Nagraj Sambrani, Wim Damen, Carlo Brena, Jacques Pradel and Yacine Graba (2011) . Selection of distinct Hox-PBC interaction modes fine-tunes Hox protein activity. ***Proc Natl Acad Sci U S A***. Feb 8;108(6):2276-81).

(b) The AERES report states that « *All of these were done in collaboration with other groups and the team members were the main executors of the work* ». This is not accurate. Two of the seven primary publications do not include any collaboration, 5 other primary papers indeed involve collaborations but for 4 of them, teams members represent a large majority of contributors and the first and last authors are from the team. This shows that these publications are truly on projects that constitute the core of the team activity.

© The AERES report states that « *...Of some concern, however, two of these PhD students have left the lab without first-authored publications.* » At the time of the AERES visit, **one**, and not 2 of the 3 PhD students did not have a first author paper.

In this context, the team wishes to shortly comment on how the inaccuracy mentioned may have impacted on:

1- Recommendation of the committee regarding our choice to refocus on Hox related projects. We understand that without integrating the two ignored papers, the strengths of the team could appear biased toward chromatin projects. Consequently the choice to operate an important refocusing on Hox projects may have appeared loosely justified to the committee.
2- Appreciation on PhD student management. While a situation where two of the three PhD students that defended their PhD during the period of evaluation may justify the concern of the committee regarding PhD student management, the PNAS article (ref2) changes this situation to only one student . The third PhD student that defended his PhD most recently will soon have a first-authored manuscript submitted for publication. The team has a good history of PhD student training, with many of the previous PhD students of the team having gained academic positions, either at the CNRS or at the University.
3- General assessment of the quality of the team: Adding two primary papers with good impact factors (PNAS and BMC Biology) to the scientific production of the team, as well as correcting the aspects mentioned in point 1 and 2, may have allowed an even more positive assessment of the team.

Team 10 : Development and pathologies of neuromuscular circuits:

Team leader: **Françoise HELMBACHER** (E10)

In « appreciation of the results » the following sentence is not accurate *"The team leader has found, during her postdoc, a regulatory mechanism controling neuronal cell fate involving a crosstalk between GDNF/Ret and ephrinA/EphA4 signaling pathways. This work was published in Neuron in 2006 in which the PI is a co-corresponding author"as it contracts several facts.* Indeed, the team leader has found, during its postdoc, 1- a regulatory mechanism controling neuronal cell fate (involving the feed forward propagation of PEA3, gated by GDNF and HGF), and 2- a crosstalk between GDNF/Ret and ephrinA/EphA4 signaling pathways for motor axon guidance. This work was published mainly through two papers, one in Neuron in 2003 as first author, and which settled the bases of her team's projects, and the second in Neuron in 2006 as co-senior author.

En accord avec les deux autres établissements d'Aix-Marseille

Le Président
de l'Université de la Méditerranée

Yvon BERLAND

Le Vice-président du Conseil Scientifique
de l'Université de la Méditerranée

Pierre CHIAPPETTA