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

Section des Unités de recherche

AERES report on the research unit

Center for Developmental Biology

From the

University Toulouse 3

CNRS

Mai 2010

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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

Mai 2010

Research Unit

Name of the research unit : Center for Developmental Biology

Requested label : UMR CNRS

N° in the case of renewal : UMR 5547

Name of the director : M. Marc HAENLIN

Members of the review committee

Chairperson

M. Patrick CHARNAY, INSERM, Paris

Other committee members

M. James CASTELLI-GAIR HOMBRIA, University Pablo de Olivade, Spain

M. Antoine GUICHET, University Paris Diderot, France

Mrs Corinne HOUART, King's College London, UK

M. Vassilis PACHNIS, National Institute for Medical Research, UK

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Committee members nomminated by staff evaluation committees

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AERES scientific advisor

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University or School representatives

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Research Organization representatives

M. André LE BIVIC, INSB-CNRS

Mrs Carine DESAULTY, Deputy-Head of Midi-Pyrénées regional, CNRS administration

Report

1 • Introduction

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

The visit occurred on December 1 and 2, 2009. The overall organization of the visit was satisfactory. The written information provided was adequate, but the groups should have been numbered in the same way in all documents, including the program of the oral presentations. The presentation of the Director, of all group leaders and the discussion with the technical staff occurred in front of the entire committee, whereas, for the presentations of the imaging and animal platforms, and the discussions with the PhD/postdocs and with staff scientists, the committee split into two groups. A large number of members of the lab attended the presentation of the Director. In contrast, the laboratory had decided that the team members would not attend the presentation of their leader. Therefore, those were either alone or assisted by one member of their group. Some members of the committee considered this decision surprising and inappropriate. A discussion was engaged within the committee on that matter, but no consensus emerged. Nevertheless the committee suggests that in the future the AERES should decide on a rule for the presence or absence of group members during the presentation of each group leader. In addition, a hand out with explanation of abbreviations used in France (e.g. ITA, CR1, DR2) would be very helpful for committee members from abroad.

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

The laboratory was created in 1992, as a mixed Unit between the University Paul Sabatier-Toulouse 3 and the CNRS, with the objective of promoting the research on genetics and molecular biology of embryonic development, using both vertebrate and invertebrate models. It is called « Centre de Biologie du Développement » (CBD) since 1999. Since then it was headed by Alain Vincent (1999-2006) and then by the current Director, Marc Haenlin. The CBD is located on the campus of the University, in a building that hosts three other CNRS-University labs. Two other CNRS-University biology labs are located in a nearby building. The CBD is part of the Institut Fédératif de Recherche « Institut d'Exploration Fonctionnelle des Génomes ». The CBD presently hosts 12 teams, representing 105 people. One team will leave at the end of 2010 and two other ones are candidates for joining the CBD. The center concentrates a large part of its efforts on a few major themes (morphogenesis, neurogenesis, haematopoiesis, gene network regulation), some of them constituting essential domains of developmental biology. An originality of the CBD is to perform these studies using a variety of animal models : Drosophila, zebrafish, Xenopus, chicken and mouse.

- **Management team :**

The laboratory is managed by the Director, assisted by an administrative director (to be recruited). The Director also consults the group leaders and all important decisions (general laboratory policy, priorities for staff recruitment, laboratory budget, purchase of large equipments and recruitments of new teams…) are taken during monthly meetings, by vote at the majority of the group leaders. Then required decisions are subjected to approval by the "Comité de laboratoire".

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

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	13	13
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	26	33
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	18	19
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	24	27
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	3	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	20	12
N7: Number of staff members with a HDR or a similar grade	24	24

2 • Overall appreciation on the research unit

- **Overall opinion :**

The CBD regroups a number of teams working on various animal models (Drosophila, zebrafish, Xenopus, chicken, mouse). Although there is no strict federating theme, apart from the general involvement in developmental biology, and therefore a wide variety of projects, the structure has been very efficient in generating innovative collaborations between groups and creating a strong cohesion between them, in particular through the establishment of common services and platforms. The overall quality of the research is high, with a few outstanding groups, but also some heterogeneity. The laboratory plays a major local role, since it regroups most of the forces in the field of developmental biology in the Toulouse area and since it has strongly invested in teaching and training of PhD students. The committee therefore formulates a very positive opinion on the activities of the CBD. The creation of a centre of integrative biology that will build on the acquired experience and achievements of the CBD constitutes an excellent initiative and a rare opportunity to further increase dynamism of the structure, expand its coverage without loosing its originality and increase its visibility. However appropriate procedures have to be set up to make sure that scientific excellence will be the major determinant in modelling the future institute.

- **Strenghts and opportunities :**

The committee was unanimous to point out to:

- a coherent and efficient assembly of groups working on a large variety of animal models, which is unusual and original for a laboratory of this size.
- a high overall quality of the research with a few outstanding groups.
- the presence of a large proportion of young group leaders.
- an excellent internal interactions and cohesion, strong involvement of the personnel.
- the quality of the imaging platform.

- the solidity of the training of the PhD students and involvement of the CBD in teaching.

- the future establishment of a Federation of laboratories that will strengthen the relationship of the CBD with its campus and increase its visibility.

- the prospect for the construction of a new building in which the CBD will be the core component.

• Weaknesses and threats :

The committee was concerned with:

- the lack of clear procedures for the recruitment of new groups and the elaboration of a strategic plan.
- some heterogeneity in the quality of the research groups.
- weaknesses in the research performed with the mouse model and uncertainties on the mouse facility.
- a limited access to laser scanning microscopy because the core facility operates at full capacity.
- the lack of technical staff in some core facilities (in particular informatics and animal houses).
- an unacceptable deficiency in ordering and accounting from the University.
- the poor maintenance of the present building by the University.

• Recommendations to the head of the research unit :

The committee strongly recommend to set up rapidly a scientific advisory committee (SAC) attached to the Federation in order to advise on the future shaping of the building and to select the groups that will move in, as well as the groups joining the CBD before the opening of the new building.

In the meantime, this committee recommends the integration of one of the two postulating groups (Merdes) into the CBD, but strongly suggests finding another solution for the second one (Bélenguer). More generally, the CBD should have a strict recruitment strategy based on quality and adjustment of the new groups to the centre's research topic and strategy. The CBD should avoid the recruitment of groups with peripheral interests based solely on resolving local problems.

All the issues associated with the creation of the new building should be foreseen a long time in advance and the director should take an active role in this strategic process.

The mouse model has a strategic importance and needs to be stabilized and reinforced at the CBD even before the construction of the new building. This involves a continued effort in favour of the mouse facility and its extension, a better selection of the mouse projects and possibly the attraction of a new dynamic group working on mouse genetics. Serious thinking is required on this matter.

- **Data on the work produced :**

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

A1: Number of permanent researchers with or without teaching duties (recorded in N1 and N2) who are active in research	37 (46)
A2: Number of other researchers (recorded in N3, N4 and N5) who are active in research	16 (1)
A3: Ratio of members who are active in research among permanent researchers [(A1)/(N1 + N2)]	0.95 (1)
A4: Number of HDR granted during the past 4 years	3
A5: Number of PhD granted during the past 4 years	11

3 • Specific comments on the research unit

- **Appreciation on the results :**

Globally the research performed by the laboratory was considered to be of a high standard, with many nice publications (in the order of 30 in very good journals). Two groups have reached an outstanding level, with a prominent international visibility. Another excellent group is postulating for integration in the CBD. Nevertheless a significant heterogeneity in quality is still present, with some groups showing a productivity that could be increased and two of them raising serious interrogations. In addition, whereas the work on Drosophila maintains itself at an excellent level and the zebrafish model expands and increases its impact, the research using the mouse model is still in a rather fragile state, which might even worsen due to the evolution of some of the groups and the situation of the animal house.

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

The regrouping of teams working on various organisms works very well: it does not affect the coherence of the laboratory, offers the possibility for numerous fruitful collaborations and even leads to the development of new programs. Clearly this confrontation of various species and experimental approaches is an essential element of the originality, dynamism and visibility of the laboratory.

The proposed joining of a cell biology group constitutes an excellent move, since this team will bring in its expertise in this field and benefit from the strong potential of the CBD in developmental biology and genetics, and has several obvious interfaces with existing groups. This speaks in favour of the attractiveness of the laboratory, as well as the arrival of two external young groups with ATIP during the last 4 years period. However, further efforts clearly need to be done on this matter, since the CBD counts only few postdocs and few PhD students originating from masters outside Toulouse.

Whereas internal collaboration is very efficient and some groups have fruitful collaborations at national or international levels, it was found that the laboratory is slightly too centred on itself and not enough integrated with its immediate neighbours. In this respect the establishment of the Federation of laboratories is an excellent initiative. In relation with this observation, the work performed at the CBD, despite its multispecies character, is rarely trans-disciplinary. This point is of some concern considering the planned evolution of the lab towards an integrative biology institute with much input from systems biology.

The heterogeneity in the quality of the groups indicated above is accompanied by an heterogeneity in the capacity of the groups to raise external grants. This issue is presently buffered by the mode of redistribution of the laboratory funding but should definitively be addressed.

The technological platforms and services seem to do their best with what they have, i.e. often not very much. More specifically, the technical personnel resource devoted to the services is a very serious concern. The committee has identified four major problems: i) ordering and payment: the problem is not located within the laboratory, but rather in the financial services of the University that cannot cope with the demand. This results in unacceptable delays (months!) in the transfer of the orders and of the payments, resulting in serious perturbation of the research and additional costs for the laboratory; ii) informatics: the entire network and software are maintained by a part-time technician and part of the mainframe computers are obsolete. This is creating a very dangerous situation for the back up conservation of rapidly expanding and precious data; iii) no central service is available for the maintenance and handling of fly lines, work which is in many cases requested to be done by the groups and sometimes the scientists (a similar problem affects the zebrafish facility); iv) Despite the likely attribution of a technical position by the CNRS, the mouse facility is still in trouble: limited capacity due in part to the hosting of mice from external labs, absence of transgenesis or embryo transfer facility, uncertainty about the future since the scientist in charge, who established the animal house and devoted a lot of efforts to it, will leave the CBD in one year.

The imaging facility belongs to the "Toulouse RIO imaging" (TRI). The TRI is an open platform with high standard equipments supervised by extremely qualified people. It is dispatched among five distinct locations distributed around Toulouse. The teams of the CBD use mostly the confocal microscopes and the platform has reached saturation for those microscopes. In consequence it is very important that the TRI rapidly acquires a new confocal microscope located in close vicinity to the CBD. An additional issue that has to be solved rapidly concerns the storage of data. More generally, the platforms and services are rather saturated, and the arrival of additional groups, together with the accessibility of the platforms to external groups, without priority for the internal ones, will create additional tension.

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

No obvious problem was detected in the day-to-day governance of the laboratory. However, the committee deeply regrets that the laboratory has not followed the advice of a previous site visit and set up a scientific advisory committee (SAC) for counselling on strategic matters, in particular recruitments of new group leaders. This constitutes a major problem for an Institute of this size and ambition and should be rapidly corrected (see next §). The laboratory has adopted a policy including the free usage of all services as well as an allowance of the financial resources that establishes a strong solidarity between the groups, with a major advantage of facilitating the start or emergence of junior groups and protecting other ones that encounter a transient decrease in their external support. However two drawbacks have to be taken into account with this system: the Drosophila groups, whose research is less costly, probably tend to subsidise the vertebrate groups, and weak groups might be artificially maintained in activity beyond a reasonable period. In any case, not knowing whether this system is the cause or the consequence, it was noted that the atmosphere of the laboratory was excellent, with essentially no complains from Technical staff, PhD students/postdocs or staff scientists, who were satisfied with the organisation of the laboratory, their relationship with the group leaders and the direction, their opportunities to follow trainings and attend conferences. In particular PhD students and postdocs also considered that they would get good professional opportunities following their passage in the laboratory. Internal and external communication was judged appropriate, but frequency of external seminars should be increased. Emergence of projects and taking of risks is essentially directly supported by the groups. The involvement of the laboratory in teaching activities is excellent. It implicates not only the teaching-researchers, but also the pure researchers, some of them being largely involved in teaching or organisation of higher education.

- **Appreciation on the project :**

The strategic project can be judged on different time-scales. On the short-term, it is essentially team-driven and can be appreciated at this level. On the medium-term, it concerns the recruitment of new teams and the establishment of a life science research federation (FRBT), which will regroup six laboratories of this campus, including the CBD. Finally, on the long-term (4-6 years), there is a project of establishment of a new building centred on integrative biology, the core of which would be provided by the CBD.

The establishment of the Federation seems to be an excellent initiative, in particular for the CBD. It aims at a better structuration of the campus, the development of the technological platforms, the increase in scientific exchanges between the different laboratories, the development of their global visibility, and the promotion of interdisciplinary research, all things that the CBD needs and will benefit from. However, it is also important that the CBD, like the other laboratories, does not become diluted within this large Federation since this would be at the expense of its originality and therefore of its own visibility.

The Federation will also be the pilot of the establishment of the integrative biology building. This development constitutes a major strategic event and a decisive opportunity for the CBD. It should be used to create novel dynamics, to expand the laboratory and to bring it to a further level of excellence, eventually to reshape its orientation and attract additional groups of the highest standard, and not simply to relocate the groups of the present building with better working conditions or to solve location problems of other groups in the campus. Presently the outlines of this new building, of its contents and scientific orientation appear rather fuzzy. Although 4-6 years may seem a long period, it is very important to start seriously thinking about these issues as soon as possible. Indeed they underlie the conception of the building (e.g. type of platforms and animal houses that should be hosted) and the orientation of the teams that should be recruited, and these latter processes will extend over several years. Equally important is the procedure established to manage these issues. Considering the importance of the project and the fact that it will be necessary to arbitrate between possibly conflicting local interests, it appears essential to establish an external and international scientific advisory committee (SAC) to the Federation, with a composition that will reflect the fact that its first major mission will concern the new building. After consultation of various representatives from the CBD, the Federation, Paul Sabatier University and CNRS, the SAC should first come up with a precise proposition for the objectives and contents of the future building intended for the governing bodies. Once the project has been approved, the SAC should participate in its implementation by selecting the local teams and external new groups that will move into the building. For the coherence of the project, the SAC should provide advice for the selection of new groups that may join the CBD before the new construction. It is unlikely that a SAC will be set in time to advice about the convenience of accepting the two groups presently applying to join the CBD, and this committee has therefore made a recommendation on that matter.

The SAC will only take care of strategic orientations, but the development of the future building will generate a number of other issues (some of them very important, like the fate of local groups that may not move to the new building) that should be anticipated a long time in advance. The director should be strongly involved in this anticipation, together with the Federation, the SAC and the governing bodies.

4 • Appreciation team by team and/or project by project

Team E01 : "Role of ionic messengers during early embryogenesis"

Team leader : Marc MOREAU

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

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

- **Appreciation on the results :**

The group works on the role of Ca2+ during amphibian development. Their data leads to the proposal that Ca2+ plays an instructive role in the choice of ectodermal cell fate towards neural determination. Ca2+ increase would result from the activation of DHP-Ca2+ channels and involve the recruitment of the calcineurine phosphatase. The group embarked on a screen for early Ca2+-sensitive target genes expressed in the neural territories. One of these genes, an arginine methyltransferase, controls the expression of the early proneural gene, Zic3. The team initiated the analysis of the involvement of the transcriptional repressor DREAM in the regulation of Ca2+-sensitive target genes in the neural territories. A second topic addressed the question of how Ca2+ signalling might play a role in the development of the pronephros. Their data, based on intracellular Ca2+ dynamic recording in ex-vivo systems as well as in Xenopus intact embryos, suggest that Ca2+ is a necessary signal in the process of pronephric tubule formation. In a collaborative work, it was shown that in Danio rerio, Ca2+ plays a significant role in the positioning and morphology of the pronephric anlagen, but does not affect the fate determination of mesoderm cells.

Besides these core projects, the group conducted collaborative works related to the implication of Ca2+ in Th2 lymphocyte differentiation in mouse and human, and in long term memory acquisition in honeybee. In addition, the group leader developed new imaging techniques to analyze Ca2+ channel activity by optical patch clamp technique, aiming to image single Ca2+ channel activity.

The group has revealed a potential interesting and original role of Ca2+ in neural induction. Preliminary results are also promising concerning Ca2+ involvement in nephrogenesis. To convince the scientific community of the specific developmental role played by Ca2+, an ion involved in a pleiotropic way in the basic process of cell life, the group would have gained advantage in sharply focussing their work on one topic and functional analysis. They should have more relied on their past heavy investment in constructing and screening a subtractive cDNA library, by further analyzing the results of this screen, rather than pursuing the role of potential new candidate actors found in the literature.

Although interesting, the results accumulated on lymphocytes and long term memory in honeybee probably contributed to the dispersion of the work and led to a less visibility of the team concerning the biological questions of the Ca2+ roles during early development. The use of a complementary model, the zebrafish, was initiated, and it is still in progress. Since 2005, the team has produced 18 publications in peer-reviewed journals, including 2 reviews published in international journals and 4 reviews in the French M/S journal. 4 among the 12 original papers are signed by a team member as first or last author. Most of the publications are in good, but not excellent journals. With two PhD students during the period, the training of the team seems modest.

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

The team actively participated to the constitution of one national network, entitled « Calcium GDR 2688 », and elaborated an international partnership with one group in the University of Science and Technology in Hong Kong, resulting in the LIA (Laboratoire International Associé called ROCADE). The team leader has a recognised expertise in Ca2+ and organized several national or European conferences. However, despite this activity, the team did not acquire an international leadership related to the basic biological question of Ca2+ involvement in neural cell fate. Significantly, members of the team are invited in national meetings and were invited to 3 international meetings, most of the publications are collaborative works, the team did not attract new permanent research members, and trained only two PhD students. The attractiveness of the team mainly resides in its very strong technical competence in Ca2+ methodology.

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

The team is well balanced in terms of permanent members, with three full-time CNRS researchers and one Assistant-Engineer. The flow of students and post-doctoral researchers (respectively two during the period) is low. It is proposed that the team will be managed by two group leaders during the following period, what could be beneficial. The funding of the team amounted to 305K€ for the 2005-2009 period, apart from a participation to an ANR project.

- **Appreciation on the project :**

The planned research project addresses the role of Ca2+ on cell determination and differentiation during Xenopus early development. The collaborations with other laboratories concerning the differentiation of Th2 lymphocytes in mice and the role of Ca2+ in learning and long term memory in honeybee will be pursued. The project is in the exact continuation of the past work and hence presents the same weaknesses. Too many topics will be developed, precluding a solid, in depth analysis of the mechanisms underlying Ca2+ mechanisms in neural induction. The developmental part of the project is based on the Xenopus model system and should be completed by the zebrafish one. Concerning neurogenesis and nephrogenesis, many candidates will be tested at muliple levels. Each direction is characterized by a short-term perspective. An overall clear direction is therefore missing and the proposed multidirectional strategy does not ensure the feasibility of the project.

- **Conclusion :**

The group has revealed a potentially interesting and original role of Ca2+ in neural induction. It has accumulated preliminary data showing that Ca2+ could be a necessary signal in the process of pronephric tubule formation. A strong in depth analysis has now to be conducted in order to convince the scientific community about this development-specific functions of a pleiotropic ion otherwise implicated in many basic life processes. The team could make an impact in this area if it were to focus its resources carefully on the biological questions related to early development. The past work and the proposed project however divert the efforts instead of focussing on this domain. This compromises a successful output of the research projects.

Team E02: "Control of neuronal identity in the zebrafish"

Team leader: Patrick BLADER

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

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	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	1	1

- **Appreciation on the results :**

The team aims to understand the mechanisms underlying the spatio-temporal control of neurogenesis in the vertebrate developing brain. They chose zebrafish as a model organism. The team leader began to explore these mechanisms, by studying the regulation of the bHLH proneural gene neurogenin (ngn1). In the last 4 years, the team has begun to address specificity of bHLH proteins in neuronal specification. They established new transgenic lines allowing inducible mis-expression of ngn1 and achaete-scute 1 (ascl1) and showed that induction of ngn1, but not ascl1, is able to rescue the loss of Mauthner neurons observed in the ngn1 mutants. They embarked on a screen for targets specific of Ngn1 and Ascl1. Part of their results indicates that specificity may be related to number of E-box sequences present in the regulatory regions of target genes. The team also expanded their research to neurogenesis in the dorsal diencephalon. On one hand, they showed that the left habenula starts neurogenesis earlier than the right one, due to early neurogenic signal provided by Nodal. On the other hand, they analysed in details the formation of neurons and photoreceptors in the pineal gland during development and found a key role for Notch in regulating progenitor identity.

The team has produced eight publications in peer-reviewed journals during the period under review, including 5 collaborative publications. Most of these publications are in journals of good to very good impact factor. Two more publications are in submission.

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

Team members received numerous invitations and oral presentations to national and international conferences. The team collaborates very efficiently and actively with 7 labs, 2 in France, 1 in Germany, 2 in the USA and 2 in the UK. Three small grants are reported.

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

The group is well structured, fitting well the remit of CBD. The team leader is interacting efficiently with the international community and developed collaboration with leading teams around the world. The projects developed during the review period have led to novel research directions that are original and likely to be very successful. The team is aware of its limited budget and is currently putting a lot of effort in applying for funding. The quality of the research done is very good and the team leader has accurately identified their many strengths and few weaknesses and importantly has drawn strategies to eliminate the latter.

- **Appreciation on the project :**

The project for the next 4 years is the logical continuation of the studies the team embarked on in the last four years. The aims are well defined, original and achievable. These comprise the functional studies of ngn1 and acsl1 specific targets, the dissection of the mechanism by which Nodal regulates neurogenesis in the habenula, and the understanding of the mechanism of choice between photoreceptors and projector neurons in the pineal gland. The field of research investigated is rather vast but the team has established strong collaborations that ensure the realisation of their goals.

- **Conclusion :**

The team is addressing questions of basic neurobiology that have great impact in general neuroscience as well as in neurological diseases. The quality of the team's work is very good and would be excellent if better funded. The team should therefore be further supported.

Team E03: "Control of the cell cycle and neurogenesis"

Team leader: Fabienne PITUELLO

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

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	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 other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	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 understanding the process of spinal neurogenesis, and in particular the role of the paired-box containing transcription factor Pax6. Using as a paradigm the developing spinal cord of vertebrate embryo, the group has identified and partially characterized a crosstalk between Pax6 and Ngn2. The identification of the players involved in this crosstalk is important and will shed light into the complex regulation of neuronal specification and differentiation. It is important for the team to unravel the positive regulation in addition to the negative feedback loop. In addition, the group has more recently focused on investigating the integration of the control of the cell cycle in the program of neurogenesis, with a strong investment in the role of the phosphatase CDC25B/A. However, the rational for creating a conditional CDC25B mouse model is not clear since the constitutive knockout does not present a phenotype. This is a solid team that generates data of quality. The publication record is satisfactory, with the production of 3 articles in peer-review journals, as well as a collaborative publication. In addition, another publication is currently under preparation. The team has regularly presented their work both as oral and poster presentations at international conferences. Two students have successfully defended their PhD in the reported period.

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

The impact of the team is reflected by regular invitations to give seminars, both nationally and internationally. The team has had regular external financial support over the past 4 year contract period, and has a running grant from the AFM until 2011. Although neither permanent researcher have required teaching duties, the team is involved in teaching in the Master 2 and each year is involved in training in lab Master 2 and Master 1 students. Two recent M2 students have obtained competitive grant either from the ministry or from the region to continue their work as PhD students. The team has numerous established national and international collaborations with a multidisciplinary approach.

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

This small group has an equilibrated structure and fits well the remit of CBD. External resources are too limited and efforts should be taken to increase them.

- **Appreciation on the project :**

Overall, the proposed research project will provide further insight into the mechanism of neurogenesis and the gene network involved. Elucidating the gene network downstream of Pax6 and Ngn2 is a solid project, which will in the long term provide information for understanding the decision of neuronal progenitors to differentiate into neurons. The team proposes to develop a project on understanding the mode of action of the phosphatase CDC25B. While the data in the chicken embryo appears solid, the existence of a third phosphatase, CDC25C in the mouse questions the rational for further developing this project in the mouse. The third project is probably the most high-risk project as it depends on developing live-imaging technology to follow single cell. However, the team benefits from a collaboration with the Toulouse Imaging platform which should allow the development of the necessary imaging tools and analyses.

- **Conclusion :**

In conclusion, this relatively small group has the potential and expertise to elucidate the molecular mechanisms underlying a committed neuronal precursor to differentiate as a neuron. The committee recommends concentrating the efforts of the group on the Pax6/Ngn2 crosstalk, by fully characterizing the transcriptome analysis rather than heavily relying on a candidate approach. The development of a strong collaboration internally with the group working on Ngn2 in the zebrafish should provide complementary data. As stated above, the committee has some reservation on the utilization of the mouse models for further understanding the role of CDC25B/A, and recommends to the group to focus their work on the existing models to determine the role and importance of this pathway.

Team E04: "Morphogens and Glial specification"

Team leaders: Cathy SOULA and Philippe COCHARD

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

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

- **Appreciation on the results :**

The work of the group focuses on the understanding of the regulatory mechanisms that underlie gliogenesis and control the transition of neural stem cells from neuron to glia producing progenitors. Thus far, the group has characterised the spatial and temporal origin of glial progenitors in the embryonic spinal cord and demonstrated that both the Shh and BMP signalling pathways have critical roles in the specification and differentiation of glial precursor cells. Moreover, the group has begun to characterise some of the transcription factors that control gliogenesis and define the molecular profile of gliogenic precursors. This work has led to the identification of Sulf1, which encodes a member of the extracellular 6-0-Sulfatases and occupies a central position of the group's activities and future plans. The group is addressing a fundamental question of utmost biological significance and far reaching biomedical implications. The work so far has established the foundations for further interesting developments.

The group has produced four publications in peer-reviewed journals during the period under review, as well as a collaborative publication. Although this is not an impressive publication record, aspects of several ongoing projects are likely to be completed and submitted in the near future.

- **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 numerous invitations and oral presentations to national and international congresses. In addition, several poster presentations are reported. The group has succeeded in recruiting young promising scientists who had moved abroad for postdoctoral work. Active collaborations have been developed with two European and two USA laboratories. Four small grants are reported and one larger grant from ANR Neuroscience.

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

The group is a well organised team that fits well the remit of CBD. The projects developed during the review period have led to novel cutting edge research that is going to be followed. The senior investigators have a rather heavy load of teaching consistent with their university appointments.

- **Appreciation on the project :**

These investigators use multiple approaches, including loss-of-function and gain-of-function studies in different vertebrate model systems to understand the role of Sulf1 in gliogenesis and its activity as a modulator of the Shh and Fgf signalling pathways. The proposed experiments are very interesting and well planned out and are very likely to produce valuable new insight into vertebrate gliogenesis. In addition to their studies on vertebrate gliogenesis, the group leaders are also proposing a series of studies in fruit flies to explore the mechanisms by which Sulf1 regulates Hh signalling in Drosophila.

These experiments are very interesting in their own right, but a note of caution is that they may provide very little new information relating to the central question of the team, namely the molecular and cellular mechanisms that control vertebrate gliogenesis. External collaborations that are developing recently are very likely to be mutually productive and fruitful.

- **Conclusion:**

In summary, this is a dynamic group that addresses fundamental biological questions with far reaching implications.

Team E05: "Cell-cell communication and CNS patterning"

Team leader: Alice DAVY

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

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	3
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	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	2
N7: Number of staff members with a HDR or a similar grade	1	2

- **Appreciation on the results :**

The research team has been created in January 2007 and initially funded by an CNRS ATIP award. In the almost 3 first years, the team focussed on two projects: i) the establishment of the role of Eph/Ephrin signalling in organisation of the cortex and ii) the role of the same signalling complex in innervation of the limb. For the first project, they showed that EphrinB proteins regulate neurogenesis in the cortex. The second research theme uncovered a requirement for EphrinB proteins in the limb bud mesenchyme for correct guidance of motor axons in the limb. The team has produced 3 publications in peer-reviewed journals during the period under review. They also have published 7 articles from work in their previous institute/team. The performance of the team in term of publications is not impressive but the group has been created just under three years ago. A couple of manuscripts of good quality are in submission, suggesting strongly that 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.

Team members received a small number of invitations and oral presentations to national and international conferences. The team collaborates with 6 labs, 4 in France, 1 in Canada and 1 in the UK. The team has been very successful at getting funding, being awarded 4 substantial grants.

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

The group is well balanced and fits well the priorities of CBD. The team leader is young and very dynamic. The projects developed during the review period have led to novel research directions that are likely to be very successful. The research done is of high quality. Some concerns have been raised regarding the future addition of three new team members with rather heavy teaching duties. However, there is a significant potential benefit of adding the fruitfly as model organism, brought by these members. The future change in team dynamic has therefore been seen as beneficial if well managed, and no doubt has been expressed in the ability of the team leader to exploit the change at its best.

- **Appreciation on the project :**

The project for the next 4 years is the logical continuation of the studies the team embarked on in the last three years. The aims are well defined, original and achievable. These comprise the functional studies of cortical effectors of Eph/Ephrin signalling and their role in control of migration and neurogenesis. The four candidates focussed on are likely to give original results and insights in impact of cell-cell communication in proliferation and neurogenesis. The other new research direction stems from the arrival of three lab members working on fruitfly development. It aims to assess the nature of the interplay between Hox proteins and Eph/Ephrin signalling. More specifically, the team wishes to test whether Hoxa/c4 give specificity to motor neurons via regulation of Ephrinb2. A similar regulation will be tested in the context of the development of the fruitfly head. It was felt that the importance of the fruitfly project inside the overall goals of the team was relatively small, but that it will constitute a good basis for expansion of the use of the fruitfly as a genetic tool for a more cohesive project in the future.

- **Conclusion :**

The team has an original research focus (Eph/Ephrin in control of neurogenesis) and the team leader is a young, dynamic and driven individual with a good track record.

Team E06: "Stress, chaperons and development"

Team leader: Elisabeth CHRISTIANS

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

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

- **Appreciation on the results :**

The research group is currently composed of 5 members in addition to the group leader. 3 members of the team (including the group leader) also have university appointments and spend only 50% of their time at the CBD, while 2 members are permanent research assistants and one is a PhD student. The main focus of the group's activity is on understanding the role of stress gene function in gametogenesis and, more recently, embryogenesis and cellular homeostasis. Using the mouse as a genetic model system the group has demonstrated that HSF1 is essential for oocyte meiosis and expression of Hsp90alpha and that the gene is also involved in the response of the male germ lineage to genotoxic stress induced by doxorubicin. Ongoing experiments address the role of Hsp90b1 as a maternal effect factor, while collaborative experiments have been initiated to examine the role of HSF genes in stem cell specification and differentiation.

The productivity of the group, as reflected in their publications record, is not impressive. Over the review period, one paper was published in 2009 in J Biol. Chem. and one in 2008 in Biol. Reprod. During the same period the group leader has also co-authored three other publications.

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

The rather small productivity of the group prevents its high visibility in the emerging field of the role of HSFs in mammalian developmental and homeostasis. The team reports in total 8 invitations to national and international congresses for participation and oral presentations. In addition, several poster presentations are reported. The funding record is minimal and therefore unable to support an expanding research programme as proposed in the Report.

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

The group leader has been studying the role of HSFs for several years and has accumulated considerable expertise on their role in gametogenesis and in particular oocyte meiosis. Consequently, this is an area in which the group could make an impact if it were to focus its resources carefully on it. Regrettably, there is little evidence of an in depth further analysis of some of the interesting original observations made by the investigators; instead we are witnessing an unjustified expansion into other topics that lack a clear direction.

- **Appreciation on the project :**

Some of the proposed experiments involve lengthy and complicated breeding of transgenic mice but promise little in terms of uncovering normal biological processes. It is our view that, given the available resources, the principal investigator should focus on hypothesis-driven experiments that address the role of HSFs on oocyte maturation. Many of the experiments proposed simply divert the main effort of the group and result in approaches that are "miles long but only centimetres deep".

- **Conclusion :**

This group suffers from serious difficulties in focusing its activities and its programme lacks a clear direction.

Team E07: "Transcriptional co-activators and ontogenesis"

Team leader: Laurence VANDEL

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

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

- **Appreciation on the results :**

The project is original tackling the complex problem of how chromatin remodelling proteins control gene expression. This area of research is expanding and the team has made very interesting contributions to it. Their results show that not only methyl transferases modify the histones but also methylate other chromatin regulators. The results are very important and should be highly cited. The team has published five papers. Of these, four publications were in journals regarded as very high quality for being ranked in the first quartile of their field. Four of these publications were done in collaboration with other groups and in one of them the team members were the main executors of the work. This is a satisfactory output as the group was created in 2006 and is in its initial steps of consolidation.

Recently a new member joined the team. This new member has a very good publication record from her postdoctoral period with two first author papers in high quality journals.

One PhD student successfully defended his thesis in the assessed period, which a very good output, given the size of the team. The group is of new creation.

- **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 is young and still is making her mark on the field. This point should be assessed in the future. The team has been very well funded in the recent years and the committee does not envisage it will have any problems obtaining funding in the future. The team has a number of collaborations with international groups that have resulted in a very good publication. There are no stable collaborations with international groups, but there are interactions with other groups in France.

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

The research program is ambitious which, in itself, represents a risk. The search for postdocs that are well trained in embryo manipulation and ChIP technology is a good strategy to favour the success of the project. The team is mainly focused on research. The student training consists mainly in PhD supervision and M2R student training.

- **Appreciation on the project :**

The group has developed a number of tools that give them the possibility to explore at the genome level how methylated and unmethylated CBP regulate transcription. They have done a series of ChIP experiments that are data rich and will open new avenues of investigation. They plan to analyse, in vivo, epigenetic crosstalk between important chromatin regulators. The project is very solid. The team seems well funded and is following the right steps to grow steadily.

They plan to analyse in vivo epigenetic crosstalk between two important chromatin regulators, which is very original and risky. Their genomic approach is very interesting. The management and understanding of the large datasets obtained is of great complexity.

- **Conclusion :**

This is a very active and energetic young group. Its research focuses on transcriptional regulation at the level of chromatin regulators using ChIP and genomic approaches focusing in topics of great interest on which they can make important contributions. The group is well funded and has a series of very specific tools that will help them getting a niche where they will be able to make important contributions without being easily scooped by larger groups. The small size of the group and its youth make it difficult attracting international researchers. The group is making an effort to integrate in the CBD by adapting their studies to the general topic of developmental biology. Although this is a good strategy, the team should not be distracted from the work at which they are specialist and in which they can make their best contributions.

Team E08: "Transcriptional control of morphogenesis and cell differentiation"

Team leaders: David CRIBBS and Henri-Marc BOURBON

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

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	3	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)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	1
N7: Number of staff members with a HDR or a similar grade	2	1

- **Appreciation on the results :**

The team has focused on the past four years on two aspects:

(1) Understanding how Hox genes form the highly divergent segmental structures present in the head segments of the fly,

(2) How transcription factors activate the RNA polymerase through the intermediate action of a highly conserved protein complex known as the "mediator complex".

The first project is of high interest and, although it is not in the spotlight of international research, it is still an important unsolved question. The work carried out by the team uncovered several unexpected aspects of Hox gene regulation and merited the publication of two papers in high standard journals in the field of Developmental Biology.

The second topic is very original. It tries to find out how transcription factors induce the RNA polymerase activity by modulating a complex formed by more than 20 Mediator subunits. This study extends previous seminal work of the laboratory. Its main merit has been the observation that transcription factors engage in very specific interactions with certain mediator complex proteins. These results are unexpected and open a new way of understanding transcriptional regulation. The problem is of a great complexity and is worth studying. It should be of great impact on the field of transcriptional regulation.

The publication record of the group in this period has been very satisfactory with a total of 9 papers. Of these, eight publications where in journals regarded as very high quality for being ranked in the first quartile of their field. Four of these publications were done in collaboration with other groups while in five publications the team members were the main executors of the work. Two PhD students successfully defended their thesis in this period representing a good number given the size of the team.

- **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 were invited to two national meetings and one international meeting. The group has maintained a stable structure through the assessed period without major movements except at the level of PhD students. No international researchers were recruited in this period. The group has had a reasonable amount of funding during the period assessed, although lately they have had year without any active grants. Their failure to obtain a grant is surprising given the quality of the group's research and may reflect a problem with the way the grant applications were written. This committee suggests that future grant applications of this group should be circulated among colleagues in the centre to improve any possible shortcomings in communicating the research, which in our opinion, is competitive and of high quality. We do not expect the team should have major problems in finding research funds for its work. The group has a number of international collaborations with Switzerland and the United Kingdom some of which have resulted in collaborative publications. The collaborations seem to be based on particular projects rather than being stable.

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

The team has a satisfactory relation with French and international research groups. A large amount of the team members were involved in teaching activities. This will not be true for the proposed rearranged team, which will be smaller but constituted by full-time researchers.

- **Appreciation on the project :**

The project is original, tackling the highly complex problem of analyzing the interaction between enhancer bound transcription factors with the complex of proteins directly interacting with the polymerase in the promoter. The results should be highly cited. The complexity of the project is a risk in itself.

- **Conclusion :**

The group is of high quality. The project developed is very original and may offer many opportunities for international collaboration. The lack of funding in the last year if repeated may seriously affect the group's research. The group should explore new granting opportunities at the national and international level. This committee suggests that future grant applications of this group should be circulated among colleagues in the centre to improve any possible shortcomings in communicating the research, which in our opinion, is competitive and of high quality.

Team E09: "Gene regulatory networks in Drosophila hematopoiesis and cell differentiation"

Team leaders: Michèle CROZATIER and Alain VINCENT

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

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

- **Appreciation on the results:**

This team, managed by two group leaders, is aiming to decipher the regulatory network in Drosophila hematopoiesis and myogenesis. Both projects are strongly connected by the central role of the EBF transcription factor Collier in both processes. Collier is expressed in the posterior signalling centre (PSC) of the lymph gland and essential for the differentiation of hemocytes. Recently, it has been shown by this team, that immune response upon wasp infection is controlled by JAK/STAT signalling with crucial impact from the PSC. Future work will concentrate on the identification of new components acting in the PSC, focusing on genes/proteins that are essential for the communication between PSC and hematopoetic progenitors in the neighbouring maturation zone. JAK/STAT signalling was already recognised to be crucial. Therefore a major effort for future work will be to identify targets in hematopoetic cells of this particular pathway.

The second major question addressed by this team is how muscle diversity is achieved during myogenesis. During Drosophila embryogenesis each muscle is established by the specification of one individual muscle founder cell, which - upon fusion with other myocytes – differentiates into a highly specific individual muscle. The link between the specification of founders by combinatorial codes of TFs and the realisation of individual muscle properties is still a miracle and one of the big questions in the field. A straightforward strategy would be to search for genes downstream of a founder cell identity factor that is specific for one single muscle identity. This prerequisite is fulfilled by Collier. Together with a comparative transcriptome analysis of individual muscles, the team has all tools in hand to answer the question of how muscle individuality is realised. Work of this team led already to an impressive number of excellent papers with primary data in top journals, many of them influenced the research field significantly. Efficiency and productivity of this team is very high.

- **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 high visibility in the scientific community. Several links to labs in France and from abroad are well established. The team provides a highly attractive scientific environment and has no problems to recruit excellent young scientist.

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

The research team is a very good example of the synergetic effects that can be achieved by integrating two group leaders into one team. They have been successfully working together for many years and the interactions within the group and also with other labs at the CBD appear very fruitul.

- **Appreciation on the project :**

The planned research project tackles major highly interesting and essential biological questions in an experimentally innovative way. Sharing common technologies and having excellent test systems in hand, the success of the research efforts is highly anticipated. There is no necessity to give specific recommendations on the research projects of this team. Further improvement of this team will be anticipated by providing the institute with additional technicians for animal care and computer support as outlined in the general recommendations. They would also benefit significantly from an expansion of the microscopy core facility.

- **Conclusion :**

In summary, this team was recognised as one of the strongest in the CBD and the project will be a hallmark contribution to the overall scientific profile of the institute.

Team E10: "Hematopoiesis and immunity"

Team leaders: Marc HAENLIN and Lucas WALTZER

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

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

- **Appreciation on the results:**

The main focus of the group is the understanding of the molecular and genetic control of normal and pathological blood cell development and physiology using Drosophila as model system. The different projects developed by the group are articulated around this central question with one exception with the analysis of the function of the Ly-6 gene family, in particular for cell-cell septate junction in epithelial tissues. The relevance of the research program is good and its originality is very good. The Ly-6 research project is outside the main topic of the team, but a very good research scientist carries out this project, which is original and very relevant. The quality of the results of the group is really good. The results have a good impact to the research field. The group has published 7 papers in peer-reviewed journals and 5 of them in high impact journals. The efficiency and productivity of the group is high.

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

The research output of the group is high and has a good visibility in the international scientific community. The two PIs of the group have been able to build a team with top-level scientists. The training of the students is very good. The level of funding for the different projects is good, indicating again the significant visibility of the team. Members of the team were invited to two international and one national meetings. The team has developed fruitful collaborations both with international teams and internal group within the unit (Team 08 HM Bourbon).

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

The team is managed by two PIs and its organization seems to be very good. The size of the group is relatively important and equilibrated between staff scientists, postdocs, PhDs and a technician. This group has taken benefit of the recent arrival of two staff scientists who will strengthen the scientific production of the group. The relevance of initiatives aimed at scientific coordination, emergence of cutting edge projects and taking of risks are very good. The team is mainly focused on research. The student training consists mainly in PhD supervision and Master student training, with also some participation into Master 2 lecture program.

- **Appreciation on the project :**

The existence, relevance and feasability of a medium- or long-term scientific project is very good. The group is well funded. The projects developed by the group are original in particular the development of Drosophila model system to investigate leukemia.

- **Conclusion :**

The scientific production of the group is good. The research projects are original and particularly relevant. The human skill of the group is very good. The different projects are well funded. There are no real weak points. There is no specific recommendation, except to keep going like that and to be even more successful with the output of the research projects. The recent arrival of two new staff scientist should help.

Team E11: "Control of cell shape remodeling"

Team leader: François PAYRE

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

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

- **Appreciation on the results :**

The central point developed by the team aims to understand the translation of regulatory cues controlling tissue specification leading into the remodelling of the shape of individual cells. The different projects developed by the group are articulated around this central question: their relevance is very high. The analysis of the different levels of regulation upstream and downstream the gene shavenbaby are original. The results are very important and are (and will be) highly cited. The work of this team has led already to an impressive number of excellent publications in journals with very high impact factors. The efficiency and productivity of the group is really high. The team has developed very fruitful collaborations, first with teams from other countries, in particular with the group of D. Stern, second with other groups within the unit, such as the Crozatier/Vincent group.

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

The research output of the group is very high and has a very good visibility in the international scientific community. The PI of the group has been able to built a team with top-level scientists. The training of the students is excellent. The only weak point would be the relative low number of foreign postdocs. The level of funding for the different projects is really good, indicating again the important visibility of the team. The participation to international or national networks is important as well as the level of collaboration.

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

The team has a good size. The relevance of initiatives aimed at scientific coordination, emergence of cutting edge projects and taking of risk is very good. The group is mainly focused on research, but both the group leader and other lab members participate actively in teaching, especially at the level of the Master.

- **Appreciation on the project :**

The research program developed by the team is original and innovative. The results provided by the group are very important in particular for the research fields associated to developmental and cell biology.

- **Conclusion :**

There is no necessity to give specific recommendations to the research projects of this team. However further improvement of this excellent team would be associated with the additional technicians for animal care (flies) and importantly also a real computer support as outlined in the general recommendations. They would also benefit from an expansion of the light microscopy core facility.

Team E12: "mRNA stability and development"

Team leader: Dominique MORELLO

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

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

- **Appreciation on the results :**

This research team works on mRNA stability in the context of differentiation and development. They found that often an uridine and alanine rich 3´UTR element (AREs) in many mRNAs is responsible for mRNA stability. This conserved motif provides the binding site for several factors, either proteins from the so-called AUBP class or small RNAs. The group has successfully established three models to study the function of AREs in depth and the role of trans-acting factors of the AUBP class. They utilise the genetically tractable Drosophila system, the mouse germ cell differentiation and they study post-transcriptional control in lymphoma. The project is of high interest and the results obtained so far are significant contributions to the research field. The team has published eight papers in peer-reviewed journals. Some of them appeared in high impact journals (e.g., Dev. Cell, Blood). Given the size of this group, the overall output is very good.

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

Work of this group is visible on the national and international level. The team leader as well as members of the group participated in several international meetings and were invited for giving talks. Research in this group was well funded during the last years. Although not listed explicitly in the report, the team seems to be well connected with other groups in Toulouse.

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

The team will be closed at the CBD in the near future for personal reasons. Although the group works on several aspects of mRNA stability in different systems, it was successful and published well. Therefore strategy and life of the team has to be judged as being very good.

- **Appreciation on the project :**

No project was proposed because the team will be closed.

- **Conclusion :**

Work of this team has had an impact on the general profile of the CBD. The major involvement of the group leader in setting up and maintaining the mouse facility should also be underlined. Her departure may create a serious problem in that matter. The group published well and raised solid funding over the last years.

New Team EN12: "Mitochondrial dynamics, from neurogenesis to neurodegeneration"

Team leader: Pascale BELANGUER

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

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	Team not member of unit	4
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		0.80
N6: Number of Ph.D. students (Form 2.7 of the application file)		0
N7: Number of staff members with a HDR or a similar grade		0

- **Appreciation on the results :**

This group, currently part of the UMR5241 "Métabolisme Plasticité Mitochondrie" directed by Dr. Casteilla, is applying for setting up a new group at the CBD in 2011 to study the mitochondrial dynamics from neurogenesis to neurodegeneration. The group has been studying for many years the function of the dynamin Msp1/OPA1 in mitochondrial dynamics, with a particular interest in the fusion/fission dynamics. Using the yeast as a model organism, the group has shown that Msp1 is implicated in mitochondrial inner membrane fusion. They contributed to show that mutations in the human homolog, OPA1, were responsible for Autosomal Dominant Optic Atrophy type 1 (ADOA1). More recently, through studies of the different isoforms in yeast, the team has shown that Msp1 is involved both in mitochondrial dynamics and mitochondrial genome maintenance, and that these two functions are not coupled. Furthermore, they have identified a new protein partner of OPA1, the pro-apoptotic BNIP3, strengthening the role of OPA1 in apoptosis. The physiological significance of the protein partners still remains to be understood. Finally, recent studies suggest that cells expressing protein carrying pathogenic mutations are more sensitive to apoptosis than control cells, suggesting a possible pathophysiological mechanism of cell death for retinal cells. The field of study of mitochondrial fusion/fission is relatively new and highly competitive. Since 2005, the team has published 11 papers in specialized peer-reviewed journals, 5 of which are primary work of the team members. However, most of these publications are not in high impact journals.

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

The team members have regularly presented their work at conferences, although only one oral presentation at an international conference. The committee recommends to the senior team members to attend and present their results at international conference in order to confront their work with the rapid evolution of their field. The team has had regular funding through national patient association (Retina and AFM) as well as one competitive grant through the National Granting Agency (ANR).

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

Due to the presence of 4 members having teaching duties, the team has a strong involvement in teaching and in training, in particular with the training of 5 PhD students since 2005. On the other hand, such a composition of the group limits its capacity to devote its efforts towards research.

- **Appreciation on the project :**

The present domain of research of the group is very far from the interests of the CBD. Because of this situation, the group has developed a project that is not in its current line of study. While the project proposes to continue to understand the influence of mitochondrial dynamics, in particular OPA1, on the neurodegenerative process, the project also proposes to extend their study to the impact of mitochondrial dynamics on the functions and plasticity of mature and developing neurons. The team expertise in molecular biology and in functional studies in the yeast is clearly appropriate for the first project, and the committee strongly suggests focusing on understanding the role of OPA1 mutations and dysfunction of mitochondrial dynamics in neurodegeneration. Although there has been a recent recruitment in the team of a neurobiologist, who will take in charge the project on the influence of mitochondrial dynamics on neurogenesis as well as neuronal plasticity and function, the committee was not convinced by the strategy or the presence of the appropriate expertise within the team for the development of the second project. In particular, despite a new collaboration with one of the CBD team for setting up the chicken embryo as a tool to address the question in the developing neural tube, the project does not appear viable in the short term.

- **Conclusion:**

The committee believes that the integration of this group in the CBD is neither appropriate for the CBD, nor for the group itself. Because of its present field of research the group will not bring much to the CBD and, on the other hand, because of its size, it will constitute an additional burden to the common services. Furthermore, part of the project, proposed to better fit into the CBD, does not correspond to the expertise of the group and does not appear to be viable. The committee thinks that recruitements of additional groups in the CBD should obey at least two rules : very high quality of the research group and potential for fruitful interactions and high mutual benefits. In the present case, none of these requirements are fulfilled.

New team EN13: "Biology of the centrosome"

Tem leader: Andreas MERDES

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

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	Team not member of the unit	
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		4
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		0
N6: Number of Ph.D. students (Form 2.7 of the application file)		0
N7: Number of staff members with a HDR or a similar grade		2

- **Appreciation on the results :**

This team studies the molecular composition and function of centrosomes and will join the CBD in 2011. The research focusses on three major aspects: the analysis of Nesprins, a class of proteins that are assumed to anchor centrosome proteins to the outer nuclear envelope, secondly, the analysis of the y-Tubulin ring complex and in particular the functional analysis of Nedd1/GCP-WD that may play a central role in connecting centrosomes and microtubules and thirdly, the analysis of centrosome clustering in cancer cells. All projects are of innovative character and it is anticipated that the results will lead to several solid publications with a high international visibility. Work of this team led to 21 high impact publications in the last 5 years. Among these, 10 papers were signed by the group leader as last author. Publications in prestigious journals like Curr. Biol., JCB and others reflect the outstanding quality of research in this team.

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

The group leader belongs already to the world´s top researchers in the field. One senior scientist will leave the group in December 2010 and one PhD student will finish at the end of 2010. The attractiveness of the team is already high and will even increase after joining the CBD. Therefore the committee is not suspecting any problems to recruit excellent young scientists in the future. The team is very well funded. Successful and stable collaboration were already established with groups in Toulouse and Paris.

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

The team is not yet part of the CBD, nevertheless several interactions between this team and other labs of the CBD are possible and the success of collaboration is anticipated. The proposed research program for the next years already points to such fruitful interactions, e.g. to study muscle differentiation and centrosome dynamics together with the CROZATIER/VINCENT team.

- **Appreciation on the project :**

The work program for the next years focuses on the in depth analysis of the role of centrosomes in a cellular context. On the one hand, the team aims to understand the molecular mechanisms of microtubular nucleation and dynamics during spindle formation and on the other hand, the team aims to decipher the role of centrosomes during developmental processes. This is an ambitious program that will have a very strong impact on our current understanding of fundamental cell biology processes. All parts of the proposed project are well planned and feasible. It is anticipated, that the team will be able to renew active grants and to obtain new funding after relocation to the CBD. The research field is highly competitive but the committee is convinced that this team will be one of the leading edge groups in this research area, not only in France but worldwide. Original projects like this one are not free of risk but absolutely worth to go for.

- **Conclusion :**

This group will bring to the CBD an outstanding expertise in cell biology that will be beneficial to many groups. Collaborations are not only possible and already planned, such interactions are highly recommended. On the other hand, the Merdes team will also benefit from being located at the CBD by utilising the available animal model systems for their studies. A planned collaboration with the Crozatier/Vincent team to study nuclear migration in muscle cells, a process which is affected in nesprin mutant background in cell culture systems, seems to be a very good entry point to start local collaborations. In summary, this team has been recognised as one of the strongest in the CBD and the proposed project will be a hallmark contribution to the scientific profile of the institute. The committee strongly supports the integration of this group in the CBD.

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

Nom de l'équipe : *ROLE OF IONIC MESSENGERS DURING EARLY EMBRYOGENESIS*

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

Nom de l'équipe : *CONTROL OF NEURONAL IDENTITY IN THE ZEBRAFISH*

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

Nom de l'équipe : *CONTROL OF THE CELL CYCLE AND NEUROGENESIS*

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

Nom de l'équipe : *MORPHOGENS AND GLIAL SPECIFICATION*

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

Nom de l'équipe : *CELL-CELL COMMUNICATION AND CNS PATTERNING*

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

Nom de l'équipe : *STRESS, CHAPERONS AND DEVELOPMENT*

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

Nom de l'équipe : *TRANSCRIPTIONAL CO-ACTIVATORS AND ONTOGENESIS*

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

Nom de l'équipe : *TRANSCRIPTIONAL CONTROL OF MORPHOGENESIS AND CELL DIFFERENTIATION*

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

Nom de l'équipe : *GENE REGULATORY NETWORKS IN DROSOPHILA HEMATOPOIESIS AND CELL DIFFERENTIATION*

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

Nom de l'équipe : *HEMATOPOIESIS AND IMMUNITY*

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

Nom de l'équipe : *CONTROL OF CELL SHAPE REMODELING*

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

Nom de l'équipe : *MRNA STABILITY AND DEVELOPMENT*

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

Nom de l'équipe : *MITOCHONDRIAL DYNAMICS, FROM NEUROGENESIS TO NEURODEGENERATION*

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

Nom de l'équipe : *BIOLOGY OF THE CENTROSOME*

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