# Bases génétiques, moléculaires et cellulaires du développement

Rapport Hcéres

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

Section des Unités de recherche

# AERES report on the research unit

## Genetic, molecular and cellular basis of development

## Department of Developmental Biology

## From the

## Pasteur Institute

## 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: Genetic, molecular and cellular basis of development

Requested label: URA CNRS

N° in the case of renewal

Name of the director: Mrs Margaret BUCKINGHAM

# Members of the review committee

## Chairperson

M. Richard BEHRINGER, UTMD Anderson Cancer Center, Houston, USA

## Other committee members

M. Peter BECKER, Ludwig-Maximilians Universität München, Germany

M. Jonathan EPSTEIN, University of Pennsylvania, Philadelphia, USA

M. Patrick HARDY, EMEA, Saint-Vulbas, France

M. Roger PATIENT, University of Oxford, United-Kingdom

M. Philippe SORIANO, Mount Sinai Medical Center, New-York, USA

M. Thierry GRANGE, Institut Jacques Monod, Paris, France

M. Richard MOXON, Weatherall Institute of Molecular Medicine, Oxford, United-Kingdom

M. Gabriel WAKSMAN, University of London, United-Kingdom

## Committee members nominated by staff evaluation committees

M. Pascal DOLLE, CoNRS member

# Observers

## AERES scientific advisor

M. Jean-Antoine LEPESANT

## Pasteur Institute representatives

M. Tony PUGSLEY

M. Alain ISRAEL

## CNRS representative

M. André LE BIVIC

# Report

## 1 • Introduction

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

The review of the Département de Biologie du Développment/URA 2578 was held on March 1-3, 2010.

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

The Département de Biologie du Développment/URA 2578 has a strong emphasis on mouse developmental genetics, initiated by its founders in the 1970's. However, over the last 10 years new model systems have been added, including Drosophila, zebrafish, and amphioxus as well as human genetics. The research focuses on the developmental processes that occur from fertilization to the generation and homeostasis of multicellular organisms. Areas of research emphasis include cell differentiation and lineage, organogenesis, gene regulation, RNA metabolism, epigenetics, Notch signaling, and disease resistance.

- **Management team:**

The URA is headed by Mrs Margaret Buckingham, whereas the Department is headed by Mr. Philip Avner. They work closely together to manage a highly cohesive, interactive, and productive enterprise.

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

| | Past **1-09-2007** | Future **1-01-2011** |
|---|---|---|
| N1: Number of researchers with teaching duties (Form 2.1 of the application file) | 1,50 | 1 |
| N2: Number of full time researchers from research organizations (Form 2.3 of the application file) = Permanent researchers EPST + I.PASTEUR | 32,5 | 36,5 |
| N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file) = researchers on short term contract-Postdocs | 19 | 18 |
| N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file) = ITA EPST + I. PASTEUR including research engineers | 30,756 | 33,655 |
| N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file) = ITA on short term contract | 0 | 0 |
| N6: Number of Ph.D. students (Form 2.8 of the report and 2.7 of the project file) | 23 | 20 |
| N7: Number of staff members with a HDR or a similar grade | 18 | 19 |

## 2 • Overall appreciation on the research unit

- **Overall opinion:**

This research unit is considered one of the top developmental biology departments in the world, with multiple internationally recognized stars. The research themes of the teams comprehensively cover the central questions of developmental biology. There is a great tradition and strength in mouse genetics and embryology but also outstanding groups utilizing Drosophila, zebrafish, and other vertebrate systems. There is a good critical mass of research teams, with numerous tenured scientists, postdoctoral fellows, graduate students and technical staff. The department has a strong record of training, leading to tenured scientists being promoted within the department to Group or Unit leader status or leaving the department to initiate their own research groups at other institutions. The publication record overall is outstanding with papers in top peer reviewed journals. There is outstanding European and international visibility. Indeed, the head of the unit has just received the Lifetime Achievement Award from the Society of Developmental Biology based in the USA. The Department also appears very cohesive and well run with a focused research seminar program, technology seminars, symposia on special topics (Bio-Imaging), journal club, student-initiated Developmental Biology Club, monthly lab head meetings, and scientific retreats.

Although the Department excels in these areas, there are minor but potentially significant concerns by the tenured scientists, postdoctoral fellows, graduate students and technical staff that should be addressed to enhance training, mentoring, and communication. For graduate students, there was a desire to have regular research mentoring committees for feedback on their thesis research. For postdoctoral fellows, there was a desire for more infrastructure to facilitate research, particularly for information services (computing) such as wireless internet, site licenses for commonly used software and restrictions on computer hardware acquisition. For tenured scientists, there was a desire for enhanced core facilities and concerns about opportunities to supervise graduate students, applying for independent funding and publishing as last authors. For the technical staff, there was a desire for more communication between Institut Pasteur, Team Leaders and the above groups about the research enterprise.

The two Core facilities based in the Department are outstanding, however, deficiencies in certain IP Cores have significantly held back research progress by the departmental teams that must be addressed.

- **Strenghts and opportunities:**

Many of the research teams are examining cutting edge topics. The group as a whole has scientific bravery addressing ambitious questions in genetics, developmental biology, and infectious disease. The Department has an outstanding international reputation. There appear to be a reasonable number of departmental collaborations that provide both intellectual and social cohesion. There are two outstanding Cores within Department, including the Mouse Genetics Engineering Center and Central Mouse Facilities. The creation of a Scientific Advisory Board would likely be beneficial to the Department, especially at this time when several senior faculty are nearing retirement age.

- **Weaknesses and threats:**

The teams require standard and cutting edge technologies to move their research forward and remain internationally competitive. These technologies include sophisticated microscopy, transgenic and knockout mouse production, flow cytometry, mass spectrometry, RNA-seq and ChIP-seq. Whereas the Mouse Genetics Engineering Center, the Central Mouse Facilities, and Imaging Core Facility within the Department were deemed outstanding, there were very serious deficiencies in IP Core Facilities that provide DNA sequencing, flow cytometry, and mass spectrometry. In addition, there is a serious deficiency in bioinformatics support to the teams. These deficiencies are significantly hindering research and forcing the teams to seek these technologies off campus. This is a serious threat to research for the department and IP.

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

The committee appreciates that this is a time of risk and opportunity for the Department because of the pending retirements of very prominent team leaders. The loss of these two prominent teams studying mouse genetics and development will leave a large scientific and leadership vacuum in the Department.

There are times when for whatever reasons there are gaps in funding for a unit. Apparently, there is currently no formal mechanism at the IP to provide bridge funding to maintain unit research integrity during these transient times. This poses a threat to research unit continuity.

- **Data on the work produced :**

| | |
|---|---|
| A1: Number of permanent researchers with or without teaching duties (recorded in N1 and N2) who are active in research | 35 |
| A2: Number of other researchers (recorded in N3, ~~N4 and N5~~) who are active in research | 16 |
| A3: Ratio of members who are active in research among permanent researchers [(A1)/(N1 + N2)] | 1 |
| A4: Number of HDR granted during the past 4 years | 5 |
| A5: Number of PhD granted during the past 4 years | 22 |

## 3 • Appreciation team by team

Team : Drosophila Genetics and Epigenetics

Team leader : M. Christophe Antoniewski

- **Staff members:**

| | Past<br>**1-09-2007/1-01-2011** | 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 | 3 |
| 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) ) = ITA EPST + I. PASTEUR including research engineers | 1,75<br>0 | 2<br>0 |
| N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file) | 0 | 0 |
| N6: Number of Ph.D. students (Form 2.7 of the application file) | 2 | 2 |
| N7: Number of staff members with a HDR or a similar grade | 1 | 2 |

- **Appreciation on the results:**

This team have established a dynamic, innovative, ambitious and internationally competitive research program, having made interesting discoveries in highly competitive areas. They published 4 senior author papers during the review period, two of which (Mol Cell Biol and EMBO Reports) describe their concluding work on the histone acetyltransferase GCN5. They discovered a previously unappreciated synergism between the nucleosome remodeling factor NURF and demonstrated that the molecular environment – the association of the enzyme in different complexes leads to an altered substrate specificity. Antoniewski was among the first researchers to realize the potential of Drosophila as a model organism to study the role of small RNAs in gene regulation. They provided the first evidence for a nuclear role of the RNA interference machinery in heterochromatin formation; such a role had only been known for fission yeast and plants. The PNAS paper that describes their original findings is likely to have a major impact in the field. In a collaborative work with Andino, this team contributed to identifying viral suppressors of RNA interference as a way to bypass the fly antiviral defense system. This work has contributed to coauthorships in major journals (Genes Dev, Nature). The team has published 12 papers in total, which is considered very good, in particular since during the presentation it became clear that they have obtained a wealth of highly interesting data that will undoubtedly lead to excellent publications, among them the identification of an ecdysone-induced micro-RNA and the design and execution of RNAi and chemical screens for modifiers of micro-RNA-dependent repression pathways (based on the self-silencing automiR system), which has led to interesting candidate genes and compounds for further functional analyses. Much of the efforts during the reporting period have been devoted to setting up the methodological requirements for highest-levels analysis of small RNA populations by deep sequencing and their informatic analyses. His emerging expertise in the identification and characterization of small RNAs is already being recognized in the field.

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

The team leader has built a small but highly motivated team and has been able to attract two permanent staff members who are able to carry out very independent research. The funding level has been very good, partly due to the participation in international consortia (NeuroMir and FunGenDroso). Two major ANR grants are pending for decision. The team leader is not yet very visible in international conferences, but this is likely to change once his most recent results have been published.

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

The team is still very small and appears to be well motivated. It is clear that essentially all of the team projects are highly original and hold great promise. The technological developments are cutting edge; in the long run there are plans to establish a systems biology study of the small RNA network in Drosophila.

- **Appreciation on the project:**

This team proposes to follow several lines of research all centered on the identification and functional analysis of large sets of small, non-coding RNAs. His plans to exploit the power of Drosophila genetics for the study of the nuclear role of the RNA interference pathway in heterochromatin formation and gene silencing is of highest relevance to the field. He convinced the review committee that deep sequencing of small RNAs is the only way of assessing in quantitative terms the changes in the production of regulatory RNAs in diverse genetic backgrounds and upon manipulation of the systems. Establishing a list of nuclear small RNAs will be an important resource for the field. Generating fly strains containing tagged RNAi enzymes for rigorous sub-cellular localization and ChIP profiling holds great promise.

A central aspect of future research will be to develop a systems biology approach to study complex small RNA networks that regulate genetic and epigenetic programs. The team will characterize small RNA populations in various defined biological systems using chemical compounds that he has identified as affecting the small RNA machinery. They rightly see the need to developing the small RNA profiling methodology further, mainly the informatic annotation, normalization and statistical evaluation. They are poised to become a leading experts in this area, however the review panel also saw the risk of being driven by technology rather than by biological questions. The research outline lists a number of collaborative projects where they will engage in small RNA profiling. Here the

methodological expertise can have a real impact. However, there is a certain risk of spreading too thin and in using resources for these collaborations without being recognized for the biological findings by the scientific community. However, at this point there is no shortage of fascinating questions that he and his team propose to address.

- **Conclusion:**

The team leader and his team have proven that they can design and carry out an ambitious and original research proposal. They have a lot of potential, but currently their progress appears limited by access to deep sequencing and by bioinformatic support. They could make a major contribution in shaping the development of a network of next generation bioinformaticians with a systems-oriented mind-set.

Team : Molecular Mouse Genetics

Team leader : M. Philip Avner

- **Staff members:**

| | Past 1-09-2007/1-01-2011 | Future 1-09-2007/1-01-2011 |
|---|---|---|
| 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 | 4 |
| N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file) ) = ITA EPST + I. PASTEUR including research engineers | 3,801 | 4,801 |
| 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 | 2 |
| N7: Number of staff members with a HDR or a similar grade | 4 | 3 |

- **Appreciation on the results:**

The team leader is an international leader in the field of epigenetic gene regulation. His team has made seminal contributions to our understanding of the complex process of mammalian X chromosome inactivation. Among the many high-quality publications during the reporting period two seminal papers in Science stand out for their highest impact. One of them shows that the mysterious non-coding Xist RNA that is central to the process of facultative heterochromatinization evolved from a protein-coding gene; the second documents a repressive function of the pluripotency factors Nanog, Oct4 and Sox2 for the Xist gene in the pluripotent state. Remarkably, the team around the team leader also made very good progress on two other lines of research: the molecular and genetic analysis of the neuronal nucleosome assembly protein Nap1l2 and the mapping and preliminary of a candidate gene as a modifier of diabetes susceptibility. Clearly, this must be considered a significant advance in this example of a quantitative trait disease of highest societal relevance. These latter projects were directed by a very capable and independent senior scientist. A patent was filed on the role of the Arntl2 gene in mediating protection from Type 1 Diabetes. The research results are considered to be outstanding, both in terms of quality and quantity (the unit has published over 30 papers). There were 22 papers in which a member of the team was senior author and/or first author. The unit has directed several PhD and master students; three PhD theses have been successfully completed.

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

The team leader is a prominent speaker at international conferences, mainly on X inactivation. The unit has had on average between 12-14 full time staff members and were able to attract gifted international students and postdoctoral fellows. The funding level of the unit has been very good, due to several grants from the ANR and from Diabetes foundations and due to the participation in several national and European Consortia, although the animal house costs have put a significant burden on the unit. The team leader has served as the co-chair of the European Network of Excellence 'The Epigenome'. During recent years two outstanding teams have 'budded off' to the Institut Curie and more recently to the University of Paris Diderot.

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

The unit appears well structured and managed by several permanent senior staff members. The productivity is excellent. The team leader is very well connected nationally and internationally. He has been a leader in the European Network of Excellence the Epigenome. He recently organized the kick-off meeting of the 'Human Epigenome Consortium' in Paris.

The team leader plans concerning the development of the team are based on the extension of his contract until 2014. He convincingly argued that the team could be orderly dissolved until then. He has not make provisions for retirement at the end of 2011 and indeed this would lead to significant consequences for many in the group.

- **Appreciation on the project:**

The research proposal is diverse and covers a convincing blend of solid follow-up research based on previous achievements and highly original, daring projects. It is feasible and the more risky aspects are backed with fallback strategies. The proposal is planned for the next four years, until the prospective retirement of Phil Avner. The review panel was convinced that all three aspects of the proposal, (X inactivation, Nap1l2 and diabetes susceptibility) bear great potential and should be followed for the next reporting period. The senior scientist may take the latter two projects for independent research after the retirement of Phil Avner.

- **Conclusion:**

This is one of the strongest units in the Department of Developmental Biology. The overarching threat is the upcoming retirement of the team leader, which would pose a significant loss not only for the Pasteur Institute, but also for the scientific community.

Title: Molecular Genetics of Development

Team leader : Mrs Margaret Buckingham

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

| | Past<br>1-09-2007/1-01-2011 | 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) | 5 | 5 |
| N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file) | 5 | 2 |
| N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file) ) = ITA EPST + I. PASTEUR including research engineers | 5<br>0 | 5<br>1 |
| N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file) | 0 | 0 |
| N6: Number of Ph.D. students (Form 2.7 of the application file) | 1 | 2 |
| N7: Number of staff members with a HDR or a similar grade | 3 | 3 |

- **Appreciation on the results:**

This research team and its leader have long been recognized as one of the most influential teams in the fields of myogenesis and cardiac development. During the period of review, novel groundbreaking and/or significant advances have been made in two fields:

- In the context of heart development, as a follow-up to the major discovery of a second embryonic heart field contributing to the myocardium, recent work has approached the genetic regulation of this second heart field using various mutants of the fibroblast growth factor pathway, as well as a novel mutant, Prdm1. Novel cell lineage studies using the laacZ reporter facilitated the study of several events including the rotation of the outflow tract, or the lineage relationship of the arterial pole myocardium and some muscles of the head. These studies are internationally recognized as fundamental advances.

- Strong advances have also been made with respect to skeletal myogenesis, with the demonstration of a Pax3/Pax7 dependent resident muscle progenitor cell population, which eventually will correspond to the muscle satellite cells. A second groundbreaking study described a method to isolate these satellite cells and demonstrated their ability to contribute to muscle repair in a model of muscular dystrophy. Taken together, this recent body of work has provided novel and fundamental insights into both embryonic myogenesis and adult muscle repair/regeneration.

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

Recent data have been reported in several papers in journals with high impact factors (Science, Nature, Genes Dev). Overall more than 40 research papers were published over the review period. There were 34 papers in which a member of the team was senior author and/or first author. The quality, originality and impact of the work are exceptional with respect to the team size.

The team and its leader have worldwide recognition, as exemplified by invitations to many prestigious conferences. The team leader is widely recognized as among the world leaders in developmental biology, has been elected to the French Academy of Sciences, and will receive the Lifetime Achievement Award from the Society for Developmental Biology in 2010.

The team benefits from recurrent sources of funding from French sources and is involved in several European networks (4 under FP6, 3 ongoing under FP7), demonstrating its strong involvement and activity in large scale collaborative projects. Overall the group is highly successful in raising funds from national and international grant agencies.

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

The team has trained a large number of subsequently successful and independent investigators who have made important contributions on their own. Several international experts have performed sabbaticals within this unit, thus enhancing the overall research climate within the Department and Institute.

Collaborations are ongoing with several teams nationally and internationally, including through European Union funded research networks. Some fruitful collaborations exist within the department, especially with team E6 (Molecular Biology of Development) through the use of transgenic lines allowing retrospective clonal cell lineage analysis. Scientific interactions and/or prospects for joint efforts (e.g. in large scale molecular screens) may perhaps be further explored with team E11 (Stem Cells and Development), also working on the mechanisms and regulation of myogenesis, now that independence of that unit appears to have matured.

- **Appreciation on the Project:**

The project is in line with recent advances and proposes several approaches to increase knowledge on the regulation and cell lineage relationships governing skeletal myogenesis and heart development. Among the attractive aspects are the search for Pax3 cofactors, and the study of the roles of regulatory (micro) RNAs in myogenic regulation. Clonal cell analysis in cardiac development is likely to continue to be fruitful, and new approaches to mathematical and quantitative modeling of morphogenesis are exciting new directions.

- **Conclusion:**

The research achievements of this team are exceptional. The team leader is at the top of her game. The project is structured, entirely relevant with the ongoing objectives, and clearly feasible. Some aspects include appropriate risk-taking for this established group, including a prospective lineage analysis of single epiblast cells. The committee appreciated the thought and concern that has already been directed towards future prospects for the Department and for the unit team scientists and other personnel following retirement of the team leader. While encouraging these considerations, the committee also strongly supported the continued active involvement and full time contributions of the team leader as allowable for the foreseeable future.

Team: Macrophages and Development of Immunity

Team leader : M. Philippe Herbomel

- **Staff members:**

| | Past 1-09-2007/1-01-2011 | 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 | 5 |
| N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file) | 1 | 2 |
| N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file) ) = ITA EPST + I. PASTEUR including research engineers | 1,50 | 2,800 |
| 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 | 3 |
| N7: Number of staff members with a HDR or a similar grade | 1 | 2 |

- **Appreciation on the results:**

This group has made several ground breaking contributions to our understanding of the origins and migration pathways of various blood cell types, including the hematopoietic stem cell (HSC), during vertebrate development. The stem cell work has culminated in a Nature paper just published that not only finally shows the HSCs emerging from the arterial cells in the floor of the dorsal aorta, a major controversy in the field for many years, but also shows exactly how this transdifferentiation process occurs, thereby identifying a completely novel mechanism for an epithelium to mesenchyme transition. They were the first to describe a new site of hematopoiesis in the zebrafish, acting equivalently to the fetal liver in mammals, where the HSCs expand on their way to populating the thymus and the kidney, the site of adult hematopoiesis in zebrafish. Furthermore, they have described in beautiful detail the activities of both macrophages and neutrophils in the early embryo, identifying a clear difference between their activities in the circulation and on epithelial sheets. Furthermore, their discovery that neutrophils do not die after engulfing bacteria opens up possibilities for insight into inflammatory processes in the future. All this work has been published in good to excellent journals. In addition, the group took part in a EU funded screen for new genes involved in myelopoiesis and they have pulled out a large number of potentially interesting genes.

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

The international profile of the group is high. They were the first to apply leading edge imaging to this topic in zebrafish. There were 11 papers in which a member of the team was senior author and/or first author. Three of their five selected publications were selected for commentary and the latest one will almost certainly be selected, too. The PI is in constant demand to speak at international conferences and his staff scientists have also given talks. Dr. Herbomel has raised substantial external funds to supplement his Pasteur Institute funding, including prestigious Framework 6 funding from the EU.

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

The team spirit of the group appears to be very high. The enjoyment in their work is evident from all the people in the lab and from the desire to stay on in the lab by several of the postdoctoral fellows. Dr. Herbomel is very naturally a risk taker in his pursuit of the things that interest him. He organizes quality outside collaborators when he needs them. The group does not appear to need much from the department or institute apart from more technical support for their zebrafish facility, which is significantly understaffed by international standards.

- **Appreciation on the project:**

The group plans to further study their novel discovery of the 'endothelial to hematopoietic transition' (EHT) that gives rise to HSCs. They plan to carry out higher resolution imaging and molecular pathway analyses. They also plan to explore the stromal support and interactions that the various blood cells receive during their tour throughout the embryo. They also will carry out further studies of the innate immune response to bacterial and viral infections. These plans appear very likely to lead to continued quality publications for this group.

- **Conclusion:**

Overall the Committee felt that the work of this Team has been excellent and that it will continue to be so in the future.

Team : Epigenetic Regulation

Team leader : M. Christian Muchardt

- **Staff members:**

| | Past<br>**1-09-2007/1-01-2011** | 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 | 4 |
| N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file) | 2 | 1 |
| N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file) ) = ITA EPST + I. PASTEUR including research engineers | 1,200 | 2,200 |
| N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file) | 0 | 0 |
| N6: Number of Ph.D. students (Form 2.7 of the application file) | 1 | 2 |
| N7: Number of staff members with a HDR or a similar grade | 1 | 1 |

- **Appreciation on the results:**

The team has made important contributions in the last 4 years. There were 4 papers in which a member of the team was senior author and/or first author. Its 2006 publication describing links between the chromatin remodeling complex SWI/SNF and alternative splicing was a pioneering work that was followed by many other descriptions of links between chromatin and splicing. Its studies of the role of HP1 proteins in regulating chromatin remodeling and transcriptional activation are useful contributions in a competitive field. Its recent observation linking HP1g to alternative splicing represents an interesting merger between two of the main themes of the team that will further

establish its contribution to the domain of chromatin and splicing. Finally, the last results linking the peptidylarginine deiminase PADI4 to HP1-mediated repression in the context of multiple sclerosis represents an important contribution establishing the biological importance of histone citrullination. The work led to a fair number of good quality publications that are expected to have an impact in a crowded field.

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

The visibility of the team could be improved as it does not reflect the quality of the science produced. The team is however able to recruit excellent scientists and to raise funds. The team is associated with the European Epigenome Network of Excellence, which demonstrates its credibility in the field. The team has also many fruitful collaborations in particular within the Pasteur Institute.

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

There appears to be an excellent team spirit within the group. The team leader appears to manage the team in a clear direction and in a flexible manner. The group is enriched by three staff scientists that bring important expertise and contribute significantly to the quality of the research performed.

- **Appreciation on the project:**

The team is pursuing several interesting and promising projects. A major one aims at establishing a link between defects in HP1-mediated repression and multiple sclerosis. This is based on sound reasoning and promising results and this appears to be a feasible and important project. A second more risky, but highly interesting project, aims at establishing an in vitro system allowing the mechanistic analysis of the links between chromatin, transcription and splicing. This project relies on a recently recruited staff scientist that has the expertise needed to succeed. It will be important to monitor progress carefully on this line of research because of the associated risks. This project is coupled to an RNAi screen of chromatin factors affecting splicing that is also interesting but less risky. The balance between the two projects should be established clearly in the medium term when sufficient preliminary results will be obtained.

Another interesting project aims at establishing the genome-wide impact of the SWI/SNF complex on alternative splicing. It is indeed important for the team to establish firmly the general importance of this regulation to gain full impact of the pioneering work already performed. A project in collaboration with a structure group of the Pasteur Institute aimed at characterizing the contribution of RNA to nucleosomal structure might divert the energy of the team and take a lot of time to bear fruit. It seemed to the committee that the scientific question would be addressed much more efficiently if it involved collaboration with an external group with specific expertise in nucleosomal structure.

- **Conclusion:**

The team is pursuing research lines on epigenetic regulation and alternative splicing in mammalian cells that are highly relevant both to the global understanding of gene regulation and to the understanding of specific diseases. The team has made several important research contributions and the committee was convinced that the team will continue on this path with a high probability of exceeding their previous achievements. The strengths of the team are the quality of the data and of the expertise already gathered, and the balance between risky and less-risky projects. The weaknesses that could all be addressed are the reduced visibility of the team, the risk associated to some of the projects whose progress must be carefully monitored, and the lack of sufficient support in bioinformatics analyses of the data (both produced in house or available on the internet). This latter aspect would benefit from an evolution of the service offered by the bioinformatics platform of the Pasteur Institute.

Team : Molecular Biology of Development

Team leader : M. Jean-François Nicolas

- **Staff members:**

| | Past | Future |
|---|---|---|
| | **1-09-2007/1-01-2011** | |
| 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 | 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) ) = ITA EPST + I. PASTEUR including research engineers | 4<br>1 | 4<br>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 | 2 |
| N7: Number of staff members with a HDR or a similar grade | 1 | 3 |

- **Appreciation on the results:**

The team leader has been continuing a long-standing effort to study cell lineages during development, focusing on elongation processes. He has also begun to look at the evolution of this process, by comparing the results he has obtained in the mouse, the system he has used most extensively, to zebrafish and amphioxus. The research is highly original and very productive. The work is of exceedingly high scientific quality, and very well received in the developmental biology community. The work has resulted in high impact publications, in such top journals that include Developmental Cell, Nature Genetics, and Development. There were 7 papers in which a member of the team was senior author and/or first author. Dr. Nicolas has trained excellent students and postdoctoral fellows. Several of his students have moved to top developmental biology labs, where they have thrived.

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

The team leader is known internationally, and participates in international meetings, although perhaps not as many as other scientists in the team. Several postdoctoral fellows and PhD students were recruited internationally and seem to have performed very well. The oral presentations from the more junior members of the group were excellent, and they seem to have really mastered the field. Successful collaborations have been established both within the Pasteur Institute and several laboratories in France and internationally.

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

There seems to be an excellent team spirit within the group. There is no concern about this area. The group includes one staff scientist with very complementary fields of expertise (zebrafish and amphioxus). As for other groups, they could be encouraged to share this expertise through teaching, active participation in workshops and courses, conferences, etc.

- **Appreciation on the project:**

The project combines several different objectives involving 1) elongation of the renal tubules; 2) elongation of the hair follicle; 3) morphogenesis of the surface ectoderm; 4) elongation of neuro-mesodermal cells; 5) hair morphogenesis and stem cells; 6) cell lineages in amphioxus; 7) myotome morphogenesis in the zebrafish. These projects are based on clever cell lineage analysis using either a mitotic homologous recombination approach (the laacZ method) or a Cre recombinase based method. The project has provided major insights in developmental processes, and shown contrasting models of cell movement evolutionarily.

- **Conclusion:**

Overall appreciation: very positive, very original research. Weaknesses, points of concern: The group could really use its own confocal microscope. They use it extensively, and with the harvest time for amphioxus being extremely limited, there are extreme logistical difficulties in tracking cell lineages.

Team : Functional Mouse Genetics

Team leader: M. Jean-Jacques PANTHIER

- **Staff members:**

| | Past<br>**1-09-2007/1-01-2011** | 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) | 1 | 2 |
| N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file) ) = ITA EPST + I. PASTEUR<br>including research engineers | 5<br>3 | 4<br>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) | 6 | 4 |
| N7: Number of staff members with a HDR or a similar grade | 3 | 3 |

- **Appreciation on the results:**

This team has two main themes of research, the mechanisms of susceptibility to infectious agents, and the biology of self-renewal and differentiation of stem cells. The committee felt that the quality of the research was very good, with high significance for both projects. Dr. Panthier has also refocused significantly his research efforts, in response to comments from the scientific council. However, since he submitted his report before receiving these comments, the narrowed down focus was only apparent in the oral presentation, but not in the written report.

The committee was especially enthusiastic about the project on susceptibility to pathogens. This uses mouse resources available at Pasteur Institute that are unique in the world and that have resulted in the isolation of very promising candidate loci. The findings are very exciting with great potential for high impact on infectious diseases.

Although the group felt that the work on Notchless was promising for stem cell biology, the rationale for having both research directions in the same team was less clear. The team members appear to interact very well, technically this gives strengths in both genetics and functional areas, as well as assures financial stability. However the two

research projects are somewhat disparate and this leads to less cohesion, even after reducing the scope of the projects.

The work has resulted in a number of publications, in excellent journals. There were 27 papers in which a member of the team was senior author and/or first author.

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

The team leader is very well known internationally, and participates in numerous international meetings. The team leader has been very successful in obtaining research funds. About 22 research contracts have been obtained over the last 6 years from the main national funding agencies, the Pasteur Institute, and the European Union. Several postdoctoral fellows and PhD students were recruited. All of the oral presentations from the members of the group were excellent. Successful collaborations have been established both within the Pasteur Institute and several laboratories in France and internationally.

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

There appears to be an excellent team spirit within the group. In particular Drs. Panthier and Cohen-Tannoudji appear to interact very well. The group brings together a staff scientist with very complementary fields of expertise.

- **Appreciation on the project:**

The project combines two main objectives involving 1) mapping susceptibility loci for plague and Rift Valley fever; 2) clarifying the role of Notchless in hematopoietic stem cell and gut intestinal stem cell development, with an overall theme on stem cell development. This may or may not work in a Notch dependent pathway, but the approaches underway should provide significant results. The significance of both areas of research is outstanding, however as stated previously it is not entirely apparent how these two lines of research fit together.

- **Conclusion:**

Overall appreciation: very positive, very original approaches for mapping susceptibility loci. Stem cell biology research appears very promising. Weaknesses, points of concern: Despite an effort at focusing the research, the various lines of research may still not fit very well together.

Team: Molecular Genetics of Morphogenesis

Team leader: M. Benoit ROBERT

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

| | Past 1-09-2007/1-01-2011 | Future 1-01-2011 |
|---|---|---|
| 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) | 2,5 | 3,50 |
| 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) ) = ITA EPST + I. PASTEUR including research engineers | 1,75<br>0 | 1,75<br>0 |
| N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file) | 0 | 0 |
| N6: Number of Ph.D. students (Form 2.7 of the application file) | 1 | 1 |
| N7: Number of staff members with a HDR or a similar grade | 1 | 1 |

- **Appreciation on the results:**

The MSX homeodomain transcription factors play important roles during early development in many tissues. They have been exploited by this Team to enhance our knowledge of the development of the limb, the spinal cord and blood vessels in the head. In the limb, they have shown that these genes are critical for the apoptosis necessary anterior limb morphogenesis and thumb development. In the spinal cord, they have shown that these transcription factors drive expression of a transcription factor essential for a particular subset of interneurons, and that in this role they are mediating BMP signaling. In head blood vessels, they have shown that this gene family is required for recruitment of smooth muscle cells and vascular integrity. The group has generated an extensive array of impressive genetic tools, including knockouts and knock-ins to the Msx1 and 2 gene loci, that facilitate a detailed understanding of gene actions and offer promising tools for future studies.

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

The group has published at regular intervals in specialty journals that are widely read by the developmental biology community. There were 8 papers in which a member of the team was senior author and/or first author. The work is focused and directed specifically at the function of Msx homeobox genes in various organs and tissues of the body. Funding is provided by the Pasteur Institute, CNRS and the Association pour la Recherche contre le Cancer.

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

The Team has generated solid and compelling data using genetic tools that have been generated within the team with precision. Opportunities exist for future investigation of potential interactions of the Msx gene program with other signaling pathways studied within the department, including Notch and Pax.

- **Appreciation on the project:**

The team has demonstrated skill and expertise in the generation of genetically modified laboratory mice, and has used these reagents to identify new functions of known genes. The studies have focused on several organ systems and tissues, and perhaps the greatest advances have come from the studies of limb development. Potential for exciting new findings in neural cell fate specification and blood vessel development also is apparent, though it may also be necessary to focus in one or two areas in order to achieve increasing depth and fundamental insight.

- **Conclusion:**

Overall the Committee felt that the work of this Team has been relatively solid and steady, with a very clear focus on the function of Msx genes. In subsequent years, potential for increasing novelty and focus on new and exciting biological questions is possible which may allow for optimal advantage to be taken of clear expertise and skill.

Team : Drosophila Developmental Genetics

Team leader : M. SCHWEISGUTH François

- **Staff members:**

| | |
|---|---|
| N1: Number of researchers with teaching duties (Form 2.1 of the application file) | 0 |
| N2: Number of full time researchers from research organizations (Form 2.3 of the application file) | 3 |
| N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file) | 3 |
| N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file) ) = ITA EPST + I. PASTEUR including research engineers | 4,50 |
| 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 Team studies questions of cell fate specification, asymmetric cell division and stem cell self renewal using the fruit fly (Drosophila) as a model organism. The work focuses on the role of Notch signaling, which has been strongly implicated in stem cell biology and cell fate choices in numerous systems, including Drosophila where it was first described. While much is already known about Notch receptor signaling and the regulation and activities of Notch ligands, the Team continues to make substantive and innovative discoveries that have materially advanced the field. These discoveries have been described in a steady stream of high profile and high impact publications and authoritative review articles. There were 13 papers in which a member of the team was senior author and/or first author.

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

The Team leader directs an attractive research program with a track record and potential for recruiting some of the best trainees and scientists from around the world. The Team leader is an internationally highly respected scientist who has co-organized a prestigious Keystone Symposium and delivered scientific seminars around the world. For example, he has repeatedly been invited to the International Notch meetings held in Athens, Greece, which are considered among the leading meetings in the field. The Team has been successful in attracting appropriate funding to support the research program and continues to demonstrate productivity and innovation. This team has been active at the Pasteur Institute only since May of 2008, and interactions and collaborations with other research programs at the Institute are still evolving.

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

The Team represents a relatively small research group with strong leadership and clearly defined roles. The research program is, to a large extent, self-contained with the necessary tools and resources to continue to pursue exciting discoveries using the Drosophila system. Scientific presentations from group members suggested a vibrant and expert team who work collaboratively within an interactive environment. Collaborative interactions with laboratories outside of the Institute have provided important and substantive advances and a strong desire to share data and research tools was evident.

- **Appreciation on the project:**

The work in this team is characterized by the fearless investigation of important fundamental questions of stem cell and developmental biology that take advantage of the strengths of the Drosophila model system which include powerful genetics and single cell resolution. Although unifying themes permeate the research studies, a series of distinct areas of investigation are simultaneously underway. These include the study of the mechanism of lateral inhibition, mediated by Notch, in clusters of proneural cells which can become sensory organ precursor cells. A novel family of genes that modify Notch signaling have been discovered that are known as bearded genes, and these function to modify how Notch ligands are processed by neurulized, an E3 ubiquitin ligase. The group has used genetic screens in Drosophila to uncover a novel function for glycosphingolipids in the regulation of Notch ligand endocytosis and signaling. This discovery offers great potential for future productive studies to extend our understanding of Notch-mediated cell fate specification and patterning, and exemplifies the innovative potential of the group. Additional investigations suggest that Notch pathways may intersect with the apical cell polarity pathway (including crumbs) in previously unappreciated ways.

Another project focuses on the role of Notch in self-renewal and differentiation, including binary cell fate decisions, in intestinal stem cells. This project has potential to impact our understanding of stem cell biology, cancer and fate specification. Genetic screens and other approaches suggest that fucosylation of Notch may modify activity and may affect cell polarity, thus offering additional novel avenues for future investigations.

- **Conclusion:**

In summary, this is an outstanding research team that has been productive and which demonstrates outstanding potential for future growth and success. The work is characterized by a focused and logical approach that takes excellent advantage of the model systems and which studies timely and important aspects of stem cell and developmental biology. The committee considered the recent establishment of this research team as an outstanding addition to the Department, and continued strong support for this internationally recognized team was encouraged.

Team : Stem Cells and Development

Team leader: M. Shahragim TAJBAKHSH

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

| | Past 1-09-2007/1-01-2011 | Future |
|---|---|---|
| N1: Number of researchers with teaching duties (Form 2.1 of the application file) | 0,50 | 0 |
| N2: Number of full time researchers from research organizations (Form 2.3 of the application file) | 3,25 | 3 |
| 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) ) = ITA EPST + I. PASTEUR including research engineers | 3,10 | 2,50 |
| 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 | 3 |
| N7: Number of staff members with a HDR or a similar grade | 3 | 2 |

- **Appreciation on the results:**

This group was created in 2001 and has significantly shifted his research towards stem cell biology, to understand how tissues develop and regenerate after injury. The team is employing a number of cutting edge approaches to decipher the regulatory mechanisms operating during lineage progression of myogenic stem cells, both during development and for the adult resident stem population, the muscle satellite cells. The work is highly significant in regenerative biology and medicine. The work is of the highest scientific quality, and very well viewed in the myogenesis community worldwide. Although there have been relatively few (5) senior author publications, these have had considerable impact in the field. As a result, several recent papers have all been published in high impact journals (Cell, Genes Dev, Nature Cell Biol, Developmental Cell, Stem Cells). There were 17 papers in which a member of the team was senior author and/or first author. In addition, a significant number of manuscripts are either submitted or in preparation, so there is no concern whatsoever about the productivity of this laboratory. Last, the Team leader has written several prominent review articles that are very helpful to the field.

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

The team leader is internationally recognized, with many participations as invited speaker to conferences, workshops, and summer courses. Furthermore, he has been acting as organizer of several symposia and conferences locally and internationally. The team leader is highly successful in raising funds. About 20 research contracts have been obtained over the last 6 years from the main national funding agencies and the European Union. Several post-docs and PhD students were recruited internationally and seem to perform very well. Even the more junior members of the group took part in the presentations, and have obviously mastered the field as judged by the way they answered questions. A number of successful collaborations have been established both within the Pasteur Institute and several laboratories in France and internationally.

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

There seems to be very good leadership and management of the team, with weekly lab meetings, and personal follow-up of each individual. There is no concern about the overall team spirit and synergies within the group. The group includes three staff scientists with relatively complementary fields of expertise. They are encouraged to share this expertise through teaching, active participation in workshops and courses, conferences, etc.

- **Appreciation on the project:**

The project combines four different objectives involving (1) genetic regulation of the skeletal myogenic lineage, (2) asymmetric cell divisions and template DNA strand segregation (3) adult myogenic stem/progenitors and muscle regeneration, (4) identification of genes and small non-coding RNAs regulating self-renewal, stress response and muscle survival. Cumulatively, the project is anticipated to make significant inroads into the myogenesis stem cell field. Although the multitude of objectives might be considered ambitious, the team has a number of positive preliminary results which gives confidence that high quality publications will arise from this work. Ample funding has been obtained in particular through three FP7 networks, up to the next four years.

- **Conclusion:**

Overall appreciation is very positive.

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

Nom de l'équipe : *DROSOPHILA GENETICS AND EPIGENETICS*

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

Nom de l'équipe : *MOLECULAR MOUSE GENETICS*

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

Nom de l'équipe : *MOLECULAR GENETICS OF DEVELOPMENT*

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

Nom de l'équipe : *MACROPHAGES AND DEVELOPMENT OF 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 : *EPIGENETIC REGULATION*

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

Nom de l'équipe : *MOLECULAR BIOLOGY OF DEVELOPMENT*

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

Nom de l'équipe : *FUNCTIONAL MOUSE GENETICS*

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

Nom de l'équipe : *MOLECULAR GENETICS OF MORPHOGENESIS*

| 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 : *DROSOPHILA DEVELOPMENTAL GENETICS*

| 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 : *STEM CELLS AND DEVELOPMENT*

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

Institut Pasteur

Paris, 23rd April 2010

*CNRS: URA 2578*
*Bases génétiques, moléculaires*
*et cellulaires du développement*
*Dir. : Margaret Buckingham*

Reply to the AERES Visiting Committee

On behalf of the URA 2578, I would like to thank the AERES committee for the time and effort they gave to our review. We are very pleased that the overall evaluation was positive and appreciate their comments about the outstanding international reputation of our URA in the field of developmental biology. We also take note of pertinent comments on aspects that we shall try to improve.

On the general points about the URA in the overall appreciation we would like to clarify the following:

**Overall opinion** – "Restrictions on computer hardware acquisition" in fact reflect the Pasteur Institute's agreement with a company that rents computer hardware and provides useful technical support. Non Pasteur funds can always be used, or, with a well argued scientific case, Pasteur will waive this restriction.
Although "deficiencies in certain IP Cores" have been noted, the campus provides an excellent research environment.

Some team leaders wished to respond to specific points as presented below.

**C. Antoniewski** – International consortia in which the team participates include AKROSS.

**JF Nicolas** – Appreciation on the results: the number of papers in which a member of the team was senior author and/or first author is 8, not 7. We would like to add that in addition to the two methods mentioned in the document, our group is also using extensively 4D imaging (3D timelapses) and reconstruction of biological samples (hair follicles, embryos) as the basis of an *in silico* clonal analysis approach that complements RCA and GICL.
Appreciation on the impact…: In response to the comment about raising funds, we have participated in a number of European contracts which provided full financing until June 2009; other applications are ongoing and we are confident about future funding.

**B. Robert** – For the Conclusion, we already have had a reflexion on the evolution of the scientific projects. We regret that we did not succeed in communicating better the strategies we are setting up to build on our expertise and tackle novel and exciting biological questions.

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