Institut de biologie du développement et cancer

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Institute of Developmental Biology and Cancer

From the

University of Nice

January 2011

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Le Président de l'AERES

Didier Houssin

Section des unités de recherche

Le Directeur

Pierre Glorieux

January 2011

Research Unit

Name of the research unit: Institute of Developmental Biology and Cancer

Requested label: UMR CNRS

N° in the case of renewal

Name of the director: Mr. Stéphane NOSELLI

Members of the review committee

Committee chairman

Mr Olivier POURQUIÉ, University of Strasbourg, Illkirch, France

Other committee members

Mr Markus AFFOLTER, Biozentrum, Switzerland

Mr James BRISCOE, NIMR, London, Great-Britain

Mr Pascal DOLLE, University of Strasbourg, Illkirch, France

Mr Andreas FAISSNER, Ruhr-University, Bochum, Germany

Ms Laura JOHNSTON, Columbia University, New-YorK, USA

Mr François SCHWEISGUTH, Pasteur Institute, Paris, France

Mr Serge ROCHE, CNRS, University of Montpellier, Montpellier, France (CNRS)

Mr Jean-Marc REICHHART, University of Strasbourg, Strasbourg, France (CNU)

Observers

AERES scientific advisor

Mr Jean-Antoine LEPESANT

University, School and Research Organization representatives

Mr Stanislas TOMAVO, CNRS

Mr Jean-Marc LARDEAUX, University of Nice

Report

1 • Introduction

• Date and execution of the visit

The visit was conducted on January 17 and 18, 2011 and essentially took place in Nice at the Valrose center in the Centre de Biochimie where most of the Institute of Developmental Biology and Cancer (IDBC) teams are located. The overall organization of the visit was excellent. The committee listened first to a general presentation of the director and then all the group leaders presented their recent work and future projects in 20 minutes, followed by a 20 minutes discussion. Whereas the lab members of the presenting team leader attended the presentation, the committee requested the 20 minutes question period to be spent only in the presence of the group leader. The committee attended all the 18 presentations, followed by a short presentation and discussion with the University of Nice and CNRS representatives and then splitted in three groups for independent discussions with the technicians, the Statutory personnel (CR and MCUs) and the students and post-docs. Finally the committee had a discussion about the future federation between IDBC and the INSERM U636, with the current directors of the two units. The visit closed with a discussion with the future director S. Noselli and a closed doors discussion between committee members. The document prepared and presented to each member of the committee was found to be excellent in its presentation and content.

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

The IDBC was created in 2008 as a joint CNRS and UNS Unit originating from a complex series of fusions and reorganisations of the local scientific landscape. It currently contains teams located on the Valrose and Pasteur Campus but due to the retirement of some senior principal investigators and the decision of the Centre Antoine Lacassagne (CAL) to discontinue its relationship with IDBC, most of its groups will join the Valrose Campus where they will be located in the Centre de Biochimie and the Sciences Naturelles building. Renovation of research floors in the Centre de Biochimie and in the Sciences Naturelles building have begun but much remains to be done. Only the Team 5 will remain in the Pasteur campus in the tour Pasteur. Two other groups, currently occupying 700 square meters in the CAL, will be relocated in the Sciences Naturelles building where most IDBC teams should be regrouped after renovation of the building. Since 2008 a zebrafish facility (the first one in Nice) has been constructed and a high performance Ibisa imaging platform (PRISM) has been established. The IDBC currently counts 18 teams for a total of 184 staff. Since 2008, teams 3 and 6 have been integrated from the FRE3094 CNRS/UNS, and five young group leaders have been recruited (2 ATIPE, 1 ATIPE/Avenir, 1 professor UNS and 1 chaire d'excellence (CNRS/UNS). Four groups will not be renewed in the IDBC. The activities of the IDBC are essentially related to developmental and cell biology and signaling (teams 1, 2, 3, 4, 5, 7, 9, 11, 12, 13) and cancer studies (8 and 14) with however a significant component interested in physiology (6 and 10).

• Management team

The director of the Unit is Stéphane Noselli and he is assisted by a deputy-director. They recently recruited an IDBC project officer to help the management with grant applications.

- 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)	12	12
Number of full time researchers from research organizations (Form 2.3 of the application file)	37	37
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	16	20
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	36.10	38.10
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	9	
N6: Number of Ph.D. students (Form 2.7 of the application file)	33	
N7: Number of staff members with a HDR or a similar grade	27	27

2 • Overall appreciation on the research unit

- Summary

Research at IDBC was overall judged excellent and highly visible at the international level for a fair number of groups. The grouping of the teams on a single site and the future federation with the nearby INSERM unit U636 was perceived as a very positive move which should both increase the visibility of IDBC research and optimize access to resources for IDBC scientists. CNRS and UNS need to make sure that appropriate space and support is provided for this key reorganisation.

- Strengths and opportunities

In their majority, the IDBC group leaders are mid-career scientists and several of them are highly visible at the international level. This recognition has favored the recruitment of several outstanding young scientists who recently joined the IDBC as ATIPE/Avenir group leaders. The IDBC has been constituted by integrating several smaller structures to establish a larger biology institute. This trend has been perceived as a very positive move by the committee. The perspective of an association with the nearby INSERM unit U636 largely focused on mouse genetics and developmental biology within a federation, was also felt as a very positive action by the committee. This will increase the IDBC critical mass allowing to mutualize equipment and personnel by the two structures, and will ultimately allow the creation of a new institute called Institut de Biologie Valrose spanning two building (Sciences Naturelles and Centre de Biochimie) with 500 employees. The fusion of the two units into a mixed CNRS, INSERM and UNS unit seems a natural goal to achieve as it would provide the current IDBC with better access to mouse models and increase the potential sources of funding. The current leadership was judged excellent by the committee.

- Weaknesses and threats

A major weakness appears to be the current space allocated to IDBC since plans to relocate in the Sciences Naturelles (SN) Building the teams currently hosted in the CAL does not seem to be accompanied by a clear strategy by CNRS and UNS. Thus whereas the prospect of obtaining floors to host IDBC in the SN building to relocate the CAL teams and to recruit new teams appears to be feasible, a clearer commitment from CNRS and UNS with respect to the IDBC is important. Currently, access to mouse models which are critical for cancer and translational research developed at IDBC appears to be limiting. This problem might be solved with the federation and eventually fusion with the INSERM unit, however this will require careful consideration of resource allocation to ensure that adequate support is given to sustain the mouse facility. Another weak point of the Institute appears to be computing resources. With the anticipated growth of the structure this problem is expected to become more acute. While the efforts to organize a high-performance imaging platform was appreciated by the committee, core facilities in general were perceived as a weakness.

- Recommendations to the head of the university

The committee strongly recommends the funding bodies to commit for infrastructure support and renovation of the laboratory. Currently there is no visibility at this level and the ambitious reorganisation plans presented will strongly depend on the availability of appropriate lab space for new teams and core facilities. Furthermore, current efforts to develop strong core facilities and computing support must be encouraged.

- Production results

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	12
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	36
A3: Ratio of members who are active in research among staff members [(A1 + A2)/(N1 + N2)]	0.9795
A4: Number of HDR granted during the past 4 years	5
A5: Number of PhD granted during the past 4 years	29

3 • Specific comments

- Appreciation on the results

The research carried out at the IDBC is widely recognized at the international level. The institute has developed a very strong community in Developmental Biology, particularly in the Drosophila field with world-leading groups in highly competitive fields such as signaling or growth control. The research developed at IDBC is highly original and IDBC is clearly one of the leading centers in Developmental Biology in France.

The quality and number of publications are outstanding with a total of 331 publications since 2006 including 26 in journals with IF>10 in which an IDBC group leader is either first or last author.

Several landmark publications in various fields have been published in top-tier journals by IDBC teams. However, there is some heterogenity among the teams and this will be pointed out in more details in the report. Several IDBC group leaders are widely recognized internationally and frequently invited to present in scientific meetings.

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

The IDBC members have been awarded a number of prestigious awards including one ERC advanced , 2 EMBO membership, 7 ATIP/CNRS and one ATIPE/Avenir, 3 EMBO YIP, 1 Schlumberger Foundation and several scientific prizes, 1 CNRS Silver and 4 bronze medals, as well as a number of competitive grants including HFSP, EU.

Since 2008, the IDBC has recruited five highly promising group leaders, including several recipients of the competitive ATIPE grant. There are several foreign scientists among the IDBC PIs and all efforts are done to foster an international ambiance. About half of the personnel of the IDBC is non-permanent counting 31 post-docs and 30 students. Around 20 different nationalities are represented. The number of foreign students and post-docs varies depending on the groups and the recruitment of foreign scientists, while good compared to most French institutions, can still be improved.

The ability to raise funds is good with close to 3 million euros external funding raised by the Institute for an internal funding (CNRS-UNS) of around 1 million euros. Most of these external funds are provided from competitive grants from ANR, ARC, INCA, FRM, LNCC and FRM. Funding from EU amounts to 188 700 euros for 2010 which is not very high but should increase significantly next year with the ERC grant. Some Institute members have active collaborations with the private pharmaceutical industry which funds research projects.

The IDBC obtained a very competitive Marie Curie grant for an international PhD program in Developmental and cellular decision. This grant allowed them to recruit several high quality PhD students in a 4 year programme. The IDBC is also involved in a Labex grant application together with the Laboratoire Dieudonné de Matémathiques, and the Nice Chemistry Institute.

- Appreciation on the management and life of the research unit

The research Unit is headed by Stéphane Noselli with a deputy director. Strategic issues including recruitments are discussed in regular PI meetings and at the Laboratoy council which meets three times a year. The Institute provides one technician to each of the teams as well as free access to the PRISM imaging facility and support for animal house facilities. No overheads are taken on PI grants by IDBC, meaning that little funds are available for developing core facilities. Overall the quality of management was judged excellent by the committee.

Several initiatives aiming at developing scientific animation have been taken and include the organization of a prestigious IDBC lecture series (227 seminars since January 2006), IDBC retreats, an IDBC/INRIA meeting to promote interaction with the local community of bioinformaticians, as well as international meetings such as the EDRC 2009, 2 EMBO meetings, the SFBD/BSDB meeting.

56 masters students, 37 PhD students and 34 post-docs have been trained at IDBC since 2006. Among the 37 permanent scientists of IDBC, 20 hold an HDR and can therefore train PhD students. IDBC is hosting 3 professors and 9 assistant professors (MCU) with three of them being group leaders.

The meetings of the committee with students and post-docs, technicians and statutory personnel were held in a very positive and interactive spirit. Collectively the students and post-docs consider the IBDC as a very good institute to learn and practice science, and appreciate the very good scientific and relational environment and interactions.

Some issues and ideas for improvements were discussed - as a matter of fact the most significant ones were beyond the institute level and concerned organizational problems at the University, as well as regulations, status and attractiveness of research positions in France. With respect to scientific animation and life of the institute, students/post-docs appreciate the fact that seminars, meetings, and daily work language is English.

They consider that there is a good organization of the internal/external seminars schedule. It was pointed out that some individual teams are more "visible" nationally and internationally, than the institute as a whole. They also feel that locally, the visibility and attractiveness of the institute could be improved at the level of undergraduates (in particular, there are relatively few candidates for undergraduate lab rotations "M1-M2" in the institute). This could be improved for instance if PIs had opportunities to give lectures, tutorials or practical teaching already at the undergraduate (M1 or below) level. Students also pointed out a number of problems at the level of the University administration, some quite unacceptable. This may particularly affect foreign students.

One issue raised is the splitting of the institute between different sites, which creates practical problems for experiments involving transfer of samples between sites, and hinders daily interactions between certain groups. The lack of a facility (e.g. small cafeteria with vending machines) for informal reunions, discussions and breaks, was pointed out. Presently the institute does not have a students/post-doc board that may organize animation, events, and provide advice to candidates or newcomers. The technicians (ITA) were concerned by the future of IBDC and particularly by its steady growth, which impacts the core resources and facilities of the institute such as administration, information technology, imaging. It was also pointed out that some rules of the French system, in particular the one limiting the numbers of years one can serve under "short-term contracts", had a disruptive effect on employee(s) within the institute. In particular, this applies for 30% of the ITA who are on short-term contracts.

- Appreciation on the scientific strategy and the project

The scientific strategy and the project for the next four years presented to the committee was in general considered excellent with several cutting edge projects presented by the group leaders. The policy of general resources allocation was also deemed satisfactory. Notably the efforts to set up high-performance facilities such as the PRISM imaging platform were appreciated by the committee and are to be encouraged.The strategy of attempting to regroup most of IDBC research teams in one single location in the Valrose campus and to create a federation with the INSERM U636 was enthusiastically welcomed by the committee. More funds should be secured by CNRS and University to allow this transition that will undoubtedly lead to the emerging of a strong actor in the French and international scientific landscape.

4 • Appreciation team by team

Team 1 - Polarized growth in yeast
Team leader - Robert ARKOWITZ

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	
N7: Number of staff members with a HDR or a similar grade	2	

- Appreciation on the results

The team leader has been continuing a long-standing effort to dissect the roles of small G proteins in polarized growth in yeast, focusing on Cdc42 and related Rho G-proteins in both S. cerevisiae and C. albicans. Amongst other findings, the group has shown that Cdc42 and its activator Cdc24 play a critical role in cell-cell fusion during yeast mating. The group also identified and characterized a Rac1 signaling pathway required for invasive filamentous growth in C. albicans. This work has been more recently extended to the study of phosphoinositides in S. cerevisiae. Finally, a more systematic analysis of the C. albicans kinome has been initiated as part of an international collaborative project. This screen identified three genes of interest.

- 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 known internationally and participates in international meetings. The team leader was also coordinator of an international ERANET pathogenomics project and co-coordinator of an EU Marie Curie grant for an international PhD program in Developmental and Cellular Decisions. The work has resulted in several papers published in good journals such as Mol. Biol. Cell and J. Biol. Chem. There were 6 original papers and 3 reviews in which a member of the team was senior and/or first author. Two very promising collaborations have been established. These collaborative projects have received good level of funding from competitive sources. The team is small but can attract PhD students and post-docs.

- Appreciation on the scientific strategy and the project

Since the team will remain relatively small, sensible strategic decisions have been taken to focus the work on: i) the role of phosphoinositides in S. cerevisiae and C. albicans; ii) the role of Gbeta phosphorylation in pheromone gradient sensing (collaborative project); iii) and the genetic analysis of the hits identified in the systematic analysis of the C. albicans kinome (collaborative project). However, studies on Cdcd42 regulation and function will no longer be pursued.

The phosphoinositides project is solid and will yield interesting information. The Gbeta project is very interesting and lends itself to quantitative studies. The combination of two yeast systems is clearly a strength : C. albicans displays spectacular morphogenesis that is great for live imaging, photoactivation studies, and gradient quantification but is diploid whereas S. cerevisiae is haploid and therefore great for genetics.

- Conclusion

— Summary

The team has very solid results in fields of major interest with the initiation of promising collaborations

— Strengths and opportunities

This is a rather small but well supervised group. The project is interesting with the possibility to make major impact.

— Weaknesses and threats

Since the research fields are competitive , it is important to try to keep touch with the rest of the field, and eventualy think of enlarging the group somewhat.

— Recommendations

Concentrate on issues of central interest to the group, profit from uniqueness of combining C. albicans and S.cerevisiae.

Team 2 - Post-transcriptional control of axon growth and guidance in Drosophila

Team leader - Florence BESSE

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	
N7: Number of staff members with a HDR or a similar grade	0	

- Appreciation on the results

This is a recently established group by a newly independent investigator who has published two papers in high impact journals (J. Cell Biol. and Genes & Dev) during her post-doctoral studies at the EMBL.

The molecular mechanism by which growing axons respond to guidance cues is an important and topical issue. The recent evidence that post-transcriptional mechanisms and the subcellular restriction in the translation of mRNAs play a role in this process has prompted renewed interest in the subject. Team 2 proposes to address the mechanism of axonal targeting and translation using Drosophila mushroom body neurons. This has relevance to the development of the nervous system and more broadly in the field of cell biology. The group has obtained encouraging preliminary data that a factor implicated in mRNA transport is required for axon growth. They have also identified putative target mRNAs for this factor. In addition the group has established a live imaging preparation that allows imaging of axon growth and ribonucleoprotein particle transport.

- 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 has been very successful in attracting start-up funds for the lab. She has also recruited researchers to her lab and appears well positioned to make progress towards the aims of her programme. Relevant collaboration with a bioinformatician has been established and the imaging appears to be an ongoing collaboration with the team leader's previous lab at EMBL.

- Appreciation on the scientific strategy and the project

The questions addressed by this programme are significant and of broad interest to cell biologists. The use of Drosophila genetics together with cutting edge imaging is a strong combination and the system studied provides a distinct niche to this programme. In particular the in vivo genome wide screen for the function of mRNA binding proteins is a strength of the proposal. The preliminary data suggest that the aims of the project are feasible and attainable.

One question that the team leader will need to address is whether the function of the proposed Imp targets, which is assessed by RNAi knock-down, actually depends on the regulation by Imp. Testing the functional relevance of the proposed Imp binding motifs would optimally require genomic rescue experiments of mutations disrupting the proposed target genes.

- Conclusion :

The team leader has successfully begun to establish a lab and independent research programme. The preliminary data places the group in a strong position to make significant contributions to the field in coming years. The project has great potential to deliver new insight into a fundamental aspect of biology. However, the IBDC should ensure that the team leader has the necessary capacity to perform the imaging necessary for her project in-house.

Team 3 - Membrane proteins, transport, signaling, pathologies

Team leader - Franck BORGESE

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	7	7
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	
N7: Number of staff members with a HDR or a similar grade	5	5

- Appreciation on the results

The major theme of Borgese's lab is the study of the Sig1R membrane protein, the function of which is still unknown. Functional interactions between this protein and the Patched receptor of the hedgehog pathway are also under investigation by this group. One project has made significant contributions to the isolation and biochemical analysis of the Hedgehog receptor proteins involved in this pathway.

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

The pace of progress seems insufficiently dynamic considering the competitiveness of the field. The team lists an overall record of 23 manuscripts that are published or in press. Of these, 10 have been issued under the responsibilities of Borgese and two other team members. Publications in Blood (1) and J Biological Chemistry (2) represent the most prominent publications with regard to the impact.

Collaborations with external partners have been developed, but this axis of activities could and should be emphasized further.

- Appreciation on the scientific strategy and the project

The present project resulted from the fusion of three individual projects. So far, the interactions between these groups have not yet translated into joint publications with one exception. The expertises comprise the analysis of membrane proteins, in particular Sig1R, the study of channel activities and the Hedgehog-signalling pathway.

The receptor Sig1R is the central and unifying topic of the different themes of the present project. It is expressed on all membrane systems and may serve as a useful tumour marker in some cases. The functions of Sig1R remain, however, poorly understood. Diverse roles in channel function, cell-substrate adhesion and the Hedgehog pathway are taken into consideration. At present, the major line of investigations has not definitively been defined.

Because of the uncertainties linked to Sig1R function the project design was found to lack focus. Some of the projects seem to be motivated by the formal fusion of project groups rather than by scientific logic. The committee also came to the view that the project should place more emphasis on in vivo functional studies, e.g. by including knock-out models for Sig1R and, possibly, aspects of the Hedgehog pathway regulation.

- Conclusion :

— Summary

The projects which result from the fusion of three themes from three independent groups, needs more focus.

— Strengths and opportunities

The main topic, i.e. the study of the Sig1R receptor, is clearly of interest knowing that its function is still unknown. Patched function is also an important and competitive topic.

— Weaknesses and threats

The link between the two major themes (Sig1R and Patched) resulting from the fusion of two exisiting teams was not obvious. Hedgehog signaling is an extremely competitive field and the assets of this team in this competition were not evident. The publication level was also average for a fairly large group.

— Recommendations

A better integration of the projects will be necessary in order to be competitive in their field.

Team 4 - Gene-environment interactions in development and evolution

Team Leader - Christian BRAENDLE

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	
N7: Number of staff members with a HDR or a similar grade	2	2

- Appreciation on the results

This group uses C. elegans to determine the molecular mechanisms that underlie phenotypic robustness. The PI has been quite productive during his previous post-docs with 4 first-author primary research publications in high impact journals (Dev Cell, PloS Genetics, Current Biology, Heredity), 4 reviews (Current Topics in Dev Biol, Current Biology), and a book chapter (Oxford U press). Overall, the team leader's track record 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

The PI was appointed to the IBDC at the end of 2008, and has assembled a team that includes one CR1, 2 PhD students, and an INSERM DR2. He has obtained funding from several sources, including an ATIP start-up package and a prize from the FSER in 2009, as well as a grant from the CNRS as co-PI with two external collaborators. The group's visibility has been increased by several invitations to speak at international meetings. The PI has established collaborations with several international researchers in France, Europe and USA.

- Appreciation on the scientific strategy and the project

The team leader proposes a conceptually innovative project that aims to understand how genetic regulation is influenced by the environment, and how adaptations to changes in the environment evolve. The proposed work focuses on the formation of C. elegans gonads, an ideal system because it is genetically and molecularly well characterized, easily scored and a critical target of evolution.

Three approaches are proposed. In the first, animals will be subject to different environments and the plasticity of the germline assessed and characterized, and linked to reproductive success. Second, reproductive plasticity will be assessed in several different species of nematodes to examine evolutionary variation. Third, direct evolutionary studies will be performed, in collaboration with a group at the Gulbenkian Institute in Lisbon, Portugal. The approaches are straightforward and well focussed. The project is wide in scope, but the combination of expertise of the team leader, strong team and collaborators, and use of an outstanding model system, all predict success.

The project is clearly outlined, with solid background and creative prospects combined with good international collaborations. The team leader is considered an outstanding addition to the IDBC.

Team 5 - Stem cells and differentiation

Team leader - Christian DANI

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	3	3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	5	5
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)	3	3
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	2	
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	
N7: Number of staff members with a HDR or a similar grade	5	5

- Appreciation on the results

This is a large, well-established research group. The main focus of the team over the last quadriennium has been to dissect the molecular and cellular mechanism of adipocyte differentiation. This is an important topic with foundations in developmental biology but wide ranging implications for translational approaches. The increasing importance of obesity and metabolic diseases in European countries has focused attention on this subject.

The team has significantly contributed to our understanding of the molecular mechanisms underlying adipocyte differentiation using a combination of assays in embryonic stem cells and a cell line previously generated by the lab. In addition, they have reported the surprising and novel finding that some adipocytes are derived from neural crest cells – a neuroectoderm derivative. Finally, the group has investigated the differentiation of myocytes and adipocytes in skeletal muscle, a topic that has particular relevance to muscular dystrophies.

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

The PI is a recognized leader in the field and his team has produced a large number of publications and patents and they have been successful in raising academic and industrial funding for their research. This success has included participation in international networks of researchers and these will undoubtedly add value to their research efforts. In addition the team has initiated or participated in the clinical translation of some of their research findings.

Overall the team appears to have made excellent efforts to maximize the impact of their research.

- Appreciation on the scientific strategy and the project

The main theme of this research programme is highly significant and of potential high impact. The programme has the potential to provide new insight into adipocyte biology and information of direct relevance to therapeutic translation.

The track record of the team and their recent novel findings are a clear strength of this team. The diversity of the projects has the potential to provide fundamental insight into important biological problems and generate clinically applicable knowledge.

- Conclusion :

— Summary

The team has significantly contributed to our understanding of the molecular mechanisms underlying adipocyte differentiation.

— Strengths and opportunities

The PI is a recognized leader in the field and his team has produced a large number of publications and patents and they have been successful in raising academic and industrial funding for their research. This is an exciting and fast moving field and this team is well placed to exploit the translation benefits of the research.

— Weaknesses and threats

This is a broad programme and it will be important to keep the research focussed.

— Recommendations

The track record of the team and their recent novel findings indicate that this team should continue to receive the full support of the IDBC.

Team 6 - Circadian system biology

Team leader - Franck DELAUNAY

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	3	3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	
N7: Number of staff members with a HDR or a similar grade	2	2

- Appreciation on the results

The team is interested in the molecular control of the circadian clock and its link with the cell cycle in peripheral organs. They use the liver as a model system to identify molecular pathways through which clock genes control key physiological processes. Genome wide transcriptome analysis has been performed to identify circadian oscillating genes in liver, and in depth functional analyses have focused on key regulators such as the cell cycle inhibitor p21 and the Kruppel-like factor KLF10. Work from this group contributed to current models linking the circadian clock to the activity of cell cycle genes. The group has also been involved in several collaborations with international expert teams, which led to additional discoveries on the involvement of nuclear receptors (PPAR alpha and ER beta) as targets and/or regulators of circadian clock genes.

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

The team is recognized internationally. This work led to a dozen of scientific publications over the period of review, of which 4 primarily report the team's work, all published in well ranked - albeit not in top impact factor - journals (Mol. Cell. Biol., J. Biol. Chem., etc). The PI is invited to national and international meetings and workshops, and both the PI and team members largely participate to teaching activities at the University of Nice and as invited lecturers for other Universities. They have been successful in raising funds, both nationally and internationally through two FP6 programs. The team leader also has management and administrative responsabilities, formerly (2008-2010) as director of a CNRS laboratory (FRE3094) and presently as director of the Life Sciences department of the Faculty of Sciences.

Despite this international recognition and an involvement in teaching activities, it is surprising that the team hosts currently 1 Master student and no PhD students. Post-docs appeared to have been recruited nationally, rather than internationally.

- Appreciation on the scientific strategy and the project

The research project is well laid out and involves an ambitious combination of experimental (mRNA profiling, ChIP, RNA interference) and in silico global approaches to characterize regulatory networks linking cell cycle regulators to the circadian clock. The cellular models to be analyzed have been essentially validated through previous work. Collaborations are in place to ensure access to the relevant circadian clock mutant murine models. As the experiments will be performed on primary cell lines (synchronized MEFs and hepatocytes) from clock mutant and/or reporter mice, one major challenge will be to demonstrate that the identified networks are indeed operating under physiological conditions in real life.

Another aspect of the project will be an in-depth study of the role of KLF10 in circadian regulation in relation to feeding behavior. This will involve generation of tamoxifen inducible, liver specific, mouse mutants. The required conditional/transgenic lines are available from collaborating teams, and the planned metabolic and molecular studies do not raise any concern about feasibility.

- Conclusion :

— Summary

The team has capitalized on its significant work on the regulation of several circadian regulators. It is definitely in a good position both with respect to its personnel and resources to carry out the research program.

— Strengths and opportunities

Establishment of a strong network of international collaborators, and comfortable current funding, are clear assets for the future. One of the major axis of research involves global profiling approaches, whose outcomes are open ended and offer the potential for novel discoveries in circadian regulatory networks.

— Weaknesses and threats

Global analysis of the various profiling approaches, and prioritization of the gene networks to be functionally investigated (especially in the whole animal, rather than in cultured cells) may be challenging. International visibility and publication standards could be improved.

— Recommendations

Ideally the team should host and train more students, especially since it includes five permanent scientists, three with teaching positions. Recruitment of foreign post-docs could also be beneficial.

Team 7 - Endocytic trafficking and asymmetric cell division

Team leader - Maximilian FURTHAUER

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	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	0	0

- Appreciation on the results

The team leader has published a number of important papers in the fish and the fly system as a PhD student and a postdoc. Both his work on zebrafish and flies are very well cited. His training in these two developmental model systems is uncommon and should allow him to ask original questions using one or the other of the two systems, depending on available tools and feasibility.

- 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 just started his laboratory a little more than a year ago and it is therefore too early to comment on the work performed since he started his independent group at the IBDC. The fish facility is now up and running and his group consists of three people.

- Appreciation on the scientific strategy and the project

The group plans to study the role of membrane dynamics in signaling in animal development. Although his aim is to study similar aspect of development both in flies and in fish, he intends to concentrate on the fish work in the next two years. His lab will study the role of the ESCRT complex on cilia formation, as well as the apical-basal transport of Delta ligands in the neuroepithelium. This is a sensible decision. Great effort should be made to do the work in the most rigorous manner, aiming at using mutants rather than MO technology. It is important that the very first papers of the group are of top technical quality, since this is key for the future positioning of the group in the respective model community.

- Conclusion :

Overall the Committee felt that the team leader is in an excellent position to combine genetics with cutting-edge live imaging of developmental processes to address novel cell biology questions.

Team 8 - Death receptors signalling and cancer therapy

Team leader - Anne-Odile HUEBER

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	7	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1.5	1.5
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	3	
N6: Number of Ph.D. students (Form 2.7 of the application file)	5	
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

This middle-sized team is focused on the molecular characterization of FAS receptor signaling. The PI has made several significant observations in this domain, specifically on the role of plasma membrane receptor partitioning in the initiation of cell death signaling. The biological relevance of these observations in a physiological or a pathological setting has not been investigated. The team has been very productive these last 4 years, including 14 main publications signed in a senior or co-senior position and continues to publish regularly in very good journals of molecular and cellular biology (4 Cell Death and Diff, 1 EMBO J, 1 Blood, 1 PNAS). Besides, the PI has hosted several PhD students during the last 4 years and most have published as a first author, highlighting the good capacity of the PI to lead PhD students. However, no PhD student is currently involved in the team.

- 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 very good as a whole. The PI has established several national partnerships and the team is also involved in translational projects in collaboration with the hospital locally. An important strength of the team is the capacity of the PI to obtain grants, which allowed the recruitment of several post-docs and technicians as well as a secure accomplishment of the research programme. However the visibility of the research team at the international level could have been improved by, for example, attending international meetings.

- Appreciation on the scientific strategy and the project

The project lies in the continuation of the past research activity but aims at deciphering a poorly understood and non-apoptotic role of FAS in colorectal cancer (CRC). The project is well focused and is of very good quality as a whole. However it raises several concerns that have been partly clarified during the interview. The investigation of FAS signaling in appropriate animal models may address some of these issues and would bring valuable insight into the role of this receptor in CRC tumorigenesis.

- Conclusion :

— Strengths and opportunities:

The PI has been successful in obtaining grants on an unexpected and interesting role of FAS in colorectal cancer.

— Weaknesses and threats:

In vivo approaches that would give important information on the role of FAS in colorectal cancer are missing. Many responsibilities of the PI outside the laboratory may affect a secure accomplishment of the research program.

— Recommendations

A collaborative work on the role of FAS signaling in CRC animal models would certainly increase the scientific quality of the project.

The project displays several strengths in regards to the role of FAS signalling in solid cancer, the translational research in the overall project and the success in grant acquisition. Addressing the role of FAS in well established animal models of intestinal tumours would however strengthen and expand the strategy chosen.

The committee also noted that the PI is burdened with many responsibilities outside of her laboratory.

Team 9 - Dynamic exploration of homeobox gene functions in the mammalian

Team leader - Thomas LAMONERIE

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

This team relocated to IDBC in 2009 after recruitment of the PI as a Professor at the University of Nice. Work of the team focuses on the function of the transcription factor Otx2 in the central nervous system. They have generated mouse transgenic lines that allow the controlled, conditional knock-out of Otx2 and/or the tracing of the Otx2-expressing cell lineages in embryonic or adult tissues. Using these animals they have characterized the time periods during development during which Otx2 is required for various functions. In addition the team has identified a function for Otx2 in posterior cerebellum and a possible novel origin of the granular neurons in this region. Finally the authors have also found that deletion of Otx2 in the adult retina leads to a progressive degeneration of photoreceptor cells neurodegenerative phenotype. As mutations of Otx2 are implicated in retinal degenerative diseases in human, this offers an interesting animal model for functional studies.

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

Although the research is highly significant and deals with important developmental regulatory processes, its impact is somewhat limited by the relatively small number of recent publications. The participation of team members to international meetings is recommended to advertise their work and strengthen their visibility with respect to developmental biology/neurobiology, and eye research communities. The PI has been successful in securing some external funding for their research. Now that the team is established in Nice one would expect further external funding should be forthcoming in the next few years. As the team has been recently established at the IBDC, it is too early to comment on its attractiveness in terms of recruitment of personnel.

- Appreciation on the scientific strategy and the project

The main research programme is addressing important and significant questions. The proposed future projects are focused and develop naturally from the previous findings of the team. The development of the proposed transgenic lines will be of use to this team as well as their international collaborators.

An issue that the proposal should address is the question of the level of Otx2 expression. The endogenous levels of Otx2 are clearly important for normal function since heterozygous phenotypes are well documented. This raises the question of whether the transgenic expression line for conditional overexpression (using the Rosa26 locus) will provide an appropriate amount of Otx2 expression. It also suggests that Otx2 will have different targets depending on the level of expression. This needs to be taken in consideration for the molecular studies of Otx2 targets that are proposed.

It is unclear, from the information provided, how feasible the transcriptomic and ChIP experiments will be. The proposal suggests using tissue from mutant mouse lines. This raises questions about whether the amount of material will be sufficient and whether the complexity of cell types in the samples will make the analysis difficult.

Nonetheless, the project has strong potential for further discoveries on the mechanisms of Otx2 function in development and disease, for instance in cerebellum precursor cell populations where the involvement of this gene in tumoral transformation will be directly investigated. Funding sources may be an issue, as the project will involve quite large mouse numbers; presently the team is mainly funded by several modest contracts. For related reasons personnel may also be limiting. The team is currently operating with three PhD students under direct supervision of the PI.

- Conclusion :

— Summary

The PI has developed a solid research program within 2 years of its move at the IBDC, and had a strong personal involvment in training and mentoring, the team being mainly composed of PhD students. The research project is addressing important and significant questions. It is well focused and logically follows current lines of investigation.

— Strengths and opportunities

The system the team studies and the transgenic lines created provides them with a unique approach to study the function of an important transcriptional regulator, in the context of development and tumorigenesis. The research topic and the approaches used should also be attractive for future recruitment of personnel.

— Weaknesses and threats

State of the art molecular approaches – transcriptional profiling and chromatin immunoprecipitation on highly limiting biological material – are a major part of the project. It is important that the feasiblity of these are carefully considered and the design of the experiments take into account foreseeable limitations. Funding of the research could become an issue, as the team is currently funded by several modest contracts. International visibility could be further improved, by participating to high level symposia or giving invited lectures.

— Recommendations

The team leader is strongly dedicated to research and doctoral training - three PhD students being currently trained under his supervision. However, these efforts could eventually be jeopardized considering the additional load of teaching and administrative activities as a full professor. Recruitement of a permanent researcher, foreseen through the possible opening of an assistant professor position, will be critical both for scientific progress and to ensure a high level in doctoral training.

Team 10 - Growth and Development in Drosophila

Team leader - Pierre LÉOPOLD

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	5	5
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	
N7: Number of staff members with a HDR or a similar grade	2	2

- Appreciation on the results

The PI is a highly regarded leader in the field of developmental control of growth in response to environmental cues, specifically in the area of control of the "developmental clock" linked to nutrition. The team uses Drosophila as a model system to study growth control with state-of-the-art genetic and imaging approaches. The team has made several contributions of landmark quality to the field, which have been published in high profile journals (6 primary research papers, 2 Cell Metabolism, 3 Developmental Cell, 3 reviews, Science, Cell Metab, Current Biol and a Book chapter, an additional review having been co-authored in Nature). The work of this team can clearly be considered as cutting-edge science of the highest quality.

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

The previous work of this team is of huge impact and international visibility, documented by the above-summarized publications and multiple invitations to speak at international and national conferences and institutions for the PI. The team organized three important meetings in Nice and has numerous collaborations in Europe and USA. This international status has been recognized by strong financial support, among which an ERC advanced grant. In the field of "developmental control of Growth", the contribution of this team to our current status of knowledge can be viewed as among the top groups in the field.

- Appreciation on the scientific strategy and the project

This team has outlined projects clearly based on results emerging from previous work. The projects are original, based on several genetic screens that are highly promising and should lead to important results in the field. Another aspect concerns more challenging projects including proteomic approaches and biochemical purification steps aimed at the identification of the "fat body factor", a circulating factor that is produced by the fat body and appears to couple nutrition to control of the rate of growth. This is a highly promising project based on excellent past work with documented achievements record. The research group has been highly productive with solid local, national and international collaborations. The prospects are clear with strong, competitive, hypothesis driven but creative and cutting-edge research.

— Summary :

This is an outstanding team producing cutting-edge science at the top international level.

— Strength and opportunities

The team produces cutting-edge science of the highest quality using full power of fly genetics. The ERC advanced grant should help to develop the team by recruiting Post-docs and students.

— Weaknesses and threats

There is a lack of recruitment of good PhD students from the Nice University and region. Proteomic approaches and biochemical purification steps is really challenging in the fly model.

— Recommendation

Continue to produce the same quality of science.

Team 11 - Epithelial morphogenesis and left-right asymmetry in Drosophila

Team leader - Stéphane NOSELLI

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	4
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

Over the past five years, the group of Stephane Noselli has made major progress along the three lines of research they pursue using Drosophila as a model system, i.e. dorsal closure, border cell migration and Left/Right asymmetry. In particular, the group has pioneered the study of L/R asymmetry, using both genetic approaches with the identification of the role of Type 1D unconventional myosin in L/R asymmetry and live imaging approaches with the direct observation of genitalia rotation during pupal development. The group has also made the intriguing and unexpected observation that, specific leading edge cells, which they called 'mixer cells' can switch compartment identity during dorsal closure of the embryo.

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

The group is internationally very well recognised. The work on JNK signalling has generated international interest, and so has his most recent work on L/R asymmetry in gonad formation. There were 9 original papers and 4 reviews in which a member of the team was senior and/or first author. Most of these papers were published in journals of high impact (Nature, PLoS Biology, Development, Current Biology, etc.). The work is of outstanding scientific quality, and it is expected that his group will again publish in the top scientific journals in the years to come. The team leader has raised substantial external funding from various national sources. The group attracts students and post-docs, mostly French.

- Appreciation on the scientific strategy and the project

The new projects propose to gather more insight into the three processes studied in the lab. The discovery of mixer cells in the dorsal epidermis will be followed up by trying to understand the underlying cell biology (cell re-determination, cell intercalation, contribution to dorsal closure, …). The border cell migration project has gained more momentum and a number of genes isolated in a screen will now be further characterized. Concerning L/R symmetry, another genetic screen has been undertaken to identify modifiers for MyoID interacting genes, and interesting results are expected upon identifying and characterizing the corresponding genes.

- Conclusion :

— Summary

The team leader has put together an excellent and very productive group. Stephane Noselli has maintained a highly productive group over many years, despite his time-consuming job as an acting director of the Institute, which is quite remarkable.

— Strengths and opportunities

This a well supervised and organized group with expertise in fly genetics and avant garde technologies used in this field.

— Weaknesses and threats

Thera are any different projects, but the research focus has already been reset to hinder too much diversity.

— Recommendations

Go on with the same vigor as in the past, try to cristalize out the most interesting questions to be addressed regarding the mixer cells.

Team 12 – Role of basement membrane structural components in morphogen signaling in Drosophila

Team leader - Sandrine PIZETTE

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	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)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	
N7: Number of staff members with a HDR or a similar grade	0	0

- Appreciation on the results

The team leader formerly worked as post-doc with Team 13 leader (2006-present). Part of her post-doctoral studies investigated the regulation of a morphogen gradient in Drosophila ovaries. This work led to one first-author publication in Development for which the team leader is the corresponding author. She also co-authored another paper in Developmental Biology as well as one review. Overall, the team leader's track record is good.

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

S. Pizette has very recently been appointed as an MCU (assistant professor) by the University of Nice and recruited as a team leader at the IBDC. She is just beginning to recruit the members of her team and to apply for external funding. Thus, these aspects were not evaluated. However, the committee views favourably that Dr. Pizette has been appointed to a chaire d'excellence as MCU, which will leave more time for research.

- Appreciation on the scientific strategy and the project

The team leader proposes an ambitious and broad project on the interplay between the composition, structure and function of the basement membrane and the activity of morphogens. This interplay will be investigated in the Drosophila wing imaginal discs as a model system. This complex issue is not novel but has remained relatively poorly explored. Functional (genetics), structural (electron microscopy) and expression studies will be combined to address whether and how the basement membrane regulates the activity of various extracellular signaling molecules of the Wnt, TGFbeta and EGF families.

Two complementary strategies are being proposed, one based on a comprehensive analysis of the spatio-temporal changes in basement membrane, the other based on the functional analysis of a specific basement membrane component. These studies should shed light on the role of the basement membrane on morphogen activity and, conversely, on the regulation of basement membrane genes by morphogens.

The team leader is in a good position to establish an independent line of research. The strong research experience of the team leader in fly genetics and developmental biology makes it likely that this research will produce interesting and novel findings. However, considering the relatively large scope of the project, the potential complexity of the addressed issue and the initial small size of the group, prioritization will have to be made to ensure steady progress. The team leader might consider complementing in vivo studies with biochemical approaches that investigate possible molecular interactions between morphogens and basement membrane components.

Team 13 - Signal transduction and control of morphogenesis in Drosophila

Team leader - Pascal THÉROND

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	
N7: Number of staff members with a HDR or a similar grade	2	2

- Appreciation on the results

A detailed understanding of the molecular and cellular mechanisms of Hh signalling is of fundamental importance. Such an understanding will illuminate basic principles of embryonic development but at the same time provide knowledge that will help in the development of therapies for diseases in which Hh signalling is deregulated. This group has made major contributions to our understanding of the hedgehog signalling pathway, a very competitive field of research. The team has firmly established its reputation as a leading research group in this field. As an international comparison, the publication output of the group is equivalent to other leading groups in this field and there have been several publications in high impact journals over the last 4-5 year period.

More specifically, the group has made novel contributions to understanding how Hh proteins are spread through tissues and how cells perceive and respond to Hh. The team has established several collaborations with groups with complementary research expertise. For example the collaboration with a group in Utrecht appears to have yielded novel and interesting data that the team proposes to continue to pursue.

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

The team has been successful in attracting external funding for their research from both national and international funding agencies. In addition, the group has several long-standing and productive collaborations with internationally recognized research groups.

The group has attracted talented researchers of all levels of experience and is comprised of a good mix of trainee and mature researchers.

The programme leader has been proactive in organizing scientific conferences in Nice and elsewhere (EMBO workshops). This is a strong indication of his commitment and standing in the field and has contributed to the overall visibility of the unit.

- Appreciation on the scientific strategy and the project

The main theme of this research programme is significant and of potential high impact. The proposal builds on the success of the previous programme of work and is likely to continue to be productive. The proposed project is feasible and focused, comprising several related individual projects. The preliminary data and experimental models available to the team are well established. The proposal suggests a more "cell biological" direction to some of the future projects and suitable collaborations have been put in place to reach these aims. The programme is likely to maintain its prominence in the field and provide new insight into the mechanisms of Hh signalling.

- Conclusion :

— Summary

The track record of the team and their recent novel findings are a clear strength of this team. This is a competitive field and there are several groups that are likely to be pursuing similar goals. Nevertheless the importance of the question, the excellent track record of the team and preliminary data suggest that there is a good chance of success.

The future work appears to be more focussed on the secretion, spread and cell membrane reception of Hh, resulting in less emphasis on the intracellular signal transduction. If resources allowed, the continuation of the projects aimed at understanding the intracellular signal transduction should also be encouraged.

— Strengths and opportunities

The group is internationaly well recognized and in a good position to continue to make major contributions.

— Weaknesses and threats

With the decision to go more into the biochemistry of Hh signaling, the group somewhat leaves its well known territory and needs to make all efforts possible to keep the high quality of research they are known for.

— Recommendations

The future work appears to be more focused on the secretion, spread and cell membrane reception of Hh, resulting in less emphasis on the intracellular signal transduction. If resources allowed, the continuation of the projects aimed at understanding the intracellular signal transduction should also be encouraged.

Team 14 - Adhesion Signaling in the Tumor Microenvironment

Team leader - Ellen Van OBBERGHEN-SCHILLING

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

The project of Obberghen-Schilling focuses on the cell biology of cancer cells. The models of the work are cell lines of squamous cell carcinomas of the head and neck (SCCHN), which are studied in various assays in vitro. The interactions of these cells and other cell types with the glycoprotein of the extracellular matrix (ECM) fibronectin are at the center of these studies. In this context, the roles of the fibronectin receptor integrin b5a1 and the ilk-"kinase" downstream of integrin activation for angiogenesis and growth of tumour and blood vessel cells are studied. 14 papers published or in press, with 10 listing the Pi as last or 1st author underline a good publication activity. A publication in Blood stands out in terms of impact, but dates from 2006.

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

The project addresses an important topic of translational research, namely the biology of cancer cells. The importance of the project and its visibility in France is reflected by a total of 7 grants, where the Pi served as coordinator for larger networks in 4 cases. Beyond collaborations with clinicians onsite cooperations with Strasbourg and Marseille laboratories are noteworthy. The work concerning the ilk-kinase is carried out in the framework of an international collaboration with a group at MPI in Munich. The Pi is also well visible in national and international meetings.

- Appreciation on the scientific strategy and the project

The topic of regulation of angiogenesis by the ECM in the field of cancer is of interest and important both on academic grounds and in the clinical context. The theme is relevant for translational research and for interactions with clinical groups on the campus in Nice. The analyses of the Itg b5a1 with the ilk-kinase downstream, as well as the signalling of the EGFR in tumours represent pertinent topics. The expertise of the group with cell culture is well documented. By comparison, the analysis in more complex models involving whole organisms could be emphasized more strongly.

- Conclusion :

The project of E. van Obberghen-Schilling displays strong points with respect to the importance of the topic, the representation of cancer and translational research in the overall project, the success in grant acquisition and the pronounced national and international visibility. The integration of animal models, e.g. transplantation strategies, possibly in combination with genetically modified recipients, would further strengthen and expand the strategy chosen.

— Strengths and opportunities

The group has found an interesting niche in the study of the role of integrin b5a1 and the ilk-"kinase" in angiogenesis associated to tumor formation. Significant grant funding has been secured

— Weaknesses and threats

The publication level could be higher and the use of more in vivo models to test for the physiological relevance of their findings is to be encouraged.

— Recommendations

The group is encouraged to increase its international visibility by raising the profile of its publications.

Team 15 - Cellular and molecular regulation of fat mass

Team leader - Ez-Zoubir AMRI

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

This is a proposal from an applicant group leader for IDBC. The previous work of the applicant group leader was undertaken in Team 5 and consisted of the analysis of extrinsic signals and intrinsic factors that influenced the adipocyte differentiation of hMADS cells. This generated novel and interesting data that were published in timely manner in several papers. The data has also formed the basis of patent applications.

The future proposal is to investigate the molecular mechanisms that control the interconversion of white and brown adipose tissue and to examine the effect of oxytocin in ovariectomized mice. The previously published work and the preliminary data offer a strong basis for these projects. The applicant programme leader has a strong track record, having published a significant number of papers in this field and co-authored patents. He has acted as the senior author on several recent papers. The questions addressed in this proposal are timely and of medical relevance and the establishment of this programme is strongly supported by his former supervisor.

The applicant programme leader has successfully participated in applications for external funding for his research. This should provide a good basis to attract talented researchers to his group, once established. Suitable collaborations with clinical colleagues have been initiated.

The applicant programme leader has made excellent efforts to maximize the protection of the intellectual property emanating from the work.

- Appreciation on the scientific strategy and the project

The main theme of this research programme is significant and of potential high impact. Understanding the differentiation of adipocytes is an interesting developmental biology question with clinical relevance.

The continuation of the current successful research projects suggests that the programme is likely to be successful. The programme consists of two separate projects and it will be important for this newly established group to ensure adequate prioritization and resources are dedicated to each project. The programme has the potential to offer new insight into adipocyte biology and provide information that is directly medically relevant.

Whereas the overall impression of the committee on the applicant was positive, it was felt that for such an appointment, in depth evaluation of the detailed scientific proposal by experts in the field was necessary.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
INSTITUT DE BIOLOGIE DU DÉVELOPPEMENT ET CANCER	**A+**	**A+**	**A+**	**A+**	**A+**
RÉGULATION CELLULAIRE ET MOLÉCULAIRE DE LA MASSE ADIPEUSE [NOSELLI-AMRI]	Non noté	Non noté	Non noté	Non noté	Non noté
CROISSANCE POLARISÉE CHEZ LA LEVURE [NOSELLI-ARKOWITZ]	A	A	Non noté	A	A
CONTRÔLE POST-TRANSCRIPTIONNEL DE LA CROISSANCE ET DU GUIDAGE AXONAL CHEZ LA DROSOPHILE [NOSELLI-BESSE]	Non noté	A+	Non noté	A+	A+
PROTÉINES MEMBRANAIRES, TRANSPORT, SIGNALISATION, PATHOLOGIES [NOSELLI-BORGESE]	B	B	Non noté	B	B
INTERACTIONS GÈNE-ENVIRONNEMENT AU COURS DU DÉVELOPPEMENT ET DE L'ÉVOLUTION [NOSELLI-BRAENDLE]	Non noté	A+	Non noté	A+	A+
CELLULES SOUCHES ET DIFFÉRENCIATION [NOSELLI-DANI]	A+	A+	Non noté	A+	A+
BIOLOGIE SYSTÉMIQUE DU RYTHME CIRCADIEN [NOSELLI-DELAUNAY]	A	A	Non noté	A	A
TRAFIC ENDOCYTAIRE ET DIVISION ASYMÉTRIQUE [NOSELLI-FURTHAUER]	Non noté	A+	Non noté	A+	A+
SIGNALISATION PAR LES RÉCEPTEURS DE MORT ET THÉRAPIE DU CANCER [NOSELLI-HUEBER]	A	A	Non noté	A	A
EXPLORATION DYNAMIQUE DES FONCTIONS DES GÈNES À HOMEOBOX CHEZ LE MAMMIFÈRE [NOSELLI-LAMONERIE]	Non noté	A	Non noté	A	A
CROISSANCE ET DÉVELOPPEMENT CHEZ LA DROSOPHILE [NOSELLI-LÉOPOLD]	A+	A+	Non noté	A+	A+
MORPHOGENÈSE ÉPITHÉLIALE. [NOSELLI-NOSELLI]	A+	A+	Non noté	A+	A+
SIGNALISATION ET ADHÉRENCE DANS LE MICROENVIRONNEMENT TUMORAL [NOSELLI-OBBERGHEN-SCHILLING]	B	A	Non noté	A	A
GLYCOSYLATION ET SIGNALISATION CHEZ LA DROSOPHILE, SECRETION DU MORPHOGÈNE HEDGEHOG CHEZ LA DROSOPHILE [NOSELLI-PIZETTE]	Non noté	A	Non noté	A	A
TRANSDUCTION DU SIGNAL ET CONTRÔLE DE LA MORPHOGENÈSE CHEZ LA DROSOPHILE [NOSELLI-THÉROND]	A+	A+	Non noté	A+	A+

C1 Qualité scientifique et production

C2 Rayonnement et attractivité, intégration dans l'environnement

C3 Gouvernance et vie du laboratoire

C4 Stratégie et projet scientifique

Statistiques de notes globales par domaines scientifiques

(État au 06/05/2011)

Sciences du Vivant et Environnement

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

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

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

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

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

Présidence et
Services centraux

Université Nice Sophia Antipolis

Nice, le 15 avril 2011

Affaire suivie par :
Eric DJAMAKORZIAN

Tél. : 04 92 07 66.05
Fax : 04 92 07 66 00

N/REF : 2011-1819

AERES
M. Pierre GLORIEUX
Directeur de la section des Unités de recherche
20 rue Vivienne
75002 – PARIS

Ref : Rapport d'évaluation Rapport d'évaluation S2UR120001726 - Institut de Biologie du Développement et Cancer - 0060931E

Monsieur le Directeur,

Faisant suite au travail effectué par le comité de visite de l'AERES et du rapport d'évaluation émis sur l'Unité de Recherche « S2UR120001726 - Institut de Biologie du Développement et Cancer - 0060931E-» portée par l'Université Nice Sophia Antipolis, vous voudrez bien trouver ci-joint la réponse que nous désirons apporter à ce rapport.

Celle-ci comporte uniquement des observations de portée générale qui s'inscrivent en droite ligne des recommandations très positives faites par le Comité de visite que nous remercions pour son travail constructif.

Vous en souhaitant bonne réception,
Je vous prie de croire, Monsieur le Directeur, en l'expression de mes sentiments distingués

GRAND CHÂTEAU
28, AV. VALROSE
06103 NICE CEDEX 2

UNIVERSITE DE NICE - SOPHIA ANTIPOLIS
1.1.1990

Pour le Président de l'Université de Nice-Sophia Antipolis et par délégation
Vice-Président délégué au Pilotage de l'Autonomie et des Moyens

Robert TELLER

Dear AERES Evaluation Committee,

On behalf of IBDC group leaders and members, I would like to thank the evaluation committee for a thorough and very positive evaluation. The high quality of the scientific discussions was much appreciated by all of the participants.

We are very pleased that the committee judged the research done at IBDC to be '*excellent*', '*highly original*', '*widely recognized at the international level*' and that '*IBDC is clearly one of the leading centers in Developmental Biology in France*'.

Also, it is much appreciated that the committee considered the current leadership to be '*excellent*' and that future projects to develop Biology on the Valrose campus through the building of the "institut de Biologie Valrose" (iBV) were considered as being '*a very positive move*' deserving strong support.

Finally, we are pleased that our efforts to provide an interactive, lively and international environment were also recognized and contributed in making IBDC '*a very good institute to learn and practice science*'.

IBDC has developed a '*high performance*' IBiSA imaging platform as well as mouse and zebrafish facilities. The committee also considered that IBDC should further develop its core facilities, in particular an in house computing facility. Applying overheads, which is currently not the case and contributes to the uniqueness of the IBDC, may represent a means of further developing core facilities. We completely agree with the committee that the development of core facilities represents a major objective for an institute such as IBDC, both to maintain competitiveness of the existing teams and as an element of attractivity to future teams. Specific actions to develop computing facilities have been taken including setting up scientific collaborations with INRIA (through the organization of a joint IBDC-INRIA meeting); furthermore, plans to attract a high profile group leader in bioinformatics represent one of IBDC's priorities for the next recruitment session. Finally, IBDC is augmenting its pluridisciplinarity in particular with neighboring institutes working in mathematics, chemistry and physics, which provides open access to specific platforms/facilities (Atomic Force Microscopy, molecular chemical design, drug screening, modeling, *etc.*).

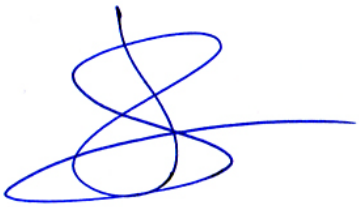
One current weakness of IBDC, well appreciated by the committee, is the current lack of a clear commitment from the funding organizations and institutions specifically with respect to allocation of new space and funding, to take into account the moving of teams from the Pasteur/CAL to the Valrose site as well as for developing the ambitious "institut de Biologie Valrose" project. We are fully convinced that our funding organizations will hear this message and that a clear and strong commitment from University of Nice, CNRS and INSERM will follow, as all these institutions have expressed their strongest support for this structuring project.

Institut Biologie du Développement & Cancer, Parc Valrose, 06108 NICE cedex 2 – France
Directeur: Stéphane NOSELLI Tel: +33 4 92 07 64 00 – FAX: +33 4 92 07 64 03 - noselli@unice.fr

In conclusion, we are grateful to the committee for providing such strong support of IBDC scientific achievements and strategy. Every effort from IBDC direction, services and teams will be dedicated to pursue and increase scientific excellence within the framework of the future "institut de Biologie Valrose".

April, 13th, 2011

NOSELLI, Stéphane



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Specific typos/omissions and clarifications regarding the text and some of the group's recommendations are listed below:

On p3 (end of paragraph 2), team 2 is not listed.
On p31-32, 'a5b1' should read 'b5a1'.
On p28, the title of the project should be changed into "Role of basement membrane structural components in morphogen signaling in Drosophila", instead of "Glycosylation and signaling in Drosophila, secretion of the Drosophila Hedgehog morphogen" corresponding to previous work.

TEAM 1
Omissions in "Appreciation on the impact" section":
- There were three reviews in which a member of the team was senior or first author.
- The team leader was also coordinator of an international ERANET pathogenomics project and co-coordinator of an EU Marie Curie grant for an international PhD program in Developmental and Cellular Decisions.

TEAM 3
The current team stems from the recent merging of the groups of Borgese and Mus-Veteau, previously members of the FRE3094 CNRS that joined IBDC in 2010 in the context of the reorganization of biology on the campus. Those two teams have previously contributed on the molecular mechanism of cation permeability in hereditary stomatocytosis, the modulation of ion channel activities by Sigma1 receptor expression and the production and biochemical characterization of the human Hedgehog receptor proteins, leading to a total of 24 publications. Following the recommendations of the committee, restructuration of this team will take place rapidly, in order to refocus the scientific project and regain in visibility and productivity.

TEAM 6
The team hosted 3 master students in the past and is currently hosting one.

TEAM 8

We are grateful to the committee for the positive comments on the team's work, that was judged "*very productive*" both in terms of grants and of publications, despite several responsibilities of the PI.

On p20, several important typos are found in the "Staff members" table: N2 line, future should read 3 instead of 2; N3 past should read 7 instead of 0; N5 past should read 3 instead of 2; N6 past should read 5 instead of 0.

Update: one of the post doc in the lab just got a CR2 CNRS tenure position to work in the team.

We appreciate the committee's recommendation regarding the use of animal models in our studies, as these have contributed much to our understanding in life science and can lead to medical advances. However we would like to mention a number of studies discussing the value of animal models in predicting human responses in terms of clinical translation. A systematic review of animal studies published in seven high-impact factor, influential journals found that only 37% of these studies translated to randomized human trials and only 10% of these interventions were subsequently approved for use in patients (Hackam, D. 2006 JAMA; Van der Worp, H. B, et al., 2010 PLoS Medicine; Knight, A. Reviews on Recent Clinical Trials). One of the limitations when translating knowledge from animals to humans is the genetic differences between human and animals. While chimpanzees and humans differ only by 1-2% in nucleotide content, this leads to 80% difference in protein expression (Glazko, G., Gene 2005). Such difference could likely lead to a multitude of differences in etiology and progression of diseases, metabolism, toxicity and efficacy of pharmaceuticals. Other laboratory animals with even less similarity to human both genetically and phenotypically are therefore less likely to accurately model the progression of human diseases or responses to therapeutic agents. Indeed, clinical trials are essential because animal studies do not predict sufficiently what will happen in humans. As is acknowledged by many scientists, much of valuable information that has been successfully translated into medical advances does not come from animal experiments but from direct observation of 'human information' (e.g. the role of KRas mutations as predictive factor in cetuximab treatment of colorectal cancer).

Therefore, we believe that despite the interests of using animal models, efforts to use non-animal models to investigate cancer should certainly be encouraged as well. By aiming to study human samples (human cell lines, biopsies, primary cells, blood samples) in close collaboration with experts clinicians (Nice, Marseille, Paris), we strongly believe that we can obtain human-directed information that can be translated into valuable clinical use (e.g. predictive factors, physicopathologic markers, relevant therapeutic targets).

TEAM 9

As recommended by the committee, the team has recruited a permanent researcher (CR1 CNRS level) to reinforce the scientific progress and doctoral training.

NOSELLI, Stéphane