Signalisation normale et pathologique de l'embryon aux thérapies innovantes des cancers

Rapport Hcéres

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

Section des Unités de recherche

Rapport d'évaluation

Unité de recherche :

Signalisation normale et pathologique, de l'embryon aux thérapies innovantes des cancers

de l'Institut Curie

Mars 2009

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Le Président de l'AERES	Section des unités de recherche
	Le Directeur
Jean-François Dhainaut	Pierre Glorieux

Mars 2009

Rapport d'évaluation

L'unité de recherche :

Nom de l'unité : Signalisation normale et pathologique de l'embryon aux thérapies innovantes des cancers

Label demandé : UMR_S INSERM, UMR CNRS.

N° si renouvellement :

Nom du directeur : M. Simon SAULE

Université ou école principale :

Université Paris 11

Autres établissements et organismes de rattachement :

Institut Curie

CNRS

INSERM

Date(s) de la visite :

30 Janvier 2009

Membres du comité d'évaluation

Président :

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Experts :

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Observateurs

Délégué scientifique de l'AERES :

M. Charles Dumontet, Lyon

Représentant de l'université ou école, établissement principal :

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Représentants des organismes tutelles de l'unité :

M. Daniel Louvard, Institut Curie

Mme Marie-Josephe Leroy-Zamia, INSERM

Mme Martine Defais, CNRS

Mme Annick Salini, INSERM

Mme Michèle Saumon, CNRS

Rapport d'évaluation

1 • Présentation succincte de l'unité

- Effectif au 30/01/09 ; 45 personnes ; 03 enseignants-chercheurs ; 10 chercheurs ; 06 ingénieurs (3IE et 2AI, plus 1 en CDD), 5 techniciens (dont 1 en CDD), 12 doctorants, 9 post doctorants
- Nombre de HDR, nombre de HDR encadrant des thèses ; 09 HDR ; 07 encadrants des thèses
- Nombre de thèses soutenues et durée moyenne lors des 4 dernières années, nombre de thèses en cours, taux d'abandon, nombre de thésards financés (détailler selon le type de financement)
- 14 thèses soutenues (pour les thèses soutenues : 8 allocataires du ministère, 1 allocataire étranger, 1 bourse Institut Curie, 2 bourses d'associations, 1 bourse ingenieur du privé, 1 bourse ANR ; les allocataires de recherches ont une bourse d'association pour leur 4eme année)
- 4 ans en moyenne par thèse
- 12 thèses en cours (3 allocataires du ministère, 2 collectivité territoriales, 1 ATER, 2 bourses INCA, 1 bourse CIFFRE, 2 bourses d'association, 1 bourse de l'Institut Curie)
- aucun abandon ; tous les thésards sont financés.
- nombre de membres bénéficiant d'une PEDR : 01
- nombre de publiants : 12 (le non publiant est DR CNRS émerite, 01 publication en 2007).

This unit will be located on the Curie Orsay campus. It will comprise 4 groups originating from the UMR146 on the same campus and 2 new groups. The two newcomers have already collaborated with groups of the UMR146. The applicant unit totals approximately 50 persons.

Although multidisciplinary, the applicant research unit will have a strong federating theme, melanoma, which will directly involve 4 groups. Other connected issues will also be addressed: (i) neural crest induction in relation to the generation of the melanocytic lineage and (ii) the study of other cancers. Cognitive questions will be addressed using mouse, chicken and Xenopus as animal models. They will be complemented by analyses of human situations both in terms of clinical studies and development of potential new therapeutical approaches.

All equipments required for the success of the project (including animal facilities and imaging platforms) are already available locally. The unit also benefits from common facilities available at the Paris campus of the Curie Institute (transcriptomic- and proteomic platforms, etc…). A redistribution of space will however be necessary both to accommodate the new groups and to have all teams in proximity.

2 • Déroulement de l'évaluation

— Two months prior to the visit, the members of the committee received an informative document (i) presenting the project of the applicant research unit and (ii) containing annexes reporting on the recent activity of both the former UMR 146 and two new groups. Useful complementary information concerning the management plans of the unit was provided during the visit.

— The visit took place on January 30, 2009. The committee first met in a closed-door meeting with the scientific delegate of the Aeres who gave explanations on Aeres policy and on the evaluation criteria.

Oral communications started in the morning with a general presentation by the scientific director of the Curie Institute, D. Louvard. This was followed, first, by a presentation of the overall project of the applicant research unit by the candidate director, and, then, scientific presentations by each one of the 6 group leaders. In the afternoon, the committee successively met and discussed openly with four categories of personnel: (i) the group leaders together with the candidate director, (ii) the ITA/IATOS, (iii) the students and post-docs and (iv) the staff scientists and assistant professors. These discussions were followed by a meeting with the

delegates of research organizations (Inserm, Cnrs and Université Paris-Sud 11) in the presence of Daniel Louvard. After a closed-door meeting of approximately one hour, the committee shortly met with the director of the applicant unit for further discussion.

3 • Analyse globale de l'unité, de son évolution et de son positionnement local, régional et européen

Although the committee noticed some heterogeneity between the groups in terms of past achievements and project standards, all of its members were favorably impressed by the overall quality and the originality of the research developed by the constituent groups of the applicant unit on the basis of several elements: (i) the past achievements, (ii) the publication records, (iii) the quality and ambition of most group projects, (iv) the reputation of certain group leaders, (v) the robust networks of collaborations of most group leaders, (vi) the efforts for translational research and (vii) the real connection to human disease.

Moreover, the committee has favorably appreciated the real connection of all groups to a strong federating theme, melanoma, within a collective project. This collective project will address various issues ranging from the most fundamental issues (development of the neural crest and of the melanocyte lineage, etc…) to the most applied ones (clinical studies, search for new drugs, etc…) via the study of the cellular and molecular mechanisms responsible for melanomagenesis. This concentration of means on the same topic should allow the applicant unit to create both a real task force and a unique identity. This should be helped by the current structuring role of one of its founding groups (Larue) in the melanoma medical and scientific community.

The applicant unit will be headed by a director helped by an deputy-director. From the discussions the Committee had with each category of personnel, the project director appeared as a consensual person who received the support of all of the members of the unit through a vote following an internal debate on the governance of the future research unit. It must be underlined that the project leader was recently appointed as professor at the Paris 11 University. This will be an important asset for the applicant unit owing to the wish of Paris 11 University to reinforce cell- and development biology on the Orsay Campus, as stated by its representatives. The committee also supported the choice for the deputy-director. His reputation as a melanoma specialist combined with his demonstrated organizational abilities (see below) should, not only help the director in the management of his unit, but will also increase the visibility of the unit in the melanoma field. Importantly, all categories of personnel were very supportive and expressed their satisfaction/enthusiasm concerning the prospective of establishing this new unit as well as their own future contribution.

Finally, it must be underlined that most group leaders have (i) exerted expert responsibilities (papers, grant applications, scientific advisory boards, editorial work, visit committees, etc…), (ii) undertaken organizational activities (organization of meetings, responsibilities in scientific societies, etc…) and (iii) been invited for numerous seminars and to numerous meetings. Additionally, two of them are co-founders of a young start-up (see below). This testifies for the quality of the science currently conducted by the founding groups of the applicant unit and for its insertion in scientific networks.

4 • Analyse équipe par équipe et par projet

Team 1 : Recombination, repair and cancer

The situation of this team (9 persons) is particular in the sense that, after a period of technological development leading to the launching of a start-up company (DNA therapeutics), the leader now wants to return to more fundamental research. After having postulated that it might be possible to saturate DNA repair systems because mammalian cells cannot discriminate between their own DNA and exogenous DNA, she has developed a number of small DNA-derived molecules (called Dbait) capable of radiosensitizing tumor cells. This interesting work has led to several publications and patents and, as already mentioned, the launching of DNA therapeutics. This was achieved with the Curie Institute Transfer Department, with which the team leader is currently working. Preclinical studies are currently ongoing and a clinical trial is foreseen in 2011.

As melanoma (and glioma, another interest of the team leader) is a tumor particularly resistant to chemo- and radiotherapy, there is an obvious reciprocal interest in the team leader joining other teams in the unit project. In her project, the team leader proposes (i) to study Dbait trafficking into cells, (ii) to analyze transcriptome changes in radioresistant tumor cells in response to ionizing radiations, (iii) to characterize the cellular mechanisms of response to Dbaits, (iv) to model this response and (v) to develop new small interfering DNAs (SiDNA) mimicking different types of DNA damage with the idea of eventually using them to potentiate chemotherapies. The Committee has clearly perceived (i) the overall interest of the project and its potentiality for anticancer applications and (ii) the potential of connections with other teams of the applicant unit. It has also appreciated the enthusiasm of the group leader for translational research and her reasons to return to more fundamental research. The committee has, however, felt the proposed project to be ill-defined on a

number of points, at least as it has been presented in the written application and orally. A better definition of the specific objectives and a real focus on the most important ones to avoid the fragmentation of efforts is clearly necessary. The committee also recommends selection of these objectives according to possible collaborations with other groups of the unit project, which would reinforce the overall dynamics of the future research unit.

Strong points: The project on « Dbait » is highly novel and original. The team has recognized expertise in translational research. There is a firm link of the project to melanoma as a cancer resistant to apoptosis and requiring novel therapeutic approaches. There are clear possibilities of collaborations with other groups of the unit projects. The team leader has already collaborated with the melanocyte development team (whose leader is also a co-founder of DNA Therapeutics).

Weak points: There are too many too vague objectives. Therefore, the specific aims and internal collaborations still need to be better defined.

Nom de l'équipe : Recombination, repair and cancer

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

Team 2: Raf and Maf in signaling in oncogenesis and development

This is a 7-person team, which has made very interesting contributions on the role, function and regulation of Raf and Maf family proteins in carcinogenesis. Till a recent past, the studies were largely, but not exclusively, conducted using cell lines and primary cells. Interesting results concerning the role of Raf kinases in melanoma and the control of MafA transcriptional activity by phosphorylation were obtained in the recent period. These have led to a number of publications in very good to excellent journals (Mol. Cell, Nat Review Cell Biol, MCB….).

The group has recently (2005) turned towards mouse models (KO and KI) to better understand the roles of Raf and Maf proteins in pathophysiology. Two major lines of research are being developed. One is the study of Raf-1 and B-Raf during development of the melanocytic lineage and induction of cutaneous melanoma. The latter aspect is justified by the fact that activating mutations are often found in N-Ras or B-Raf in these tumors. The second project is the study of MafA and its phosphorylation during normal development and carcinogenesis. There are two reasons underlying this study: (i) MafA, MafB and c-Maf genes are translocated in 10% of multiple myelomas (MM) and that of c-Maf is dysregulated in 50% of MM and (ii) transcriptional activity of Maf proteins is stimulated by phosphorylation. Turning towards mouse engineering-based approaches has requested a real conversion of half of the members of the group in the recent period. These efforts have been rewarding as the first phenotypes were recently obtained. This makes the committee confident concerning the future achievements of the team. Of note, conditional gene knock-out in melanoblasts and melanocytes is based on the system developed in the melanocyte development team.

This constitutes testimony, among others, to the ability of the unit members to collaborate. The committee has however raised the point that conducting two highly competitive projects in parallel most probably represent a weakness for such a small group. Unless it can increase in size, the committee recommend the group to consider focusing on just one aspect in order to reach higher achievements.

The group leader has organized several meetings and held several administrative and scientific animation responsibilities. He is regularly solicited for paper- and grant application reviewing, which testifies to the scientific reputation of the group. He also has regular teaching activities at the Master level and is responsible for the mouse colony at Curie Orsay.

Strong points: This group has a long-standing, strong and acknowledged expertise in the oncogenesis field. It has obtained interesting results in the recent period. Its publication record of the last 4 years is very good. The team has successfully converted half of its personnel to mouse model work. It also has a robust network of collaborations.

Weak points: There may be too numerous points related to both cancer and development. In consequence there exists a real risk of dispersion. As mentionned above, it is likely that running two projects in parallel (despite some connections between them and some success on the two subjects) has already impeded higher

impact achievements in the past. The group should gain from either increasing its size, including via recruiting one or two additional senior scientists, or focusing on just one them.

Nom de l'équipe : Raf and Maf in signaling in oncogenesis and development

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

Team 3: Normal and pathological development of melanocytes

This is a 12-person team with, probably, the highest scientific impact of the applicant unit. This group has made many interesting and noted observations on normal melanocyte development and cutaneous melanoma during the recent period. -catenin (bcat) is the molecule at the heart of its research. The group project combines molecular, cellular and in vivo approaches to better understand normal and pathological development of melanocytes and follows several lines of research. They are: (i) the study of the role of bcat during establishment/maintenance of the melanocyte lineage, (ii) the study of the regulation of bcat activity via its direct interactions with cadherins and Icat and via its indirect interactions with the PI3K/Pten/Akt signaling pathway, (iii) the study of Brn2, Mitf and p16 gene regulation by bcat and the role of these proteins in the melanocyte lineage and (iv) the study of the integrated function of bcat in melanomagenesis through its functional cooperation with proteins involved in proliferation, migration and invasion. Many of these studies are based on the use of engineered mice. Indeed, the collection of transgenic mice of the group provides a specific strength. Interestingly also, the team has developed its own system to obtain conditional and inducible KO mice in the melanocyte lineage. This system probably constitutes one of the best animal models to study melanomagenesis. The work carried out by the group has led to many publications of excellent quality (Genes Dev., Nature, J. Cell Biol, Canc. Res, Oncogene MCB….). Many of these publications were shared with other laboratories, which strongly testifies to the ability of the group to collaborate.

In addition to its scientific activity, the team leader has many other activities (scientific director of the animal colony of the Curie Institute, teaching responsibilities, organizer of several meetings, various expert responsibilities, etc….). He is also the co-founder of the young start-up company, "DNA therapeutics". The quality of the work conducted in his group is acknowledged at the national and international level through invitations to many seminars and meetings, participation in thesis committees, etc…. The team leader has also

played an important role in the structuring of melanoma research, not only at the national level (Canceropole Ile-de-France), but also at the European level.

Strong points: This team is the most productive of the unit both in quantity and quality. Its past achievements are of very high quality. The overall project is strong with, sometimes, imaginative specific objectives. The team leader has developed an impressive network of collaborations at the local, national and international levels. He has also demonstrated his ability to develop technological tools as well as to make connections with the clinic and to structure research on a large scale.

Weak points: There is a possibility of dispersion as often occurs in imaginative and active groups.

Nom de l'équipe : Normal and pathological development of melanocytes

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+

Team 4: Shh/TGF signaling in the development and progression of melanoma

This group currently comprises 3-4 persons. It is due to move from Saint-Louis Hospital (Paris) to Curie Orsay where it has already collaborated with the melanocyte development team. Its main focus is melanomagenesis with a particular emphasis on TGF signaling. Many very interesting observations were made these past years. Among the main findings, one can cite: (i) the demonstration of the importance of autocrine TGF signaling in melanoma invasion and metastasis, (ii) the interest of targeting this pathway, as suggested in a preclinical mouse model of melanoma, (iii) the identification of the GLI2 transcription factor as a transcriptional target of TGF signaling, this observation being all the more interesting in that GLI2 is independently known to be a target of Sonic Hedgehog signaling in other cancers, and (iv) the demonstration that GLI2 expression is negatively correlated with that of MITF and E-cadherin and associated with invasion and metastasis. This work is at the origin of many publications in high-level journals (Cancer Res., Oncogene, J. Cell Phys., Carcinogenesis….). Importantly, many of them are highly cited.

The proposed project is the logical continuation of the past work. Its major cognitive aims (non-exhaustively) are (i) to characterize the molecular mechanisms of GLI2 gene transcription and (ii) to characterize the role of GLI2 in the initiation and progression of melanoma as well as during the maturation of the melanocyte lineage. The research program also has translational research objectives that include (i) the establishment of whether measuring the GLI2/MITF ratio may represent an interesting diagnostic/prognostic indication in melanoma and (i) testing several drugs and monoclonal antibodies as potential therapeutics in the treatment of melanoma.

Besides his research activity, the group leader has also had administrative responsibilities as director of an Inserm unit. His scientific value is acknowledged by numerous invitations as speaker in international meetings and regular solicitations for expert activities.

Strong points: The team has a longstanding expertise in the field. Its project is built on a robust corpus of original observations. There are already ongoing collaborations with the melanocyte development group. There are also many possibilities of interactions with other groups of the applicant unit. The team leader has an acknowledged international reputation and has been very productive these past years. The overall goal of the lab is of high interest and the past work is of very good to excellent quality. The committee feels that having the team leader join the unit project would both strongly strengthen the "melanoma" identity and enhance the international visibility of this future unit. The committee also noticed the clear enthusiasm of the team leader about the UNIT project and, reciprocally, the explicitly expressed interest of the other group leaders to have him join them.

Weak points: There might be too many objectives in the project with respect to the current size of the group. The team may gain by more in-depth analysis of selected issues, which might be facilitated by the complementary expertise already present at Curie Orsay. Increasing the critical mass of the team must, therefore, be a priority to maintain the quality of its science. Securing this development might be one of the priorities of the future director.

Nom de l'équipe : Shh/TGF signaling in the development and progression of melanoma

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

Team 5: Signaling and neural crest development

This is the smallest and most recent group of the UNIT project currently present on the Curie Orsay campus (4 persons till recently). It was established, first, as a Curie team in 2004 and, then, as a CNRS ATIP in 2005. Its focus is the molecular network controlling both the induction of neural crest during neuronal tube patterning and the generation of the cell lineages originating from the neural crest. This issue is of particular interest for the whole applicant unit as neural crest is at the origin of the melanocyte lineage and constitutes a particularly interesting system to study the epithelial-to-mesenchymal transition (EMT), which is critical in the metastatic process.

In the recent period, the team has identified a number of secreted factors and transcription factors driving neural crest induction using Xenopus, and to a lesser extent chicken, as animal models. This group now aims at

understanding further the molecular mechanisms of this induction in terms of signal transduction, EMT control and neural crest-derived lineage determination. Its specific objectives are to understand (i) how the neural progenitor domain is established during early neurulation, (ii) what are the molecular mechanisms whereby the Pax3 transcription factor and its partners induce neural crest and (iii) how these molecular interactions control EMT in the embryo and other contexts. Though the production of this group is still modest, the committee has favorably appreciated its recent articles (2 papers in Dev Biol, one in 2007 and the other in press, and a contribution to CSH protocols), taking into consideration both the small size and the recent start of this team. One of the current weaknesses of the group is its small size. It, however, appeared during the visit that new students may joint it. Due to the convincing oral presentation of the group leader and the fact that the group has begun to be productive, the committee is confident about its chances of success, provided that certain observations are confirmed and that the group can reach a reasonable critical mass.

Strong points: This is an interesting and well-conceived project conducted by an intelligent, competent and enthusiastic person. The team leader is expert with Xenopus, which provides one of the most amenable systems to study very early embryonic events. The first publications specific to the group constitute an encouraging sign. The study of the neural crest stage has a good chance of being relevant to melanoma, as the spectrum of gene expression patterns suggests that some melanoma may dedifferentiate to resemble very early embryonic precursor cells and this hypothesis can be tested fully only by knowing more about neural crest biology.

Weak points: Increasing the size of the group is one necessary condition to reach the highest achievement standards. Securing this development might be one of the priorities of the future director.

Nom de l'équipe : Signaling and neural crest development

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

Team 6: Pax and Mitf in signaling, eye development and melanoma

This is a 7-person group studying the genetic control of neuronal and pigmentary cell differentiation using the eye as an experimental system. With respect to cognitive research, this team aims towards a better understanding of the development of ocular function and of ocular tumors, namely uveal melanoma and retinoblastoma. During the past years, the team has addressed the role of the Pax 6 and Mitf transcription factors in eye development using various approaches. This has led to several interesting observations published in good journals (JBC, Dev Biol., J Cell Biochem, Genome Res ….). In parallel, this group has also coordinated a

study of transcriptome and genomic alterations found in uveal melanoma and its liver metastasis. To achieve this goal, it has taken advantage of the unique recruitment of uveal melanoma patients by the Curie Hospital. This original study has been conducted in collaboration with the Transfer Department of the Curie Institute. Very interesting observations were made, which may constitute new original avenues for future stimulating research.

Strong points: The group has a long-standing expertise in the field of eye development, which constitutes a very interesting system. The uveal melanoma study is entirely original and should be at the origin of interesting new investigations.

Weak points: Despite the fact that a number of interesting observations were made throughout the recent years, the committee has felt some tendency of the group to get distracted with details of secondary interest

to the detriment of the most important issues. The committee therefore recommends a refocusing of the activity on the strongest lines of research and a better exploitation of the most important findings of the recent period. Keeping on the uveal melanoma study may, for example, lead to important and original achievements.

Nom de l'équipe : Pax and Mitf in signaling, eye development and melanoma

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

5 • Analyse de la vie de l'unité

The working conditions (space, equipment of the laboratory, common facilities, budget, support of the Curie Institute, scientific animation, access to technological platforms, excellent relationships between people and groups, etc…) are there to guarantee the success of the proposed objectives.

As this is an applicant unit not yet opened, it is difficult to make a definitive opinion concerning the future life of the research unit. However, as 4 out of the 6 founding groups of this applicant unit originate from the UMR146 and have lived side-by-side for a long time, the committee is confident in their ability to make the best use of human resources and to develop a stimulating intellectual environment. Moreover, as already mentioned, all personnel involved in the application are enthusiastic about the project and all expressed their overall satisfaction concerning their current situation/supervision/condition of work in the UMR146. Finally, collaborations already exist between some of these groups and the newcomers. This should favor the integration of the latter teams.

6 • Conclusions

- Strong points:

Overall, the unit appears strong with complementary and added value between the groups. It should constitute a real task force on melanoma which is its federating theme. Most groups have individually made important observations and now present excellent individual and collective projects.

The expertise and the reputation of most groups of the unit project are well established. Some of these groups even have had an important role in structuring melanoma research at both the national and the European level. The links with the Curie Hospital and Transfer Department constitute particularly valuable assets. Finally, there is an enthusiastic support of all categories of personnel for this proposed unit.

- Weak points:

Certain groups need to better define certain of their specific objectives.

- Recommendations:

It is important that the critical mass of certain teams be increased, and that the main aims of certain teams be better defined.

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

institutCurie
Ensemble, prenons le cancer de vitesse.

Reply to AERES committee; visite du 30 janvier 2009

Team 1 «Recombination, repair and cancer»
The objectives of Team 1 are straightforward. A new family of drugs called siDNA that disturb DNA damage signaling and inhibit DNA repair have been characterized in the team. The objectives are (i) to get a first generation of molecules (Dbait) in preclinical assay to treat radioresistant melanoma and glioblastoma, (ii) to better characterize the mechanism of action of Dbait, (iii) to evaluate the activity of novel molecules of this family. The approaches of these three objectives are already established in team 1. In order to improve, the screening and to better evaluate the mechanism of action of these molecules, we will interact with other teams of the ETIC unit that are developing uveal and skin melanoma models.

Team 2 «Raf and Maf signaling in oncogenesis and development»
No comment

Team 3 «Normal and pathological development of melanocytes»
No comment

Team 4 «Shh/TGF signaling in the development and progression of melanoma»
The number of objectives presented by team 4 is large and is not in adequation with the current size of the group, and Team 4 has begun to search for new personnel. Four potential candidates (two students and two post-docs) are highly interested to join this team. Moreover, the early recruited CR1 (INSERM) will defend her HDR within the next year to allow official training of PhD students.

Team 5 «Signaling and neural crest cell development»
No comment

Team 6: "Pax and Mitf in signaling, eye development and melanoma"
The main goal of team 6 is to get insight in the uveal melanoma. The fundamental knowledge acquired from the functional study of transcription factors in eye development and pigmentation will be focused and useful for team 6 main goal. The descriptive and correlative pan-genomic analysis of human uveal melanoma will be challenged using appropriate cellular and animal models.

Directeur Projet ETIC
Professeur Simon SAULE

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