

BDR - Biologie du développement et reproduction

Rapport Hcéres

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

Section des Unités de recherche

Evaluation report

Research unit :

Biologie du Développement et de la Reproduction

From the Ecole Nationale Vétérinaire de
Maison Alfort UMR INRA 1198



March 2009



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et de l'enseignement supérieur

Section des Unités de recherche

Evaluation report

Research unit :

Biologie du Développement et de la Reproduction

From the Ecole Nationale Vétérinaire de
Maison Alfort UMR INRA 1198

Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

mars 2009



Evaluation report



The research unit :

Name of the research unit : Biologie du Développement et de la Reproduction

Requested label : UMR INRA

N° in case of renewal : 1198

Head of the research unit : Ms. Corinne COTINOT

University or school :

Ecole Nationale Vétérinaire de Maison-Alfort

Other institutions and research organization:

INRA

Date of the visit :

March 2th to 3th 2009



Members of the visiting committee

Chairman of the committee :

M. Marc-André SIRARD, University of Laval, Canada

Other committee members :

M. Peter BOLS, University of Antwerp, Belgique

M. Ian MOTLIK LIBECHOV, Republique Tchèque

M. Fulvio GANDOLFI, University of Milan, Italie

M. Robert FEIL, IGMM, Montpellier

CNU, CoNRS, CSS INSERM, représentant INRA, INRIA, IRD.....) representatives :

Ms. Christine BALY, CSS INRA representative

Observers

AERES scientific representative:

M. Frédéric FLAMANT

University or school representative:

M. Henri-Jean BOULOUIS, ENV representative

Research organization representative :

M. Philippe CHEMINEAU, INRA representative



Evaluation report

1 • Short presentation of the research unit

- Number of lab members : 97 including
 - o 8 researchers with teaching duties, including 2PR and 6 MCF
 - o 23 full time researchers, including 3 DR and 20 CR
 - o 2 postdoctoral fellows
 - o 44 engineers, technicians and administrative assistants (39 ETP)
 - o 20 PhD students, all with a fellowship
- Number of HDR : 13
- Number of students who have obtained their PhD during the past 4 years : 8
- Number of “publishing” lab members : 26 out of 31

2 • Preparation and execution of the visit

The documents received which were quite elaborated and were useful for the analysis of the scientific activities, the management structure and the achievements according to each team in the previous 4 years (10 teams).

The committee requested a list of publications for each individual team to better assess individual team productivity. This list was kindly provided more than a month before the visit. Therefore the documents received contained all the information required.

The oral presentations were organised not in function of the previous structure (2005-2008) but according to the new structure proposed for the next contract (2010-2013). The overall program was presented by the head of the department and then each team was introduced by the team leader who then invited each group leader to present the scientific plan for the next 4 years. Numerous questions were asked by the visiting committee to appreciate the scientific planning as well as the interaction foreseen amongst groups and teams.

The visit was well organized by the department head and no logistic problems.

Day 1:

09h15 : Door-closed meeting

09h45 : Presentation by the head of the unit

10h15 : Team 1

14h00 : Team 2

16h00 : Posters and core facilities

17h00 : Door-closed meeting

Day 2:

09h00 : Team 3

10h30-13h00 : Door-closed meeting



3 • Overall appreciation of the activity of the research unit, of its links with local, national and international partners

This unit is going through a functional and physical reorganisation characterised by the nomination of a new department head, the redistribution of the previous 10 groups in 3 teams totalising 11 groups and a regrouping of the groups located in Jouy in a unique location. Most of the original teams are now reorganised in a new topic oriented distribution. An INSERM team has been added which focuses on the impact of nutrition on maternal-placental interaction.

The unit is well positioned in France as one of the leading groups in animal reproduction as well as on the European context where several grants have been obtained in collaboration with other scientists from other countries.

The unit is quite recognised on the international scene mainly due to the unique questions/expertise constituting this department. The analysis of the embryo-maternal interaction in the context of cattle cloning is certainly the most remarkable aspect of the research program in this unit. The leadership of the previous department head has certainly had a significant impact on the recognition of this unit.

The number of publications has been satisfying although limited considering the number of permanent positions. In 85/112 lab members are either first or last authors. Out of these, 25 were in journals of high rank (IF>5). Several lab members consider that working on farm animals compromise their chance to publish in top ranked journals.

The unit is well funded, due to active seeking for contracts, of national and european origin, which represent the majority of the financial resources. This part has been growing constantly, indicating the ability of the laboratory to adapt to competitive funding.

4 • Specific appreciation team by team and/or project by project

Team 1 : Embryonic development and dynamics of the genome

This team is composed of 4 groups of different weight. The 2 smaller groups are involved in developing very unique and specific tools to study intracellular signaling during early development, and knockdown gene expression in embryos. The 2 other groups are at the forefront of transcriptomic and chromatin research. The later 2 are showing a strong productivity and high quality publications. Their work is well perceived on the national scene and the 2 young scientists leading these groups have a great potential to contribute to the understanding of gene regulation in early embryos through the precise analysis of gene expression and chromatin structure. This should result in an increase in international recognition and eventually more invitations to give lectures. The access to cloned embryos represents a unique opportunity to study perturbations in the control of gene expression and repression in bovine. No other team in the world has built a comparable set up for this work. They have access to state of the art microscopic image analysis tools but are somewhat limited by their access to transcriptomic tools (deep sequencing or pyrosequencing) and modelisation tools (although some expertise is present in team 2 and has shown good collaboration). It must be pointed out that although the unit is not as well equipped as some of their collaborators in the US, the use of their own, custom made microarrays has resulted in very interesting results that would had been missed with more standard platforms.

The study of chromatin configuration in farm animals is a very hot topic and few groups have the transcriptomic-epigenomic aspect associated within the same lab. This association is therefore promising and should lead to cutting edge research. The 2 other groups in oocyte culture and transgenesis are not closely linked to the main stream of the team but it is expected that interactions will develop about the impact of culture conditions on the epigenome and potentially on the chromatin structure especially in clone embryos. Using transgenic or specific RNA inhibition approaches will be instrumental to evaluate the importance of identified genes (ex LTR sequences) in chromatin regulation.



DEVELOPPEMENT EMBRYONNAIRE ET DYNAMIQUE DU GENOME

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 2 : Cellular and molecular mechanism involved in placenta and gonad organogenesis

This team is made of 3 groups loosely connected to each other. The first group is involved in the epigenetic analysis of the placenta and extra-embryonic tissues which is in line with the work of team 1 as embryos that show epigenetic problem from cloning go on to form placentas with sometime unique defects. The cow is very useful in that regard and represents a good model where huge perturbations are induced by cloning and therefore allow the analysis of almost all problems possible arising from incomplete epigenomic reprogramming. This is an emerging field and the projects presented are in line with the international competition although ambitious. This team is also involved in one of the most important aspect of biology research these days: modelisation and integration of genome/epigenome data. This expertise will have to be shared across teams. The interaction with teams 1 and 3 is both complementary and essential for the generation of a comprehensive image of clones and the regulation of the epigenome. Bio-informatics support seems good (one full time resource) but if not developed further could become a limiting factor for the modelisation efforts/requirements of all groups.

The second group is involved the study of lipid signalling between uterus and conceptus in the bovine. The scientist involved has developed a unique expertise in this field and has well exploited this model to generate good publications. It would be interesting if the regulation of prostaglandin synthesis would be analysed in regard of the promoter regulation by the environment, the nutrition, and the unique response of the uterus depending on the type of embryo at the interface (clone, in vitro or control) possibly in collaboration with team 3.

The third group works on organogenesis of the gonads which does not result in useful collaborations within this team as compared to across other teams. The fact that they work on different species (goat and sheep) also requires different tools, different arrays and different transgenes. They would/will benefit from the transcriptomic expertise developed in team 1 and modelisation in their own team. A possible interaction with team 3 would have looked logical in the context of the study of the environment and pollutant effects on the ovary. Their work is more fundamental and addresses long term questions of sex differentiation that may have less visibility these days compared to the effects of the environment.

MECANISMES CELLULAIRES ET MOLECULAIRES IMPLIQUÉS DANS L'ORGANOGENESE DU PLACENTA ET DES GONADES

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	C	B	B

Team 3 : Maternal conceptus interactions and long term physiological consequences

This team is comprised of 2 INRA groups, one INSERM group and one ENVA group. There is a good fit between the 2 INRA teams as they are interested in very similar paradigms: the effect of the environment on the mother/progeny interaction and later consequences of this relation. The INSERM group also fits well with this theme as they use a mouse model and human tissues associated with metabolism-related diseases. It appeared clear to the committee that there will be a benefit from such an association and the potential outcome is great. These 3 groups have strong leaders and ambitious programs to answers numerous public health questions. Their publication record is good and



knowledge transfer is expected to increase further with their association. They will benefit from exchange with group 1 and 2 especially for tool development (epigenome assessment) but their theme is becoming more and more popular amongst scientists and they should expect increase in resources from outside grants or contracts.

The ENVA group is much more clinically oriented and definitively requires collaboration with the INRA scientists to achieve a higher impact of their research. They use a unique model, the dog that has been neglected by the scientific community for a long time and there are also limited resources at ENVA. Their collaboration with INRA is essential at least to get access to state of the art equipment (QRTPCR) and cell culture expertise. The only rationale given for their association with team 3 concerns the development of dog's tubal culture which is planned in team 3 for the bovine. Besides scientific interest, the association between ENVA and INRA was based on a strategic decision that should translate in more efforts to align resources and expertise. More collaboration is expected on cattle reproduction with the return of a key investigator who had an accident and is now back at ENVA.

The 3 teams have a similar number of groups/scientists/resources and this seems to be on purpose. This distribution has the merit of creating equilibrium but remains arbitrary in terms of scientific coherence and future interactions.

INTERACTIONS MERE CONCEPTUS ET CONSEQUENCES A LONG TERME

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

5 • Appreciation of resources and of the life of the research unit

–Funding and equipments :

It is difficult for the committee to assess financial management of this unit. None of the human resources groups made complaints except the fact that some technicians have to perform some administrative duties which reduce their availability for research.

The sharing of resources does not seem problematic and most equipments are easily accessible to all. The regrouping of the groups located in Jouy in the same building appears as a very important management decision that should help the cohesion of the whole group and maintain/sustain collaborations that are expected across teams.

–Human resources :

The different types of supporting staff, technicians, assistants, engineers would appreciate a more uniform or a more defined recognition of their contribution on publications as these are now considered for their promotions. We suggest that the new department head implements some guidelines for the scientists in all 3 teams to ensure homogenous treatment of these employees.

Recruitment has been strong and still additional new scientists are expected to join this unit within the next year. The average age is not high and although several people will retire in the next few years it did not appear as a threat to this committee since the most active groups are led by rather young scientists. The number of students is satisfactory and they had quite positive comments to make about their supervisor and the working environment provided. They would like more money to go to international meetings but realise that resources are limited for this type of activities even for senior scientists.

The unit has relatively few postdoctoral researchers. This is unfortunate since having postdoctoral fellows impacts on the dynamics of the teams and their contacts with other laboratories in France and abroad. It should be advisable to enhance recruitment of (foreign) postdoctoral visitors during the coming years, funded through personal fellowships and grants.



–Communication :

This unit has been quite interactive with the press and the population in general particularly because of the general interest in biotechnologies and the fears it has generated. The unit has invested in ethical analysis of animal ethics and biotechnology through several means (conferences, lectures, book chapters and interviews).

6 • Recommendations and advice

The new unit proposed looks as a balancing effort to allow each group enough space, weight and individuality to maximise productivity without tampering collaborations. This unit seems to be in a transition period, emerging from a strong leadership that developed several biotechnologies in farm animals and moving towards a more analytical perspective where the focus is on the impact of the maternal environment and its disturbances on the offspring's quality. This transition is perceived by the committee as necessary but will create a period of wavering that may impact of the overall outcome and the focus of the unit.

–Strong points :

A good group of motivated and talented scientists moving in an emerging field of research - environment and epigenome - with good ideas, enough freedom and resources.

–Weak points :

Concerning the diverse studies on the impact of the environment and the epigenome, the many model species that are being used by the different groups do not easily facilitate integration of data and swift concerted progress. Comparative biology is fine when the analytic process is well integrated and resources are allocated for that purpose.

The need for the newly appointed scientific leaders to foster the development of a common vision of where this unit should be in 4 years from now.

–Recommendations :

The committee recommends that the proposed plan and structure should continue as described but care must be taken to ensure the emergence of a unifying scientific leadership. The potential is there amongst the group leaders and hopefully the next 4 years should be enough to achieve a more integrated vision of this restructured unit. The previous leader, who is still active and maintains a strong scientific influence, can certainly contribute to this process through the realization of the Physiopole project partly associated with the BDR activity.

UMR INRA/ENVA Biologie du Développement et Reproduction

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



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A l'attention de Monsieur le
Directeur de la section des unités
AERES

Alfort le 2 avril 2009

Monsieur le Directeur,

Je vous prie de trouver ci-joint la réponse que la Directrice de l'UMR Biologie du Développement Reproduction INRA-ENVA a souhaité vous transmettre. Cette réponse est organisée selon vos indications en deux fichiers attachés distincts, UMR 1198_général et UMR 1198_corrections.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de ma sincère considération.

Directeur Délégué à la Recherche
ENVA

Comments on the report from the visiting AERES committee

INRA-ENVA UMR 1198 “Biologie du développement et Reproduction”

On behalf of my colleagues I would like to thank the AERES Committee for their efforts and this report. I am especially pleased that the committee recognized our unit as one of the leading groups in animal reproduction in Europe with motivated and talented scientists.

However, I am surprised that the following points have not been addressed in the report:

- We have been for a long time and are still connected to stakeholders including breeder associations involved in the organization of the reproduction and selection of farm mammals and start-up companies contributing to the development of reproductive biotechnologies. This point attesting our involvement both in basic and applied research would merit to have been emphasized.

- In contrast but in a complementary manner, several groups of the unit are involved in more fundamental subjects needing the use of mouse model such as the nuclear organisation of first stages of development, the toti/multipotency transition, the role of intracellular signals (Ca²⁺ et NADH/NAD⁺) during the oocyte activation and the gonad differentiation, these themes are few or not discussed in the report. This latter theme has been particularly neglected despite its contribution to the unit in term of publications, PhD training and grant obtaining.

- Biomedical groups are now becoming attracted by our new expertise in targeted transgenesis and epigenetics; in this context, the access to several farm animal models that we are presently regrouping within a dedicated structure (the Physiopôle) has to be considered as an asset rather than a weak point of our project. Our involvement in the development of targeted transgenesis in farm mammals with its financial and time constraints should have been better recognized.

- The creation of “Very large unit” structures inside INRA Institute (and in other French Institutes) requires that the themes developed in our unit be clearly identified and visible inside of this structure and outside. This is one of the reasons of our reorganization into three teams. Each of them reflecting the three major topics developed within the unit i.e.: Embryonic development and dynamics of the genome, Cellular and Molecular mechanisms involved in placenta and gonad organogenesis and Maternal-conceptus interactions and long term physiological consequences. We are aware of the need to foster a common vision within the future unit and to develop close interactions between groups and teams. In this respect, special attention will be given to the ENVA group to include it more in the unit’s development.

Finally, I am surprised that the predominant part of the report focused on our perspectives rather than on the evaluation of our results over the past four years.

Corinne Cotinot, UMR 1198

April 2009

