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## Environnement périnatal et croissance

Rapport Hcéres

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

Department for the evaluation of  
research units

AERES report on interdisciplinary unit:

Perinatal Environment and Health

PERINATSANTE

Under the supervision of the following  
institutions and research bodies:

Université Lille 1 – Sciences et Technologies - USTL

Université Lille 2 – Droit et Santé

December 2013



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

Department for the evaluation of  
research units

*On behalf of AERES, pursuant to the Decree  
of 3 november 2006<sup>1</sup>,*

- Mr. Didier HOUSSIN, president
- Mr. Pierre GLAUDES, head of the  
evaluation of research units department

*On behalf of the expert committee,*

- Mr. Daniel VAIMAN, chair of the  
committee

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<sup>1</sup> The AERES President "signs [...], the evaluation reports, [...] countersigned for each department by the director concerned" (Article 9, paragraph 3 of the Decree n° 2006-1334 of 3 November 2006, as amended).



## Evaluation report

This report is the result of the evaluation by the experts committee, the composition of which is specified below.

The assessments contained herein are the expression of an independent and collegial deliberation of the committee.

Unit name:	Perinatal Environment and Health
Unit acronym:	PERINATALSANTE
Label requested:	EA
Present no.:	EA4889
Name of Director (2013-2014):	Mr Laurent STORME
Name of Project Leader (2015-2019):	Mr Laurent STORME

## Expert committee members

Chair:	Mr Daniel VAIMAN, INSERM
Experts:	Mr Olivier CLARIS, Lyon hospital
	Mr Yves LE BOUC, INSERM
	Ms Susan E. OZANNE, Cambridge University, UK
	Mr Umberto SIMEONI, Aix-Marseille University

### Scientific delegate representing the AERES:

Mr Jean GIRARD

### Representatives of the unit's supervising institutions and bodies:

Mr Régis BORDET, University of Lille 2 - Droit et santé  
Mr Frédéric GOTTRAND, Directoire of the University hospital of Lille  
Mr Jean-François PAUWELS, University of Lille 1 - Sciences et Technologies  
Mr Bernard SABLONNIÈRES (Head, doctoral school Biology and Health n° 446)



## 1 • Introduction

### History and geographical location of the unit

The team is located in Lille, and depends on the two Lille Universities (Lille 1 and Lille 2). It is the result of a fusion of 4 teams focusing essentially on pediatrics and neonatology with the major theme being 'perinatal care'. This geographical bi-localisation is a potential source of problems in terms of organisation but this appears to be well managed. For the moment, the direction has been able to induce a cross-competency synergy, limiting these problems, especially through weekly lab meetings that allow information to circulate efficiently between the groups.

### Management team

The management is carried out by the director and a deputy-director.

### Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
<b>N1:</b> Permanent professors and similar positions	13	13
<b>N2:</b> Permanent researchers from Institutions and similar positions		
<b>N3:</b> Other permanent staff (without research duties)		
<b>N4:</b> Other professors (Emeritus Professor, on-contract Professor, etc.)		
<b>N5:</b> Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)		
<b>N6:</b> Other contractual staff (without research duties)		
<b>TOTAL N1 to N6</b>	<b>13</b>	<b>13 (FTE~6.5)</b>

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	6	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit*	3	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	11	11



## 2 • Overall assessment of the interdisciplinary unit

### Strengths and opportunities related to the context

The team is built on important medical concerns related to the programming of adult diseases from prenatal or perinatal sub-optimal exposures. The team has developed good novel animal models that it has characterized well at the whole body level. The localization in the North of France is a very good location in terms of regional epidemiological characteristics, since it is one of the regions most affected by obesity and cardiovascular diseases, which allows a very productive interfacing with clinicians and facilitates patient recruitment in the perinatal and mother-infant field. Another strength of the team has been the development of innovative industrial equipment especially in terms of pain detection and management. Finally, the local structures (university, hospital) are very supportive and willing strongly to help to develop and maintain this research team. In addition, several members of the team are strongly involved in teaching and research training.

### Weaknesses and threats related to the context

The team is located on two different distant sites, necessitating at least 10 minutes transportation for moving from one to the other. There are no full time researchers, the only scientists being university professors and clinicians who have many draws on their time, since they are very busy with teaching and/or hospital duties. There is for the moment insufficient internal research drive and expertise to provide mechanistic insights, which relies on recently started external cooperation. From discussion with the researchers and students, it appears that they have relatively insufficient circulating information on seminars and general scientific high-level information within the institution. To note, the technical staff are shared with other teams of the university, that could eventually lead to organizational problems.

### Recommendations

None of the weak points are unsolvable, even though some aspects of the solution may be a bit difficult to implement. An important issue would be to recruit one full time high-level researcher (high scientific profile, organizational capabilities) who could be attracted by the possibility of developing freely his own research group, highly connected to the clinic with the possibility of using animal models; a package could be proposed, since the University appears very eager to maintain and develop the research structure. Another issue would be to develop the DoHAD (Developmental origin Of Health and Disease) topic under the angle of epigenetic analysis (high throughput methylation analysis, ChIP-seq with epigenetic marks, mi-RNA profiling) and the development of cell models to validate and manipulate the environmental conditions (hypoxia, serum-deprivation, serum excess could be tested in cell cultures from tissue-derived cell lines, in vivo validation of miRNA putative targets). Conjointly there is of course an immediate need to develop bioinformatic capabilities locally.

Other minor points could be easily improved, such as a widening of the competencies of the students through external conferences.



### 3 • Detailed assessments

#### Assessment of scientific quality and outputs

The scientific production is quite abundant, in a field for which few research teams are involved in France despite its extreme importance in terms of the programming of metabolic epidemics (cardiovascular diseases, obesity, type 2 diabetes). Between 2008 and 2013, 58 articles have been published with a direct connection to members of the team. Besides, one of the members through providing DNA samples for genotyping in programs linked to metabolic diseases developed mainly by another team in Lille, was a co-author of several articles in top scientific journals (Science, NEJM, Nature Genetics). The production originating directly from the work of the team is published in a priori lower impact factor journals. However, precise tracking of the articles reveals clearly their importance, at least for some of them (for instance “Maternal perinatal undernutrition drastically reduces postnatal leptin surge and affects the development of arcuate nucleus proopiomelanocortin neurons in neonatal male rat pups”, published in 2008 in *Endocrinology* has been quoted 86 times, i.e. 15 times per year; “Sex- and Diet-Specific Changes of Imprinted Gene Expression and DNA Methylation in Mouse Placenta under a High-Fat Diet”, published in *PlosONE* in 2010, has been cited 33 times (almost 9 times per year); “Maternal stress alters endocrine function of the fetoplacental unit in rats” published in 2007 in *American Journal of Physiology*, has been cited 74 times, more than 10 times a year) without decrease in the number of citations in the period under evaluation, even though this article was published one year before. These examples clearly demonstrate the scientific relevance and recognition of the team’s work in the field of perinatal and endocrine programming. To note in the field of pain management, the team obtained a ANR funding for the development of a pain monitoring device focused on new born infant applications. This device is protected by 2 international patents (classically considered as comparable to top publications).

#### Assessment of the unit's academic reputation and appeal

Several members of the team are regularly invited to international conferences around the thematic of neonatal/fetal pain and stress, as well as sub-normal maternal nutrition during pregnancy. Mr Laurent STORME is the president of the organizing committee of the 'Journées Francophones de la Recherche en Néonatalogie'.

#### Assessment of the unit's interaction with the social, economic and cultural environment

The geographic situation and the composition of the team gives access to a collection of maternal samples that could be assigned to different ‘metabolic status (BMI, precarity,...)’. There are also very good facilities for implementing alterations of maternal diets in animal models. These models are available for the clinical teams, in particular obstetric surgeons and pediatricians. This situation is not very frequent in France, where such possibilities are available only in a handful of places.

The visit revealed a team working in a good environment, with useful facilities, a good support of the university, a strong investment in teaching activities and training PhD students. The thematic are very coherent around the accumulation of knowledge linked to consequences of alterations of the perinatal environment. The use of this knowledge as a translational research tool is easy to set up given the natural link of many members of the team with patients to release information. The implementation in the north of France, where nutritional disorders, poverty, obesity are the most frequent is especially logical, and could contribute to decrease societal costs.

In connection with the management of pain and stress in fetuses and neonates, the committee was impressed by the industrial development of a tool for pain assessment, and by the success in selling this equipment throughout the world.



### Assessment of the unit's organisation and life

In terms of “A” category staff (researchers, either from university or clinicians or research institutes), EA 4489 is a research team composed of university professors, assistant professors and clinicians, but without full time researchers from national research institutes. In the “B” category staff (corresponding to technicians, engineers and administrative personal), there are 5 technicians and engineers, but only one full-time in the team. A difficulty is the fact that most of the technical staff are on a half-time basis, which may make it difficult for concentrating on specific topics and to focus the forces on a given hot-topic at a certain moment of time. In the field of staff, the committee felt strongly that the absence of fulltime researchers was a problem that should be addressed as soon as possible, since it was felt that it is the only way to develop more ambitious research programs going deeply into the mechanisms at work in terms of programming of adult disease following injuries of the early life.

There are also weaknesses that are observable in terms of structure and in terms of scientific project. In terms of structure, being divided into two sites is clearly difficult to cope with on a daily basis, and could increase significantly the difficulty of making regular contacts among the team members.

### Assessment of the unit's involvement in training through research

There are many professors in the staff and the involvement in teaching is outstanding at the levels of L3, M1, M2 and very interestingly, a European Master is in preparation around the DoHAD concept. It was also noted by the committee after discussing with the students, that while they were overall very satisfied with the daily life of the team, they appeared a bit disconnected from seminars of general interest that could help them to evolve in their scientific formation. The first point is demonstrated by the absence of detectable conflicts, meaning that the management is very well done. In addition, the direction systematically provides the means for the students to participate to international and national meetings. Encouraging the students and the direction to generate a ‘journal club’ structure could be one of the numerous ways of improving this situation.

### Assessment of the strategy and the five-year plan

There are two major projects that are the logical follow-up of the previous research topics: one deals with suboptimal nutrition, and the other with pain/stress management in newborns and fetuses. The committee observed that there are clearly strong forces in the team to describe the processes of suboptimal nutrition, but not to go further in terms of mechanisms. This project in its present form, do not encompass the use of epigenetic tools as a way of understanding the health problems possibly induced in the progeny. The committee unanimously felt that the team should engage itself in the ‘in situ’ creation of an ‘epigenetic’ know-how, not only based upon external collaborations. That way, the team may be able to give an important mechanistic bonus to its physiological observation and thus to publish in journals of much higher impact. This should increase their international recognition and visibility. Another important point would be to develop bioinformatic capacities in situ.

For the project of pain and stress, as mentioned above, the committee was impressed by the industrial development of a tool for pain assessment, and by the success in selling this equipment throughout the world. This success would be even more complete if some scientific understanding of the mechanisms at work, or some epidemiological assessment of the tool benefit could be developed in the next five-year period. Part of the project could be to concentrate on that issue.

The feeling of the committee was overall that the team has a very interesting potential for development, in terms of tools, of medical problem addressed.

Another feeling of the committee was that the team would benefit from discussing special issues of their protocols on a wider scale with external teams. Among these protocols/project,

1. The denutrition model in rats with the periods of application could be re-thought in order to dissociate the prenatal and post-natal effects (mediated for instance by milk composition).

2. The injection of opioid drugs in the amniotic liquid and their possible long-term consequences should be carefully assessed in animal models. For instance the methylation of genes encoding receptors could be analyzed.

3. There is a need to open the scientific communication to other fields and other competencies, available in Lille or elsewhere. Locally a better advertising on conferences could be achieved quite easily.





## 4 • Conduct of the visit

Visit date:

Start: 2013 december the 6<sup>th</sup>, at 09h30

End: 2013 december the 6<sup>th</sup>, at 16h00

Visit sites: Faculté de Médecine - Département Hospitalo-Universitaire de Recherche  
Expérimentale (DHURE), Université Lille 2 - Droit et Santé

Institution: Université Lille 1 - Sciences et Technologies

Address: 1, Place de Verdun 59045 Lille Cedex

Second site: Université Lille 1 - Sciences et Technologies, UFR de Biologie UPRES EA 4489

Institution: Université Lille 1 - Sciences et Technologies

Address: Bâtiment SN4 - Université Lille 1 - 59655 Villeneuve d'Ascq cedex

Conduct or programme of visit:

The visit was conducted entirely through seminars in the university Conference Room, as well as three consecutive meetings with 1) the students, 2) the technical and administrative staff and 3) the researchers.



## 5 • Supervising bodies' general comments