



# Neuroimmunologie des annélides

## 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 :

Annelid's Neuroimmune

University of Lille 1



Mars 2009



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et de l'enseignement supérieur

Section des Unités de recherche

# Evaluation report

Research unit :

Annelid's Neuroimmune

University of Lille 1



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 : Annelid's Neuroimmune

Requested label : UMR CNRS

N° in case of renewal : FRE2933

Head of the research unit : Mr Michel SALZET

## University or school :

University Lille 1

## Other institutions and research organization:

CNRS

## Date of the visit :

December, 10th 2008



# Members of the visiting committee

## Chairman of the committee :

Mr Jonathan EWBANK, CIML, University Aix-Marseille 2

## Other committee members :

Mr Steven HUSSON, University Frankfurt, Germany

Mr Edwin DE PAUW, University Liege, Belgium

Mrs Catherine LUBETZKI, University Paris 6

## CNU, CoNRS, CSS INSERM, INRA, INRIA, IRD... representatives :

Mrs Sylvie MAZAN, CoNRS representative

Mr Michel MATHIEU, CNU representative

# Observers

## AERES scientific representative:

Mr Marc BONNEVILLE

## University or school representative:

Mr Isham SHAHROUR, University Lille 1

## Research organization representative :

Mr Bernard BIOULAC, CNRS



# Evaluation report



## 1 • Short presentation of the research unit

- Total number of lab members : 28.5 including
  - researchers with teaching duties : 10
  - full time researchers : 2
  - postdoctoral fellows : 2
  - PhD students : 7 all with a fellowship:
  - engineers, technicians and administrative assistants : 6,5 including 1 on a CDD
- Numbers of HDR and of HDR who are PhD student advisors : 6
- Numbers of PhD students who have obtained their PhD during the past 4 years : 10
- Numbers of lab members who have been granted a PEDR : 3
- Numbers of “publishing” lab members : 12 out of 12

## 2 • Preparation and execution of the visit

Paper and electronic documents required by the committee were provided in a timely manner before the visit. The site visit was well organised. A number of supplementary documents (reprints, preprints) were provided during the visit. Only a cursory visit of the laboratories was made, but the committee did not consider this a problem.

The formal scientific presentations by current members of the unit were complemented by a short talk from the head of the Terahertz imaging team. This group proposes to join the unit.

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

During the period under review, the unit’s research staff was almost entirely composed of university lecturers. The interview with the representatives of the university made it very clear that the unit director is a highly-valued member of the professorial staff. He and the other members of the unit participate very actively in both teaching and administrative functions. Recently, they have been joined by two CNRS researchers, one of which heads a research group and has been co-director of the unit. The committee saw the subdivision of the unit as a very positive step. The committee also had the impression that the codirector was helping the unit to become more focused in its activities.

The lack of focus that has handicapped the unit in the past is reflected in the scientific production. A very large number of articles have been produced in the last few years on a surprisingly broad range of subjects. But, leaving aside the question of the quality of the respective journals, a very large proportion of this prolific output has had limited impact. Since this could be a sign of the unit producing truly groundbreaking work that was slow to be fully recognised, the committee examined publications pre-dating the current review period. Taking just the papers authored by the director, there were 60 articles between 2001 and 2008 referenced by ISI. At first sight, this is a commendable achievement. But of these articles, 40 were cited fewer than 10 times, and of those published at least 12 months ago, ten have never been cited at all. Given the teaching and administrative demands on the research staff, this is a particularly serious dispersion of energy.



The exception to this trend is the work concerning MALDI-imaging, which is already well cited in journals that are highly considered in the field. Similarly, this work is attracting funding in the context of competitive national programmes, and the researcher heading this program is gaining a national and international reputation for her work. That said, the unit director is also active in national and international cooperative programmes, although few might seem really top-notch.

It is too early to evaluate properly the impact that the codirector group's work will have, but they are making a positive start and bring complementary expertise.

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

### Team 1

Team 1 comprises one professor (half time), 3 assistant professors and one research assistant (adjoint-technique).

The team was created in 2007 and most of its staff was recently hired. Its research topic deals with the identification of anti-microbial peptides (AMPs) in annelids, and their role in neural regeneration in the leech model. This topic takes into account phylogenetic aspects and comparative biology within annelids, with the characterization of AMPs in several species, either through biochemical approaches or screening of EST libraries. From a functional standpoint, the main achievements of the team deal with characterization of a new induction mechanism of innate immune responses by microorganisms in lophotrochozoans, and the neurotrophic properties of AMPs during neural cord regeneration in leech, an original observation that opens promising perspectives. Characterization of a cytokine (HmEMAP II) and its chemo-attracting role in the recruitment of microglial cells is also another important finding. Exploration of the mechanisms involved in neural immunity has also led to identification of TLR/NLR-like receptors in leech neural system.

Team 1, although quite small, has proven skills in a variety of complementary experimental approaches and technologies (peptide isolation and characterization, EST library screening, RNAi gene knockdown, cellular approaches), with a very positive input of recently hired staff.

The current head of the team (helped by the unit director) is very active and has demonstrated her ability to manage properly both the technological and conceptual issues raised by her project.

The publication record is satisfactory when taking into account the heavy teaching load of the permanent researchers (who are all « enseignant-chercheurs »): 20 papers in peer-reviewed journals, 4 reviews, 7 chapters, 7 invitations at international meetings, although as emphasised below, quantity does not necessarily replace quality.

The limited number of HDR (only 2) explains the limited number of PhD students involved in this program (one PhD thesis in 2007).

Team 1 has got several grants from national (Université Lille 1, Génopole Lille, Génoscope, CNRS) and international (IRSC-Canada, FRSCQ-Canada, NIH) agencies, reflecting its international recognition. Team 1 is well integrated within an international network working on Leech EST libraries and genome sequencing.

The project proposed by team 1 is ambitious and structured around 4 topics : (i) the mode of action of neural regeneration mediators (PAMs et EMAP II), ii) the mode of pathogen sensing by danger receptors, iii) the role of blood compounds in immunity and regeneration, and iv) the comparative and phylogenetic analysis of AMPs in annelids. In terms of relevance and feasibility, this project logically extends the most recent results obtained by this team and rests on its demonstrated skills and expertise. However owing the very small size of the team (even when taking into account the recruitment in 2009 of a new assistant professor), it will be important to prioritize and better focus the various sub-projects.

Regarding topic (i), there is convergence if not overlap with the topics developed by team 2, as both teams are addressing functional aspects of molecules involved in neural regeneration. Although likely, a tight interaction and coordination of the projects run by these two teams is to be encouraged.



**Nom de l'équipe : Signaux de danger, voies de signalisation et effecteurs**

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	A	B

**Team 2**

Team 2 is codirected by two PIs, this team comprises 8 people, including 1 DR2, 4 enseignants chercheurs, 1 AJT et 1 PhD student (no postdoctoral fellows).

The project, derived from data regarding recruitment of microglial cells after neural lesions and its impact on healing, deals with the role played by 3 molecules identified from a leech EST library screening, which are upregulated in neurons after lesion: IL16 and C1q (with chemotactic properties) and progranulin (with neurotrophic properties). The aim of the project in the coming years is to identify their receptors, in particular through surface plasmon resonance approaches, analyze their signalling patterns and study their impact on healing, using blocking antibodies and RNAi-mediated gene knockdown.

The study model is original and interesting and allows analysis of some mechanisms involved in neurogenesis and/or neural regeneration. Results already obtained supports the validity and overall rationale of the approach. However the selection strategy of candidate targets from EST library screening was a bit like a fishing trip. To focus immediately on molecules homologous to known mammalian players is questionable. New approaches based on microarray hybridization are planned and should be encouraged. Another concern deals with the program proposing extrapolation to human neural pathologies covering a broad array of diseases such as multiple sclerosis, Alzheimer disease, ALS... It would be preferable in this respect to focus on a particular model with better relevance to mammalian physiopathology (eg axotomy or comparison of leech vs murine CNS). This would require stronger links with teams specialized in neurosciences.

The recent publication output is quite low (8 papers published in rather low impact journals since 2004), but this might be explained in part by the recent reorganization of the team.

**Nom de l'équipe : Cellules microgliales et réparation**

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

**Team 3**

Team 3, dedicated to mass spectrometry imaging, is the largest of the unit : it comprises one professor (Half-time), 2 assistant professors, 1 CR1, 1AJT, 2 post-doctoral fellows and 6 PhD students). It has access to good equipment, which will nevertheless need to be renewed and upgraded in the near future.

Mass spectrometry is among the physicochemical approaches that have recently revolutionized biological chemistry. The originality of the approaches developed by team 3 lies in the coupling of mass spectrometry with microscopy and histochemistry, which allows assessment of the tissue location of the molecules identified and possibly quantified. In this regard team 3 takes part actively in the implementation of molecular imaging mass spectrometry techniques. The combination of expertises in physico-chemistry and biology within the unit





allows development of an original and competitive project with good international level. It is a highly multidisciplinary project starting from a precise understanding of physico-chemical concepts and going to setting up of elegant technical strategies such as development of « tag-mass » reagents. This high quality research has led to several publications in the best specialty journals (though not cited so much, but this is improving), and significant industrial applications. The team receives invitations to international meetings on a regular basis. They have an active policy of postdoctoral recruitment that is starting to be fruitful.

Nom de l'équipe : MALDI IMAGING

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

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

### – Management

The committee was much impressed by the obvious energy and enthusiasm of the unit director. He has gathered a motivated group of individuals who clearly feel that they are part of a team. This inspiration from the director is a key point for any successful research structure. On the other hand, the unit is housed in an antiquated building that probably does not conform to current health and safety regulations. An important point raised by the director, and which the committee deplores, is the essentially non-existent possibility for promotion for the university-employed technical staff. The committee hopes that increased administrative autonomy within the university will be used to rectify this egregious situation.

The interviews that the committee had with the students and technical staff did not reveal any other real problems, but rather confirmed the committee's positive impression of the organisation of the unit. The committee commends the director for his active policy of promoting student participation in conferences and meetings.

### – Human Resources :

There is a preponderance of permanent full-time university lecturers. The director explained his desire to try to increase the number of full-time research staff. The committee encourages him in this aim, but would like to emphasize the fact that the relatively restricted impact of the unit's work will count against any candidate (regardless of their relative merit) in the intense competition for permanent posts at INSERM or CNRS.

## 6 • Recommendations and advice

### – Strong points :

The unit appears to be made of a cohesive group of individuals who are proud to be working under direction of the current head.

The MALDI-imaging group has emerged as a very promising group.



– Weak points :

The obvious enthusiasm of members of the unit for new challenges is not always accompanied by sufficient rigour or reflection on the investment required to investigate a given question.

The structure is unbalanced, with an over-reliance on permanent staff.

– Recommendations :

The unit could certainly benefit from the presence of an increased number of post-doctoral fellows. The director is encouraged to favour foreign candidates who do not wish to seek a permanent post in France to give a more balanced structure to the unit.

As noted above, there is a tendency for a lack of focus in certain projects. Curiosity-driven research is to be encouraged, but the energies of researchers with a full teaching load need absolutely to be channelled into questions that have medium- and long-term perspectives.

Again, while wholeheartedly encouraging the idea of curiosity-driven research, the committee does not believe that the adoption of further model animals, particularly those that are not experimental tractable, will aid the unit in its principal goals. The importance of the questions that could be answered with animals that are difficult to culture, or that lack any research tools is not likely to justify the investment of effort required.

The director evoked the possibility of passing on the direction to a senior permanent member of the unit. This should be seriously considered in the medium-term.

The role of MALDI team (team 3) needs to be carefully considered. The committee was told that the head of this team had applied unsuccessfully for an INSERM Avenir project to focus on the use of MALDI imaging in medical diagnostics. If this is to be the principal motivation of her group for the coming years, the time spent on developing methods for imaging leeches might need to be restricted, in which case the group would then be more in the position of a service-provider for the unit's leech projects.

The committee is in favour of the merging of the MALDI team with that of Terahertz Imaging from the IEMN.

Finally, although the committee noted a very positive evolution in the organisation of the unit, with the emergence of distinct groups, there was some residual concern regarding the current structure wherein the current director plays co-directs one group with the head of team 1 and co-directs a project nominally under the scientific responsibility of the head of team 3. They encourage the unit to take the current reorganisation to its logical conclusion. This would entail the head of team 1 taking full responsibility for her project, and the director focusing his energies on the neurogenesis/regeneration/degeneration project, within the context of a fourth group. While the current head of the unit would retain overall direction, and maintain a mentoring role for the more junior group leaders, this increased demarcation of research areas can only aid in the establishment of clear research priorities, with realistic targets being set for each group.

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	A	A+	B

*Villeneuve d'Ascq, le 7 avril 2009*

Philippe ROLLET, Président de l'Université Lille1

*A l'attention de Jean-François DHAINAUT, président de l'AERES*

Objet : Réponse au Rapport du Comité de Visite  
Laboratoire de Neuroimmunologie des Annélides (FRE 2933)

Monsieur le Président et Cher collègue,

Nous tenons à remercier le comité de visite pour l'analyse du bilan et du projet  
Laboratoire de Neuroimmunologie des Annélides (FRE 2933).

Vous trouverez ci-joint la réponse de l'unité à ce rapport. Elle comporte :

- des demandes de correction d'erreurs factuelles ;
- des observations et commentaires sur le rapport d'évaluation.

Nous vous prions d'agréer, cher collègue, l'expression de nos sincères salutations.

Signature

Le Président de l'Université  
Ph. ROLLET





## LABORATOIRE DE NEUROIMMUNOLOGIE DES ANNELIDES – FRE CNRS 2933-LIA CNRS

Pr. M. Salzet  
Directeur de l'Unité  
Villeneuve d'Ascq, le 6 Avril 2009

### Réponses au comité d'évaluation de l'unité de recherche :

#### Observations générales

Après lecture du rapport, les membres de l'unité remercient le comité pour son travail d'évaluation. Les membres du laboratoire apprécient que la restructuration de l'unité, effective depuis 2007, ait été bien perçue par la commission.

**Cependant, les membres de l'unité souhaitent apporter certains éléments complémentaires, afin de mieux traduire, dans sa globalité, le contexte dans lequel le laboratoire s'efforce de développer ses recherches.**

1- La remarque relative au facteur immédiat de citation des publications devrait être nuancée, car ce facteur dépend de la taille de la communauté scientifique travaillant sur un modèle donné. La communauté des chercheurs travaillant sur des modèles non conventionnels est beaucoup plus réduite que celle travaillant sur des animaux modèles. Il nous semble important de souligner que le laboratoire a pris le risque de travailler sur un modèle animal non conventionnel qui pourra contribuer à l'apport de connaissances fondamentales importantes dans quelques années. Il est également important de souligner la qualité de la production scientifique de l'unité sur ce dernier quadriennal.

2- Il faut également prendre en considération comme un élément de reconnaissance internationale de l'unité, le nombre d'invitation dans des congrès internationaux de renom (19 dont l'ASMS, les GRC, HUPO, ISDCI) ainsi que les contrats étrangers obtenus (NIH, NSF, IRSC, FRSQ).

3- De plus, nous souhaitons insister sur le fait qu'en général, le développement de nos thématiques de recherche repose sur l'établissement de collaborations nationales et internationales avec des équipes ayant une notoriété reconnue dans leur domaine. Dans la politique menée par le laboratoire cela se traduit par la réalisation de co-publications, de co-demandes de financement ainsi que de codirections de thèses.

4- En ce qui concerne les financements, nous souhaitons préciser que certains des contrats obtenus par le directeur (NIH, Génopôle, Génoscope) ont été des demandes communes pour l'ensemble des équipes.

5- Concernant le point relatif à l'impossibilité de succès au concours CNRS de candidats présentés par l'unité, malgré la qualité scientifique de ces derniers, qui serait lié au manque de renommée de l'unité, nous trouvons ce commentaire étonnant. Le CNRS ayant accordé son label au laboratoire, il nous apparaît donc surprenant de ne pouvoir espérer obtenir de poste au concours si le candidat présenté est excellent.

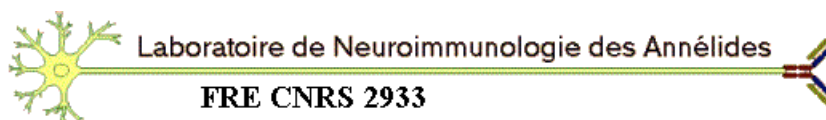
**Enfin, des commentaires spécifiques à chaque équipe doivent être ajoutés**

*Concernant l'équipe 2*, le commentaire portant sur la stratégie de recherche par « fishing » apparaît exagéré. Il aurait été, en revanche, plus opportun de souligner les efforts mis en œuvre par l'équipe pour disposer des outils nécessaires (banque d'ADNc, Ac, cellules microgliales purifiées...) pour répondre à ses recherches. Le criblage de la banque d'EST a été réalisé en gardant à l'esprit les données obtenues chez d'autres modèles, et c'est dans ce contexte qu'ont été recherchés des facteurs chimioattractants des cellules microgliales e.g. IL-16 et C1q.

*Concernant l'équipe 3*, certains éléments mentionnant le passage du responsable de l'équipe 3 devant un comité Inserm doivent être précisés. Après un processus de sélection sur dossier, une présentation orale en vue de l'obtention d'une équipe AVENIR a bien eu lieu. Cependant, selon le rapport de la commission qui a siégé, l'équipe était déjà trop structurée et autonome pour correspondre aux critères d'une labellisation AVENIR. Il a donc été recommandé par l'INSERM de faire la demande d'une unité monothématique. De plus, il semble que les programmes de financement ainsi que les efforts de valorisation (contrats industriels, brevet, Start-up) réalisés par l'équipe n'aient pas été considérés. Ses thématiques de recherche n'ont pas été décrites. Il n'a pas non plus été fait mention que cette équipe avait été créée *ex nihilo* suite à l'obtention d'une ACI Jeunes Chercheurs en 2004.

Nous espérons que ces points pourront être pris en considération dans l'évaluation globale de l'unité. Veuillez agréer Monsieur le Président l'expression de nos sentiments les plus cordiaux

Pr. Michel Salzet et les membres de l'unité\*



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