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## MMNP - Maintenance myélinique et neuropathies périphériques

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

Section des Unités de recherche

AERES report on the research unit

Maintenance Myélinique et Neuropathies

Périphériques

From the

Université de Limoges

December 2010



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Section des Unités de recherche

# AERES report on the research unit

Maintenance Myélinique et Neuropathies

Périphériques

From the

Université de Limoges

Le Président de l'AERES

**Didier Houssin**

Section des unités  
de recherche

Le Directeur

**Pierre Glorieux**

December 2010



# Research Unit

Name of the research unit: Maintenance myélinique et Neuropathies périphériques

Requested label : EA

Name of the director: Mr. Benoit FUNALOT

# Members of the review committee

## Committee chairman

Mr. Bernard ZALC, Université Paris 6, Paris

## Other committee members

Ms. Anne Baron VAN EVERCOOREN, Université Paris 6, Paris

Ms. Rebecca MATSAS, Institut Pasteur, Athènes, Grèce

Mr. Bruno BROCHET, Université de Bordeaux 2

Mr. Frédéric DUBAS, Université d'Angers, représentant du CNU

# Observers

## AERES scientific advisor

Mr. Christian GIAUME

## University, School and Research Organization representatives

Mr. Serge VERDEYME, Université de Limoges



# Report

## 1 • Introduction

- Date and execution of the visit :

The visit began at 8:30 am on December 17th 2010 and ended the same day at 5:00 pm. The agenda included the presentation of the unit past activities and project by the head of the unit, presentation of axis 1, presentation of axis 2, and successive meetings with staff members, engineers and technicians, students and post-doc and University of Limoges representatives.

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

Current activities and projects relating to peripheral nerve are based on the work of the head of the neurology department, who has for several decades developed in Limoges the morphological analyses of peripheral nerves from patients with peripheral neuropathy and corresponding animal models. This initial approach has been progressively implemented by more sophisticated technique such as biological analyses, immuno-EM, and more importantly molecular genetic analyses.

These activities are backed up by the National reference centre for rare peripheral neuropathies (created in 2006), the Departement and laboratory of neurology and the department of biochemistry and molecular genetics.

- Management team: The head of the unit is M. FUNALOT
- Staff members

|  |            |
|--|------------|
| N1: Number of researchers with teaching duties (Form 2.1 of the application file)  | 11         |
| N2: Number of full time researchers from research organizations (Form 2.3 of the application file)                       | 0          |
| N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)                | 3PH, 1 AHU |
| N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file) | 6          |
| N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file) |            |
| N6: Number of Ph.D. students (Form 2.7 of the application file)  |            |
| N7: Number of staff members with a HDR or a similar grade  | 8          |



## 2 • Overall appreciation on the research unit

- Summary

This is an excellent project relying on the existence of a superb collection of biological samples from patients presenting with a peripheral neuropathy and which have been well characterized clinically and morphologically at the EM. This is probably the best and most competitive french team in the field of peripheral neuropathy.

- Strengths and opportunities

The committee has appreciated the multidisciplinary approach, the excellent interaction between clinical and basic research, the originality of the approach based on the morphological examination to guide more molecular investigations. The ongoing collaboration with the unit at the ENS (Paris) give to this rather clinically oriented team a strong basic research back up. This scientific strategy has to be maintained. The project has a complete support from the University and has been identified as one of the 3 out of 25 projects presented this year that has already been selected by the University (based on the very positive comments by the SAB) to receive 120 k€ for a 3 year period.

- Weaknesses and threats

The experimental therapeutic part of the project needs to be more focussed. The hydrogel part of the project with its strong linked with MedinCell (a biotech company based in Montpellier) has a strong potential. However, the committee recommends the PI to choose one factor (for instance NT3) and carry on all the experimentation to prove the concept, rather than testing a battery of compounds. The high throughput project could be dropped since there is not locally the forces to develop such a costly project. The rhEPO project appears as a service prestation for an israelian company and could as well be abandoned, since the cognitive outcome seems weak. These recommendations, if followed, would allow the principal investigator to concentrate human ressources on less projects and increase dramatically his chances of success.

- Recommendations

The choosen director is an excellent scientist and he has been recognized and accepted by all the participants of the project as well as by the local academic staff as the best candidate to direct the Unit. This put him in the best position to impose to his group the above listed recommandations : namely focus the projects on those where the team is in a position of international leader and for which they have the human and financial forces to conduct the project to the best sucessful issue.

- Production results

During the past 4 years: 139 papers in journals referenced in PubMed, among them 83 had a member of the laboratory as either first or last author, 26 of which with an IF>5.

|   |    |
|---|----|
| A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research    | 11 |
| A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research | 0  |
| A3: Ratio of members who are active in research among staff members $[(A1 + A2)/(N1 + N2)]$             | 1  |
| A4: Number of HDR granted during the past 4 years   | 4  |
| A5: Number of PhD granted during the past 4 years   | 11 |



### 3 • Specific comments

- **Appreciation on the results**

A major recent finding from this group is that the depletion of Schwann cells and boundary cap cells or inactivation of *Krox20/Egr2*, a master regulatory gene for myelination in Schwann cells, results in transgression of the CNS/PNS boundary by astrocytes and oligodendrocytes and in myelination of nerve root axons by oligodendrocytes. They have analyzed a human patient affected by a congenital amyelinating neuropathy, associated with the absence of the *Krox20* protein in Schwann cells. In this case, the nerve roots were also invaded by oligodendrocytes and astrocytes, which indicates that transgression of the CNS/PNS boundary by central glia can also occur in pathological situations in humans.

In a randomized study against a placebo they have demonstrated an analgesic effect of botulinum toxin (BTX-A) in patients with diabetic painful peripheral neuropathy. A single session of multiple intradermal injection of BTX-A produces long-lasting analgesic effects in patients with focal painful neuropathies and diabetic neuropathic pain, and is particularly well tolerated.

An interesting discovery is the demonstration of mitochondrial abnormalities in axons from neuropathic patients presenting with mutations in *MFN2* et *GDAP1* genes and that severe early-onset axonal neuropathy due to *MFN2* mutations can present as an apparently recessively inherited neuropathy.

For a group of this size there is a good number of publications. However, they are somewhat heterogeneous ranging from *NEJM* to *La presse medicale* or *la revue du praticien*. The team has benefited 2 ANR grants and will deposit 2 new projects to answer the 2011 call.

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

Participants to the project receive numerous invitations to participate and communicate during national and international meetings.

One post-doc from Uruguay was recruited last year for 1 year. However, there is no full time researchers, and this year no post-doc.

The members of the unit have obtained 2 ANR grants and have 2 ANR grants pending.

This team has an international reputation. More precisely they have established collaborative programs with Australia, USA (several), Algeria, Spain, Germany....

The committee acknowledges the strong link with the biotech *MedinCell*.

They have monthly seminars with invited speakers from outside Limoges. Based a large part of the project on candidate genes is a real risk, but they like to demonstrate that this risk can pay off !

In addition, concerning the scientific animation, it is of note that they organize once a year a public debate for lay people animated by a media speaker.

- **Appreciation on the management and life of the research unit**

Each group of personnel (researchers, technicians, students) all agrees on the choice of the head of the project. They all appreciate his qualities and none has reported a single conflict. They have a weekly lab meeting.

They have monthly seminars with invited speakers from outside Limoges. Based a large part of the project on candidate genes is a real risk, but they like to demonstrate that this risk can pay off.



In addition, concerning the scientific animation, it is of note that they organize once a year a public debate for lay people animated by a prominent speaker.

Practically all the participants to the project have a heavy load of teaching and they are very active in different activities to support the regional effort of research.

- **Appreciation on the scientific strategy and the project**

This is an excellent project relying on the existence of a superb collection of biological samples from patients presenting with a peripheral neuropathy and which have been well characterized first clinically and then morphologically at the EM level.

Following an evaluation by the SAB from the University of Limoges, a support of 40 k€/year has already been obtained from the University. The SAB strongly recommended to support this team that has been ranked amount the 3 first teams of the University of Limoges.

This is probably the best and most competitive French team in the field of peripheral neuropathy.

| <b>Intitulé UR / équipe</b>                                 | <b>C1</b> | <b>C2</b> | <b>C3</b> | <b>C4</b> | <b>Note globale</b> |
|---|-----------|-----------|-----------|-----------|---------------------|
| <b>MAINTENANCE MYÉLINIQUE ET NEUROPATHIES PÉRIPHÉRIQUES</b> | <b>A</b>  | <b>A</b>  | <b>A+</b> | <b>A</b>  | <b>A</b>            |

**C1** Qualité scientifique et production

**C2** Rayonnement et attractivité, intégration dans l'environnement

**C3** Gouvernance et vie du laboratoire

**C4** Stratégie et projet scientifique





## Statistiques de notes globales par domaines scientifiques (État au 06/05/2011)

### Sciences du Vivant et Environnement

| Note globale | SVE1_LS1_LS2 | SVE1_LS3 | SVE1_LS4  | SVE1_LS5  | SVE1_LS6  | SVE1_LS7  | SVE2_LS3 * | SVE2_LS8 * | SVE2_LS9 * | Total      |
|--------------|--------------|----------|-----------|-----------|-----------|-----------|------------|------------|------------|------------|
| A+           | 7            | 3        | 1         | 4         | 7         | 6         |            | 2          |            | 30         |
| A            | 27           | 1        | 13        | 20        | 21        | 26        | 2          | 12         | 23         | 145        |
| B            | 6            | 1        | 6         | 2         | 8         | 23        | 3          | 3          | 6          | 58         |
| C            | 1            |          |           |           |           | 4         |            |            |            | 5          |
| Non noté     | 1            |          |           |           |           |           |            |            |            | 1          |
| <b>Total</b> | <b>42</b>    | <b>5</b> | <b>20</b> | <b>26</b> | <b>36</b> | <b>59</b> | <b>5</b>   | <b>17</b>  | <b>29</b>  | <b>239</b> |
| A+           | 16,7%        | 60,0%    | 5,0%      | 15,4%     | 19,4%     | 10,2%     |            | 11,8%      |            | 12,6%      |
| A            | 64,3%        | 20,0%    | 65,0%     | 76,9%     | 58,3%     | 44,1%     | 40,0%      | 70,6%      | 79,3%      | 60,7%      |
| B            | 14,3%        | 20,0%    | 30,0%     | 7,7%      | 22,2%     | 39,0%     | 60,0%      | 17,6%      | 20,7%      | 24,3%      |
| C            | 2,4%         |          |           |           |           | 6,8%      |            |            |            | 2,1%       |
| Non noté     | 2,4%         |          |           |           |           |           |            |            |            | 0,4%       |
| Total        | 100,0%       | 100,0%   | 100,0%    | 100,0%    | 100,0%    | 100,0%    | 100,0%     | 100,0%     | 100,0%     | 100,0%     |

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

### Intitulés des domaines scientifiques

#### Sciences du Vivant et Environnement

- SVE1 Biologie, santé
  - SVE1\_LS1 Biologie moléculaire, Biologie structurale, Biochimie
  - SVE1\_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes
  - SVE1\_LS3 Biologie cellulaire, Biologie du développement animal
  - SVE1\_LS4 Physiologie, Physiopathologie, Endocrinologie
  - SVE1\_LS5 Neurosciences
  - SVE1\_LS6 Immunologie, Infectiologie
  - SVE1\_LS7 Recherche clinique, Santé publique
- SVE2 Ecologie, environnement
  - SVE2\_LS8 Evolution, Ecologie, Biologie de l'environnement
  - SVE2\_LS9 Sciences et technologies du vivant, Biotechnologie
  - SVE2\_LS3 Biologie cellulaire, Biologie du développement végétal

Limoges, le 16 avril 2011

Le Président

à

Monsieur le Président  
AERES  
20 rue Vivienne  
75 002 PARIS

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**OBJET**

**General comment for the Unit Maintenance Myélinique et Neuropathies  
Périphériques – 0870669E**

Dear Mr President,

We thank the visiting committee members for their thorough evaluation and intense work. We are grateful for their positive comments and fully agree with their recommendations, which will be carefully followed. Namely, we will focus our projects "on those where the team is in a position of international leader". As suggested, the experimental therapeutic part will first be limited to a "proof of concept" study focused on a single compound, without developing a high-throughput project.

Yours faithfully,



J. FONTANILLE