



# Li2P - Physiopathologie, cibles et thérapies de la polyarthrite rhumatoïde

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 unit:

Physiopathology, Targets and Therapies of Rheumatoid  
Arthritis

Li2P

Under the supervision of  
the following institutions  
and research bodies:

University Paris 13 - Paris-Nord

January 2013



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

Research Units Department

President of AERES

**Didier Houssin**

Research Units Department

*Department Head*

**Pierre Glaudes**



# Grading

Once the visits for the 2012-2013 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).

This score (A+, A, B, C) concerned each of the six criteria defined by the AERES.

NN (not-scored) attached to a criteria indicate that this one was not applicable to the particular case of this research unit or this team.

**Criterion 1 - C1** : Scientific outputs and quality ;

**Criterion 2 - C2** : Academic reputation and appeal ;

**Criterion 3 - C3** : Interactions with the social, economic and cultural environment ;

**Criterion 4 - C4** : Organisation and life of the institution (or of the team) ;

**Criterion 5 - C5** : Involvement in training through research ;

**Criterion 6 - C6** : Strategy and five-year plan.

With respect to this score, the research unit concerned by this report received the following grades:

- Grading table of the unit: **Physiopathology, Targets and Therapies of Rheumatoid Arthritis**

C1	C2	C3	C4	C5	C6
A	A	A	A+	A+	A+



## Evaluation report

Unit name:	Physiopathology, Targets and Therapies of Rheumatoid Arthritis
Unit acronym:	Li2P
Label requested:	EA
Present no.:	EA 4222
Name of Director (2012-2013):	Mr Marie-Christophe BOISSIER
Name of Project Leader (2014-2018):	Mr Marie-Christophe BOISSIER

## Expert committee members

Chair:	Mr Jean ROUDIER, University of Aix-Marseille
Experts:	Mr Michael EHRENSTEIN , London, United Kingdom
	Mr William OLLIER, Manchester, United Kingdom
	Mr Alain SARAUX, University of Brest

Scientific delegate representing the AERES:

Mr Joost VAN MEERWIJK

Representative(s) of the unit's supervising institutions and bodies:

Mr Charles DESFRANÇOIS, Université Paris 13



# 1 • Introduction

## History and geographical location of the unit

The “Laboratoire de recherche en immunologie et immunopathologie” or Li2P was created in 1996 on the Bobigny campus by its current leader, Mr Marie-Christophe BOISSIER, after he was appointed as a Full Professor of Rheumatology at University of Paris 13 and as the Adjunct Head of Rheumatology at nearby Hôpital Avicenne.

From the start, Li2P was dedicated to the study of rheumatoid arthritis, with particular emphasis on mouse models, a field in which Mr Marie-Christophe BOISSIER had a special expertise, having trained for his PhD with a renowned researcher in the field of collagen induced arthritis.

## Management team

Mr Marie-Christophe BOISSIER leads the laboratory with the help of two co directors.

## AERES nomenclature

SVE1\_LS4

## Unit workforce

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
<b>N1:</b> Permanent professors and similar positions	4	4	4
<b>N2:</b> Permanent researchers from Institutions and similar positions	7	6	6
<b>N3:</b> Other permanent staff (without research duties)	3	3	0
<b>N4:</b> Other professors (Emeritus Professor, on-contract Professor, etc.)	0	0	0
<b>N5:</b> Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	0	0	0
<b>N6:</b> Other contractual staff (without research duties)	0	1	0
<b>TOTAL N1 to N6</b>	<b>14</b>	<b>14</b>	<b>10</b>

Percentage of producers	100 %
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Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	5	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit*	0	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	5	6



## 2 • Assessment of the unit

### Strengths and opportunities

This small group is led by a Physician Scientist who also heads the Rheumatology Clinic at Hôpital Avicenne. Its research fields cover basic and translational research on rheumatoid arthritis (RA), both in the mouse and in humans. This includes clinical trials using a TNF-Kinoïd, a compound made by coupling human TNF $\alpha$  with Keyhole Limpet Hemocyanin (KLH) in RA. The group collaborates with NEOVACS, a pharmaceutical company that produces Kinoïds and helps organizing clinical trials.

The laboratory enjoys very strong support from the University which provided lab space and five tenured positions for scientists in the last six years (one Professorship of Medicine, one Professorship at the Science-School, three Associate Professor positions). The laboratory has access to a good mouse breeding and experimentation facility on campus. The patient population served by the hospital is an important resource for clinical trials and translational research. The lab is diversifying its interests to neutrophils and continues with a strong science base.

### Weaknesses and threats

The group is somewhat isolated on the Bobigny campus and would benefit from the presence of other similar groups, which would provide sufficient critical mass for cross collaborations and greater technology (e.g. expanded flow cytometry/confocal microscopy). The group lacks administrative help. Equipment is limited (e.g., no ultracentrifuge). These limitations may account for the absence of postdoctoral students in the lab.

### Recommendations

This relatively small group is involved in a very important human vaccination project that might change the face of TNF inhibition therapy in RA. This should be their major focus. They should be more ambitious when choosing where they publish: for instance, their 2008 article describing successful treatment of arthritis in human TNF transgenic mice by immunization with human TNF kinoïds could have been published in a major journal rather than in a good rheumatology journal.





### 3 • Detailed assessments

#### Assessment of scientific quality and outputs

The number of published articles has been increasing from 12 to 24 in the last two years. However, this lab has yet to publish a major paper. It is a shame, as the quality of the vaccination project should allow publications in non-specialized journals.

For example, one of their publications reports successful protection against arthritis through TNF kinoid vaccination in TNF transgenic mice. This article was published in the *Annals of the Rheumatic Diseases*, currently the best rheumatology Journal with an impact factor of eight. Still, this data obtained in a clean transgenic model using innovative TNF kinoid technology demonstrates that TNF vaccination protects from arthritis. This may in the future change fundamentally TNF inhibition therapeutic strategies. This article warranted publication in a major journal.

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

The Head of the laboratory is regularly invited to give seminars at international meetings like EWRR and EULAR.

The Unit recruits good people (students and junior faculty) and was recently granted a “chair of excellence”.

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

This research Unit is based in a poor suburb of Paris, in one of the poorest areas in France. The unit engages well with the local population and contributes to processes that expose local youth to research: many students have been recruited from the local area.

Local integration is not limited to playing good Samaritan. Indeed, this lab has produced three patents, all of them on the treatment of RA with peptides from TNF, IL-1, VEGF, or extracts from mycobacterium tuberculosis. Finally, the lab is also involved in close interaction with the nearby rheumatology ward. The best example of this is the clinical vaccination trial currently going on in rheumatoid arthritis patients, some of whom are followed in the rheumatology clinic at Avicenne.

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

The general atmosphere is friendly and relaxed. Students, technicians and staff are happy. Everybody feels he is respected by his colleagues and line managers, has enough independence and has appropriate credit for their work. Junior staff signs as last authors on their students' articles. PhD students are first authors. Students and staff all attend two meetings a year.

The director is a well respected and charismatic leader who gives independence and credit to his collaborators.

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

The involvement of the unit in training is regarded as being highly important as assessed by the number of students: seven PhD students and two master students are currently working in the laboratory. Besides, faculty working in this lab leads two of the three Master Programs taught in Bobigny. Finally, PhD students from the lab have defended seven doctoral theses in the last five years.

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

The lab's main effort is now to speed up on the clinical side of its project, namely the phase 2b studies of vaccination with TNF kinoids to treat patients with rheumatoid arthritis. This is very promising, as the gold standard for the treatment of rheumatoid arthritis, TNF inhibitors, are very expensive (€10000 per patient per year) and must often be discontinued because of side effects (allergy, infection).



Consequently, immunization and host antibody development against human TNF boosted by TNF kinoïds, which are both safer and less expensive, may constitute an important alternative to classical anti-TNF therapy. This project may thus end up reducing the cost of TNF inhibition therapy (€40 billion per year worldwide) and may consequently become an important disruptive technology.

This development is both economically and clinically important. Such major translational innovation would be the outcome of research started and pursued in this particular laboratory, from initial idea, via experimental mouse model, to translational bedside therapy, an outstanding example of truly translational science, perhaps unique in French rheumatology.



## 4 • Conduct of the visit

Visit date:

Start: Friday, February 1st 2013 at 9:00h

End: Friday, February 1st 2013 at 16:00h

Visit site: UFR SMBH, Li2P

Institution: University of Paris 13

Address: 74, rue Marcel Cachin, 93 Bobigny

### Conduct or programme of visit:

Committee and AERES representative met from 9AM to 9.30 AM. Mr Marie-Christophe BOISSIER and his two co-directors then presented past activity and project, from 9.40 AM to 11AM. Committee members asked questions till 11.30 AM. Then they met with Mr Jean Luc DUMAS, Dean of the Medical School in Bobigny, and with Mr Charles DESFRANÇOIS, Vice President of the Scientific Council of Université Paris 13. Members of the Committee then met Students, Researchers, and Technicians, separately in three parallel meetings, from 12 to 12.45 AM.

Committee and AERES representative then met with the lab Director from 1.30 PM to 2 PM. Finally, Committee and AERES representative met to write down the pre-report and report, from 2 PM to 4 PM.

### Specific points to be mentioned:

The site visit was conducted in a collegiate and friendly manner and all scientific and administrative questions were answered in an open and honest manner. An excellent scientific dialogue between the committee and the Unit was established. One issue that was discussed and considered was whether the Unit needs additional external support and advice regarding maximizing the extent of intellectual protection (IP). Given the clinical and financial benefits that could eventually accrue should this therapeutic approach be finally adopted, this would be in the interest of all parties involved (Unit, University, collaborators and funders).

## 5 • Statistics by field: SVE on 10/06/2013

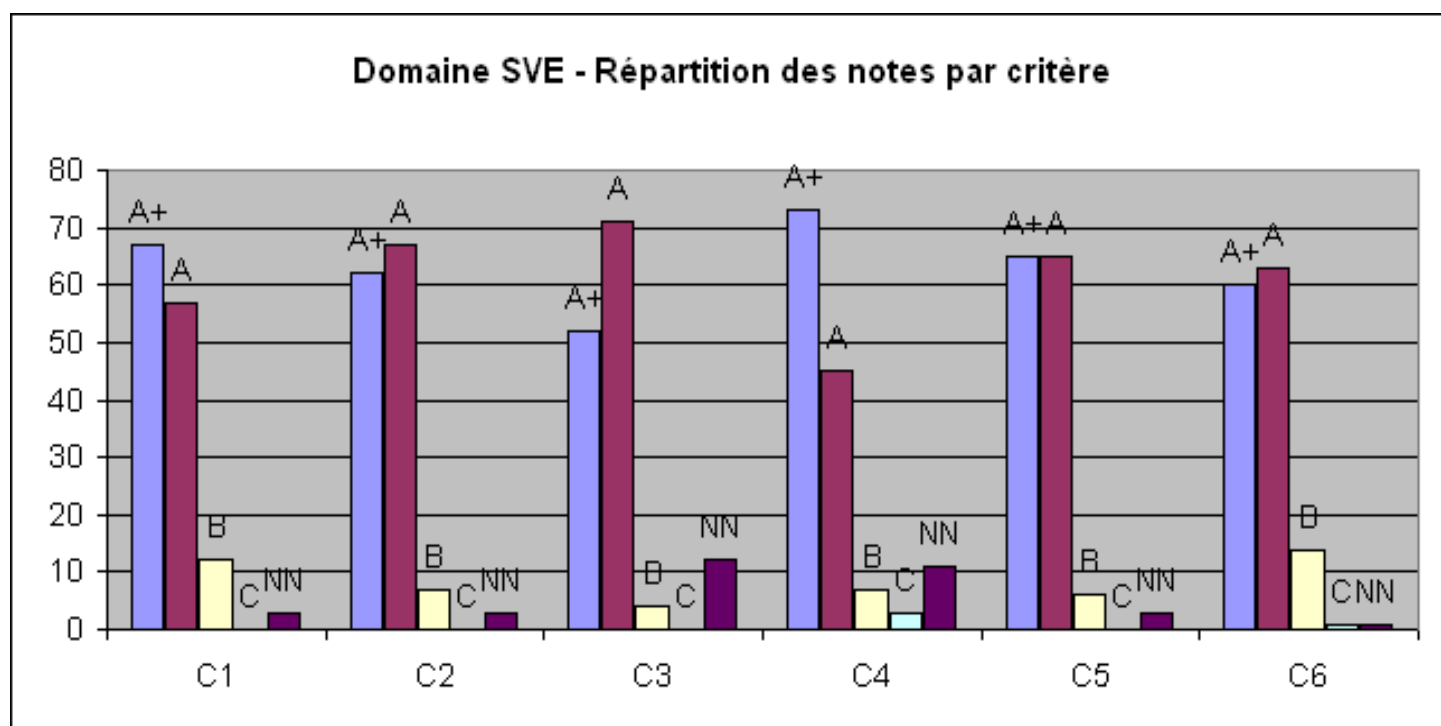
### Grades

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	67	62	52	73	65	60
A	57	67	71	45	65	63
B	12	7	4	7	6	14
C	0	0	0	3	0	1
Non Noté	3	3	12	11	3	1

### Percentages

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	48%	45%	37%	53%	47%	43%
A	41%	48%	51%	32%	47%	45%
B	9%	5%	3%	5%	4%	10%
C	0%	0%	0%	2%	0%	1%
Non Noté	2%	2%	9%	8%	2%	1%

### Histogram





## 6 • Supervising bodies' general comments

Villetaneuse, le 25 avril 2013

**Le Président**

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**Observations générales sur le rapport AERES  
de l'Unité de Recherche  
PHYSIOPATHOLOGIE, CIBLES ET THERAPIES DE LA  
POLYARTHRITE RHUMATOÏDE  
(LI2P, EA 4222)**

First, the university and the unit would like to thank the AERES evaluation committee for its report and for the recommendations.

Secondly, we totally agree with the conclusions of this evaluation report and we corroborate that the team:

- goes on the vaccination project and on a more extensive development of clinical application;
- confirms its strategy of diversification in the pathophysiology of rheumatoid arthritis (namely novel potential targets and neutrophils) and of publishing in major journals;
- enhance its translational research by a clinical engineer fully dedicated to selecting patients, collecting samples, processing them.

It is also worth noting that the team benefits from the presence of other groups involved in biomedical research that are within the same institute and, in particular, ASIH unit Inserm 978 (head by Nadine Varin-Blank) that allows us to share some skills and all equipment.

The university also notes that administrative help would be helpful to this unit.

Jean-Loup SALZMANN



Membre fondateur de :