



IMMUNO - Département d'immunologie

Rapport Hcéres

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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

Département d'Immunologie

From the

Institut Pasteur

May 2010



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et de l'enseignement supérieur

Section des Unités de recherche

AERES report on the research unit

Département d'Immunologie

From the

Institut Pasteur

Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

May 2010

Research Units

1. Name of the research unit: Activation, relaxation and homeostasis of the immune system

Requested label: URA CNRS

N° in the case of renewal: 1961

Name of the director: Antonio FREITAS

2. Name of the research unit: Physiopathology of the immune system

Requested label: INSERM

N° in the case of renewal: U668

Name of the director: James DI SANTO

3. Name of the research unit: Laboratory of dendritic cell immunobiology

Requested label: INSERM

N° in the case of renewal: U818

Name of the director: Matthew ALBERT

4. Name of the research unit: Unit of molecular and cellular allergology

Requested label: INSERM

N° in the case of renewal: U760

Name of the director: Marc DAËRON

5. Name of the research unit: Immune regulation and vaccinology

Requested label: INSERM

N° in the case of renewal: U883

Name of the director: Claude LECLERC

6. Name of the research unit: Immunobiology of Trypanosoma infections

Requested label: Pasteur unit

Name of the director: Paola MINOPRIO



Members of the review committee

Chairperson:

Mr. Adrian HAYDAY, London, UK

Other committee members

Mr. Robert SCHREIBER, Saint Louis, USA

Mr. Lewis LANIER, San Francisco, USA

Mr. Ricardo GAZZINELLI, Belo Horizonte, Brazil

Mr. Hans-Reiner RODEWALD, Ulm, Germany

Mr. Georgio TRINCHERI, Frederick, USA

Mr. David LEVY, New-York, USA

Mr. Michel NUSSENZWEIG, New-York, USA

Mr. Per BRANDTZAEG, Oslo, Norway

Mr. Bruno LUCAS, Paris, Paris

Ms. Danila VALMORI, Nantes

Observers

AERES scientific advisor

Ms. Claude-Agnès REYNAUD

University, School and Research Organization representatives

Ms Christine TUFFEREAU and Armelle REGNAULT, INSERM

Ms Evelyne MARCHE, CNRS

Report

1 • Introduction

- Preliminary statement by AERES scientific delegate:

This visit, which took place on the 30th of November and the 1st of December 2009, represents the first attempt, for AERES and Pasteur Institute, to merge their own evaluation procedures in order to avoid unnecessary duplication of site visits. In this still provisional setting, each Pasteur group was evaluated independently, without consideration for their being embedded within a larger INSERM or CNRS structure. Accordingly, the general part of this report comments on the activity of the Immunology Department as a whole, and not on the INSERM or CNRS unit entities.

- Date and execution of the visit

The visit took place over a two-day period, starting with a presentation by the scientific director and the director of evaluation. The committee then split in two to hear the different research groups make presentations of approx. 45 minutes, followed by approximately 30 minutes questions. Each reviewer had the opportunity to meet with post-docs and students within the laboratory of the respective researchers, in the absence of the team leader. Two discussions followed, with the scientific director, and with the head of the department, respectively.

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

The Immunology department is one of the ten departments of Pasteur and one with a high international visibility. It embraces a broad sweep of immunology, although its greatest focus is on cellular and molecular studies, particularly in animal models. There is relatively little human immunology, although this is growing again under the auspice of a Centre for Human Immunology. There are long-standing interests in infectious diseases, as befits Institut Pasteur, but there is currently relatively little attention paid to the immunology of the world's major pathogens. The Dept labs are located in Metchnikoff building, now shared with laboratories from other departments.

- Management team

The department is headed by a director. However, the Director seems to have little resources at his disposal to facilitate and /or promote initiatives within the Dept and between departments. This lack of overt managerial power poses some problems and acts as a disincentive for talented individuals to take on this important responsibility. The Dept includes 13 teams evaluated for renewal, distributed within 4 INSERM units (three "mono-équipes", U760, U818 and U883, and one (U668) including 2 teams and a G5 group), one CNRS unit (including 5 teams applying for renewal, with one of them evaluated with the Parasitology department, and a G5 group), and one laboratory, each of these units having their own director.

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	13	13
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	43	43
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	39	38
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	32	27
N7: Number of staff members with a HDR or a similar grade	27	26

2 • Overall appreciation on the research unit

- Overall opinion

In many respects, this is an high-achieving Dept. with several group leaders with high international recognition that respects their places at the cutting edge of their respective fields. Many publish in high quality journals and are highly cited as they show ambition in attacking some of the key questions of the day. Likewise, there is evidence of success in obtaining very supportive reviews from highly competitive funding agencies, such as the ERC, and the Gates Foundation.

- Strengths and opportunities

One overt feature is the high quality of the G5 groups that have recently matured within the Dept. This provides the Dept with a new set of mid-career, outstanding scientists. Another strong opportunity is the recent establishment of a practical structure devoted to human immunology and translational research.

- Weaknesses and threats

There has been an ongoing reduction in the size of the Dept and in particular its scientific staff. This is not a healthy symptom, since it will inevitably limit the potential achievements of such an excellent grouping. Reflecting this, there are currently no new G5 groups. Not all research groupings within the Dept were optimally organised to promote the achievements of individual researchers within them. Inevitably, this is an opportunity cost for the Dept and for the Pasteur. The viability of the Human Immunology Centre is jeopardised by the reduced connections with clinicians since the closure of the Pasteur hospital. Thus, this important initiative merits overt internal support. There is relatively little incisive interdisciplinary work, particularly with microbiology, which is ironic given the achievements of Pasteur himself. This may be contributed to by the lack of resources that Dept Heads have to incentivise inter-departmental initiatives. The fluorescence activated cell sorting facility is utterly inadequate to meet to modern needs of immunology.

- Recommendations to the head of the research unit

A redefined role of the Chair could be a powerful means to establish more cohesion among the department's initiatives; to more closely scrutinise the management styles applied in individual research groupings ; and to promote inter-disciplinary, inter-departmental initiatives. All such devices can optimise the performance of the talented individuals that the Dept is home to. At the same time, this, together with more space allocation, can promote the Dept's physical growth, which is important. There needs to be at least one new G5 group set up soon. There should be support for the Centre for Human Immunology, so that enhanced collaborations can be developed



between basic scientists and clinicians. This type of approach will be expected by the next generation of biomedical scientists who have ambition to see their expertise in basic science effectively translated. The possibility to develop a specific program to attract clinicians should be considered.

- Data on the work produced :

A1: Number of permanent researchers with or without teaching duties (recorded in N1 and N2) who are active in research	36
A2: Number of other researchers (recorded in N3, N4 and N5) who are active in research	
A3: Ratio of members who are active in research among permanent researchers $[(A1)/(N1 + N2)]$	35/36
A4: Number of HDR granted during the past 4 years	2
A5: Number of PhD granted during the past 4 years	
A6: Any other relevant item in the field	33

3 • Specific comments on the research unit

The external Scientific Review Board in Immunology, noted the outstanding reputation of Institut Pasteur for scientific creativity and productivity across a spectrum of studies that conspicuously includes immunology. Immunology at Institut Pasteur has been and continues to operate at the highest level of achievement, with numerous cases of scholarship and publication that provide the academic community with truly new insight. Moreover, this is underpinned by an evident esprit de corps, enthusiasm and ambition among younger researchers who are proud to be training in the Dept of Immunology at Institut Pasteur.

The Scientific Review Board found evidence of healthy interactions, but not necessarily strong cohesion. Even small things like the complete heterogeneity of format adopted by each lab in its presentation of review materials suggests that the Dept is not in the habit of “thinking collectively”. While there should be no undermining of individuality, a more cohesive presentation of the Dept might better position it to take maximum advantage of future funding opportunities and international initiatives. The current situation, where individual efforts conspicuously outweigh cohesion and synergy, perhaps reflects the rather disempowered role of the Chair, which many of the Scientific Review Board found peculiar and arguably unhelpful in the current, highly competitive era (Note that this does not in any way reflect any personal criticism of the present Head of Dept).

As a first case in point, the somewhat disempowered status of the Chair limits the devices available to incentivise inter-disciplinary research opportunities. Thus, while there were highly commendable examples of excellent, collaborative, highly inter-disciplinary work, the Scientific Review Board did not perceive ambitious interdisciplinary attempts to take on key challenges such as the development of vaccines fit for the 21st century. Given its excellence, its structure, and its history, Institut Pasteur might have been expected to be more ambitious in some such endeavours. While the committee acknowledges that such ambition and initiative require a bottom-up approach, such approaches can benefit enormously from empowered top-down steer, particularly when driven by the Chairs of more than one dept working together. Moreover, if bottom-up approaches cannot be easily incentivised and materially supported from the top, the Institut risks undermining many creative and promising endeavours. The committee therefore would advise that the position and power of the Chair of Immunology (and probably of related Depts) be made more substantive and less enigmatic. The Scientific Review Board suspects that there would be much to gain from improved communication between the offices of Dept Heads and the Institut's higher management structures. The committee was also concerned that the inability of departments to control space and the apparent competition between departments for Institut space could make it difficult to maintain the integrity of the discipline of Immunology. De facto, the current Dept is shrinking in physical space and personnel (see below). The Scientific Review Board would like to stress the need to guarantee a certain minimum space in order to maintain the autonomy and growth of the department.



As a second case in point, a more co-ordinated action of Chairs and the Institut's higher management could substantively promote the active involvement of clinicians in the academic programmes. This is a conspicuous weakness in the Dept of Immunology, but it likely affects other Depts too. The Institut Pasteur should interrogate the possibility of key strategic initiatives with clinical centres of excellence such as Cochin, Pitié-Salpêtrière, Necker, etc. In other institutes, the collaborative involvement of active clinicians in research is materially supported by payment for back-up service provision and for research nurses. The committee suspects that this kind of bold gesture will also be needed at Institut Pasteur. While "Translational Research" is not everything, it is important, particularly in the eyes of the next generation. It is therefore important to take it seriously and to do it well.

In this regard, the Department's presentations identified a smaller number of advanced translational projects than might have been expected for such an eminent department entering the second decade of the 21st Century. The Scientific Review Board's individual reviews note and commend some notable efforts in this arena; for example, the tumour vaccine studies or the modulation of chemokine CXCL10 cleavage by inhibiting dipeptidylpeptidase IV, to limit treatment failure in Hepatitis C Virus infection. Providing a foundation for more intensive translational work, the Scientific Review Board was impressed by the implementation of the Centre of Human Immunology (CIH). However, the CIH came across as excessively the product of individual enterprise that is not sustainable. It will not flourish without more stringent, top-down efforts to engage clinicians in incisive research projects that are a strength of Institut Pasteur. Another provision that requires overt support (and, in this case, managerial re-organisation) is flow cytometry-based cell sorting, which is currently completely unsatisfactory for the Dept of Immunology. One further area that deserves attention, although it was not a specific remit for our Scientific Review Board, is that of handling data complexity, with the need to integrate bio-informatics, systems biology, molecular epidemiology and mathematical modelling. It was not clear to the Scientific Review Board that the Pasteur investigators are as yet well served in this emerging area, and the situation should be reviewed promptly and thoroughly.

Immunology at Pasteur, in sheer numbers alone is declining. This is not appropriate. This does not simply threaten the intrinsic importance of immunology as an area of scholarship, but it is frankly hard to imagine that scholarship in virology, microbiology, parasitology, and mycology can continue to develop at Institut Pasteur without strong immunology. Furthermore, the "age-complexion" of the Dept is tilting toward senior investigators. Therefore, greater efforts should be made to grow the Dept by recruitment to G5 posts and by nurturing internal talent, when identified. At the same time, the committee enthusiastically and unanimously support the transition into Pasteur Units, of the two actual G5 investigators. The evident capacity of both to flourish at an international standard of excellence should give Institut Pasteur great confidence to invest further in the future of immunology. In so doing, one should alas endeavour to ensure that the broad representation of women among current trainees is reflected in the Faculty.



Unité : ACTIVATION, RELAXATION ET HOMEOSTASIE DU SYSTEME IMMUNITAIRE, Antonio FREITAS

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

Nom de l'équipe : BIOLOGIE CELLULAIRE DES LYMPHOCYTES - URA 1961 (FREITAS-ALCOVER)

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+

Nom de l'équipe : DÉVELOPPEMENT DES TISSUS LYMPHOÏDES (FREITAS-EBERL)

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+

Nom de l'équipe : BIOLOGIE DES POPULATIONS LYMPHOCYTAIRES URA961 (FREITAS)

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



Nom de l'équipe : SIGNALISATION DES CYTOKINES (FREITAS-PELLEGRINI)

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	B	A	A+	A

Nom de l'équipe : IMMUNORÉGULATION (FREITAS-ROGGE)

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+

Unité : PHYSIOPATHOLOGIE DU SYSTÈME IMMUNITAIRE, James DI SANTO

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

Nom de l'équipe : DYNAMIQUE DES RÉPONSES IMMUNES (DI SANTO-BOUSSO)

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+



Nom de l'équipe : DÉVELOPPEMENT DES LYMPHOCYTES (DI SANTO-CUMANO)

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

Nom de l'équipe : CYTOKINES ET DÉVELOPPEMENT LYMPHOÏDE (DI SANTO)

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+

Unité: IMMUNOBIOLOGIE DES CELLULES DENDRITIQUES, Matthew ALBERT

Note de l'unité	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+



Unité : ALLERGOLOGIE MOLECULAIRE ET CELLULAIRE, Marc DAËRON

Note de l'unité	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+

Unité : REGULATION IMMUNITAIRE ET VACCINOLOGIE - U883, Claude LECLERC

Note de l'unité	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

Unité : IMMUNOBIOLOGIE DES INFECTIONS A TRYPANOSOMA, Paola MINOPRIO

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



Response of the Head of Department to the AERES report on the evaluation of the Department of Immunology of Institut Pasteur

We thank the Site Visit Committee for having accepted the heavy task of evaluating the *Department of Immunology* of Institut Pasteur and for the document that resulted from this work. We acknowledge the accuracy and the pertinence of most points raised in this document.

We are especially grateful for the Committee's support on two major issues that were raised in the document submitted to AERES by the Head of Department. The first issue is our main concern on the evolution and future of the Department. The space allotted to Department and the personnel working in the Department have indeed been steadily decreasing over the last 5 years, as a result of the departure of 1 head of unit, the non-transformation of one G5 into a research unit and the retirement of 3 heads of units. Yet, the Department has no means to stop and correct this evolution. This issue was not considered as a priority when submitted to the Direction of the Institute. The second issue is important too, but less critical. It concerns the Flow-Cytometry Platform. In spite of long-lasting efforts, this facility still requires to be extensively reorganized in order to be functional and to fulfill the needs of the Department. Due to confusing managerial organization, the Department is unable to impact on the procedure. We therefore strongly endorse the recommendations of the Committee that the Department had with some control on these issues and be enabled to recruit at least one G5 soon.

We were also pleased that the Committee appreciated our efforts to engage the Department in Human Immunology and could measure the difficulty of the task in an Institute that has no hospital. This difficulty may explain why the Committee felt that "the number of advanced translational projects was smaller than might have been expected" and we appreciate its recommendation to "promote the active involvement of clinicians in the academic programmes", to "interrogate the possibility of key strategic initiatives with clinical centres of excellence such as Cochin, Pitié-Salpêtrière, Necker, etc" and to "materially support the involvement of active clinicians in research by payment for back-up service provision and for research nurses". These bold recommendations should indeed encourage the Direction of the Institute to further support the *Centre d'Immunologie Humaine* (CIH), as it did at the time of its creation. Indeed, contrary to the Committee's comment, the CIH did not "come across as excessively the product of individual enterprise" even though the enterprise would not

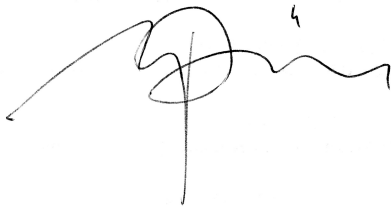
have been possible without the involvement of one outstanding individual. It has been a departmental project, which received a strong support from the Direction. This support remains a necessity, especially if one wants to keep this unique structure, which aims at developing not only biology-based translational research but also medicine-based fundamental research, exceptional.

In response to the comment of the Site Visit Committee that “there is relatively little incisive interdisciplinary work, particularly with microbiology, which is ironic given the achievements of Pasteur himself”, we wish to stress the following facts that we should have possibly emphasized on:

1. In September 2006, 44 collaborative works were recorded involving 11 units of the *Department of Immunology* and 33 units in 9 of the 10 departments of Institut Pasteur. As a result, the *Department of Immunology* published 12 papers specifically dealing with microbes or infection in 2008 (in *Nature Med.*, *Cell Host Microbe*, *Immunity*, *PLoS Genet.*, *Proc Natl Acad Sci U S A.*, *J. Exp. Med.*, *Cell Death Differentiation*, *Mol. Biochem. Parasitol.*, *Mem. Inst. Oswaldo Cruz*, *Curr. Top. Microbiol. Immunol.*, *Mucosal Immunol.*) and another 12 papers in 2009 (in *Immunity*, *Virology*, *PLoS Pathogen*, *Hepatology*, *J. Urology*, *Vaccine*, *PLoS One*, *J. Neuroimmunol.*, *PLoS Pathogen*, *Nature*).
2. A symposium, devoted to *Host-Pathogens Interactions* was created in 2006 as a joint initiative of the *Department of Immunology* and the *Department of Cell Biology and Infection* of the Institut Pasteur, and of the *Centre d’Immunology de Marseille-Luminy*. It was first held in May 2007 at the Château des Ravatys. Since then, this symposium, named *The Ravatys Symposium*, has been held yearly. It gathered members from 5 departments of the Institute (the departments of *Immunology*, *Cell Biology and Infection*, *Infection and Epidemiology*, *Virology* and *Microbiology*) in 2008, and members from 6 departments (the departments of *Immunology*, *Cell Biology and Infection*, *Infection and Epidemiology*, *Virology*, *Biology of Development* and *Parasitology and Mycology*) in 2009.
3. Institut Pasteur departments hold annual retreats. These gatherings are opportunities to bring together not only all members of a department, but also invited participants from other departments. One head of unit from the *Department Infection and Epidemiology* was invited to the annual retreat of the *Department of Immunology* and one head of unit of the *Department of Immunology* was invited to the annual retreat of the *Department Cell Biology of Infection* in 2006. A whole team of the *Department of Immunology* participated to the annual retreat of the *Department Cell Biology of Infection* and the head of the *Department of Immunology* was invited to the annual retreat of the *Department of Neurosciences* in 2007. Three heads of unit from 3 departments (*Biology of Development*, *Microbiology* and *Virology*) were invited to the annual retreat of the *Department of Immunology* and two chefs of units of the *Department of Immunology* were invited to the annual retreat of the *Department Infection and Epidemiology* in 2008. Three heads of unit from 3 departments (*Biology of Development*, *Cell Biology and Infection* and *Infection and Epidemiology*) were invited to the annual retreat of the *Department of Immunology* and one chef of unit of the *Department of Immunology* was invited to the annual retreat of the *Department of Biology of Development* in 2009. Two heads of unit from 2 departments (*Virology* and *Infection and Epidemiology*) will be invited to the annual retreat of the *Department of Immunology* in 2010.

Finally, it is interesting that “The Scientific Review Board found evidence of healthy interactions, but not necessarily strong cohesion” and that “even small things like the complete heterogeneity of format adopted by each lab in its presentation of review materials suggests that the Dept is not in the habit of “thinking collectively”. Whether “a more cohesive presentation of the Dept might better position it to take maximum advantage of future funding opportunities and international initiatives” or whether it would “undermine individuality” may be discussed. In any case, we appreciate that the Committee found evidence of healthy interactions in spite of such a heterogeneity. It shows that, rather than the habit of thinking collectively, we preferred that of exchanging and confronting the diversity of thoughts of a unique collection of individuals. Progress in scientific research indeed remains primarily a matter of creativity.

Paris, April 16, 2010

A handwritten signature in black ink, appearing to read 'Daëron', with a long horizontal stroke extending to the left.

Marc Daëron, MD, PhD,
Director

A handwritten signature in black ink, appearing to read 'Israël', with a large loop at the bottom.

ALAIN ISRAËL
DIRECTEUR DE L’ÉVALUATION
SCIENTIFIQUE
INSTITUT PASTEUR