Immunobiologie des cellules dendritiques

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Dendritic Cell Immunobiology

From the

INSERM

Pasteur Institute

Mai 2010

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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

Mai 2010

Research Unit

Name of the research unit: Laboratory of dendritic cell immunobiology

Requested label: UMR_S INSERM

N° in the case of renewal: 818

Name of the director: Mr. Matthew ALBERT

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

Committee members nomminated by staff evaluation committees (CNU, CoNRS, INSERM and INRA CSS....)

Ms. Danila VALMORI, Nantes, INSERM CSS member

Observers

AERES scientific advisor

Ms.Claude-Agnes REYNAUD

Research Organization representatives

Ms. Christine TUFFEREAU AND Armelle REGNAULT, INSERM

Report

1 • Introduction

- Date and execution of the visit

This visit, which took place on the 30th of November and the 1rst 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, a general report commenting on the activity of the Immunology Department is provided, but not on the INSERM or CNRS unit entities.

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	4	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3.5	3.5
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	2	2
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	3
N7: Number of staff members with a HDR or a similar grade	1	1

2 • Overall appreciation on the research unit

- 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	1
A2: Number of other researchers (recorded in N3, N4 and N5) who are active in research	0
A3: Ratio of members who are active in research among permanent researchers [(A1)/(N1 + N2)]	1/1
A4: Number of HDR granted during the past 4 years	0
A5: Number of PhD granted during the past 4 years	3

3 • Specific comments on the research unit

- Appreciation on the results

The team has added much to our understanding of antigen cross presentation by dendritic cells (DC). His work was some of the first to demonstrate that dying cells were the source of tumor antigens following engulfment, processing and cross presentation by dendritic cells to CD8+ T cells. The team leader, together with his former mentor at Rockefeller University, also showed that as a result of tumor antigen cross presentation, the tumor specific T cells that developed in an individual were responsible for paraneoplastic neurologic degenerations. Since establishing his group at the Institut Pasteur, he has continued the analysis of cell death and antigen cross presentation now in the context of viral infection and human bladder cancer. This work has led to the development of both mouse model systems and projects in human viral and tumor immunology. In this regard it is significant that group leader has obtained important insights into the cross presentation process and specifically into the factors/parameters that determine whether cross presentation results in generation of host protective anti-tumor/anti-viral CD8+ T cell responses or to induction of tolerance to tumor cells/viruses. It is also clear that he has made a significant commitment to human immunology and as a result has not only been responsible for establishing the Center for Human Immunology at Institut Pasteur (a very significant feat in itself) but also in establishing both translational and basic human tumor immunology projects within his own laboratory. This effort has been accompanied by a steady stream of publications in well-respected peer reviewed journals during the last 5 years, many appearing in the highest level research journals.

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

The group leader is held in very high regard by the international immunology community. This is evidenced by (a) a number of awards he has received for meritorious research; (b) the fact that he has organized or co-organized 8 international conferences during the last 6 years; and (c) has been invited to write several review articles in the area of antigen cross-presentation in extremely high profile review series such as Nature Reviews Immunology, Nature Reviews Cancer and Nature Reviews Microbiology. In addition he has been invited to deliver several talks at many world class Universities such as Yale University, Washington University in St. Louis, the NIH and King's College London, and at international meetings such as the 2nd European Congress of Immunology. The team leader is also universally acknowledged as a fine teacher and mentor and has been an active lecturer in the Institut Pasteur's courses in Vaccinology and Immunology as well as lecturing in the international immunology course in Egypt. He has also

mentored 3 Master students and 3 PhD students through their degrees and is currently mentoring one Master student and 3 Ph.D. students.

- Appreciation on the strategy, governance and life of the research unit

The team assembles remarkably talented individuals and its leader has done a superb job setting up and running his lab. This ability clearly comes naturally to Dr.the team leader and his gift for organizing his research efforts are evident everywhere one looks throughout his lab, and to some extent beyond that. Thus, in addition to setting up his own lab, he has done a wonderful job setting up the Center for Human Immunology (CIH) for the Institut Pasteur, thereby establishing an extremely unique environment in this institution that will foster human immunology research. His staff holds him in extremely high esteem and his superb management skills form the basis for a highly productive working environment.

- Appreciation on the project

The group has made a number of very interesting and exciting observations that now form the basis for the next several years of work. Basically their research will be divided into three broad areas: (a) understanding the relative importance of cell death by apoptosis versus autophagy in promoting cross priming; (b) exploring the role of immunity in BCG induced host protective responses to bladder cancer in humans and in a mouse model of bladder cancer and (c) elucidating mechanisms of HCV escape from immune control with emphasis on mechanisms of chemokine inactivation. These are all important areas of research and fit nicely into the group expressed desire to do research aimed at going from the bedside to the bench and back again. Whereas no one would argue with the importance of the subjects in general, it will be important for the group to "drill down" into the mechanistic aspects of each project and thus he will have to very soon make a commitment to assessing the molecular basis of these effects. Thus, the Scientific Review Committee urges him to prioritize. Happily, the group seems fully aware of this challenge. It has already made significant progress on defining the molecular mechanism of chemokine inactivation in HCV infected individuals, and is progressing well in extending this investigation into potential therapies. In contrast, studies on autophagy and cross presentation, and of BCG-induced responses to bladder cancer are still at a very early stage and more work is needed before they achieve the same level of mechanistic sophistication as the chemokine inactivation project. Similarly, care should be taken to first define that the mouse model of BCG treatment of bladder cancer is genuinely relevant to the actual human disease. Nevertheless, it is clear from the discussion that the group remains deeply committed to pursuing the molecular and cellular basis of these projects. Based on their very many talents and enthusiasm, there is every expectation that very exciting results will be forthcoming.

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+

INSTITUT PASTEUR

Instituts thématiques Inserm
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IMMUNOBIOLOGIE DES CELLULES DENDRITIQUES

RE : AERES REPORT – DENDRITIC CELL IMMUNOBIOLOGY

Paris, April 12th, 2010

Dear Members of the AERES Review Committee,

On behalf of myself and my research unit, we thank the Committee for their visit and review of our work. We were pleased by the positive evaluation of our accomplishments and our current research efforts. In particular, I appreciate that the Committee valued our 'bedside-to-bench' approach to translational research. These efforts have required considerable investment as they require close interactions with clinical scientists and we are proud of the network of investigators that we have organized, representing teams in France and abroad.

The only concern raised by the committee related to our ability to focus our efforts. Specifically, the report stated:

"(…) it will be important for the group to "drill down" into the mechanistic aspects of each project and thus (he) will have to soon make a commitment to assessing the molecular basis of these effects. Thus, the Scientific Review Committee urges him to prioritize."

We value this comment and of course are engaged in this activity on a regular basis. Regarding mechanistic work, we have a strong effort on defining the regulation of antigen cross-presentation; and as noted by the committee, we are deeply engaged in *"elucidating mechanisms of HCV escape from immune control with emphasis on mechanisms of chemokine inactivation."* In truth, the only area where we are needing to focus concerns our studies on bladder cancer. This work is still at an early stage and we are currently in the process of defining the questions that we will pursue in this important model of tumor immunotherapy.

Again, we thank you for your confidence and support of our research efforts.

Yours sincerely,

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