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

Section des Unités de recherche

AERES report on the research unit

Immunovirology and genetic polymorphism

From the

University of Nantes

December 2010

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

Section des Unités de recherche

AERES report on the research unit

Immunovirology and genetic polymorphism

From the

University of Nantes

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: Immunovirology and genetic polymorphism

Requested label: EA

N° in the case of renewal: 4271

Name of the director: Ms Berthe-Marie IMBERT-MARCILLE

Members of the review committee

Committee chairman:

M. Ali SAIB, CNAM, Paris

Experts:

M. Jacques IZOPET, Université Toulouse 3, Toulouse

M. François TROTTEIN, Université Lille 1, Lille

Ms Mary COLLINS, University College London, London, UK

M. Moncef GUENOUNOU (CNU), Université de Reims

M. François LEMOINE (CSS INSERM), Université Pierre & Marie Curie, Paris,

Observers

AERES scientific advisor:

M. Yves GAUDIN

University, School and Research Organization representatives

M. Jacques GIRARDEAU, University of Nantes

M. Olivier GARRAUD, Établissement Français du Sang

Report

1 • Introduction

- **Date and execution of the visit :**

The visit was performed the 13th of December 2010 from 7h45 to 12h45. After the introduction talk from the head of the laboratory, the main PIs were invited to present their work and project. This was followed by a general discussion focusing on science first, then on governance and general strategy. The committee then met successively in the absence of the director, students and post-docs, technicians and engineers, researchers and teachers/researchers. The visit ended by a closed-door debriefing of the committee.

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

The team "Immunovirology and Genetic Polymorphism" (EA4271) was created in January 2008 and resulted from the fusion of two pre-existing research groups located in Nantes (former JE2437 and EE0503). This team is located in the Faculty of Medicine and Pharmacy (former JE2437, so called “virus group”) and within the Etablissement Français du Sang (EFS, “NK group”). The EA4271 team is affiliated with the IFR26.

The unit is currently subdivided into two groups: the NK/EFS group (former EE0503) and the virus group (former JE2437). The research unit has an interest in persistent viral infections (DNA viruses and HIV), host cellular responses and genetic polymorphism (host and virus). Three research themes have been developed over the last three years. The first theme aims at evaluating the role of dendritic cell (DC)/natural killer (NK) cell cross-talk in the context of ▫-herpesvirus (cytomegalovirus and HHV6) infection, which occurs in immunocompromised individuals (allografts, HIV infection). This project is currently under development. The second theme (NK group) aims at analyzing KIR/HLA immunogenetics and the mechanisms of human NK cell alloreactivity after haematopoietic stem cell (HSC) graft. The third theme (virus group) aims at improving the understanding and therapeutic management of viral opportunistic complications (Herpesvirus) after allograft (HSCT or kidney transplanted patients) and at evaluating the efficacy of antiretroviral treatment (HIV). This theme involves a strong element of clinical research, notably in the context of multicentric trials and ANRS working groups, and is complemented by more fundamental research.

- **Management team:**

The Unit is directed by Berthe-Marie IMBERT who is PU-PH. A laboratory council has been established.

- **Staff members (on the basis of the application file submitted to the AERES):**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	5	6
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	8	5
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	5	7
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	
N7: Number of staff members with a HDR or a similar grade	5	6

2 • Overall appreciation on the research unit

- **Summary:**

The team deals with persistent viral infections (CMV, BKV, HIV and more recently HCV), host cellular responses and host genetic polymorphism. The overall relevance and originality of the research performed by this team is good. There is a strong element of clinical research and a more fundamental research program, the most visible element being the analysis of KIR receptors. Although the local environment has played a role in different research themes, efforts to focus on a unifying research project will be helpful for the future structuralization of the team.

- **Strengths and opportunities:**

- Arrival of the HCV team to reinforce the fundamental research in Virology.

- Quality of the clinical trials. Strong and visible expertise in this field.

- Very good support of the EFS (2 full-time scientists, two technicians).

- **Weaknesses and threats:**

- Low impact of publication and lack of visibility in Virology.

- Insufficient external grants.

- Lack of patents regarding the applied research.

- Low number of PhD awarded.

- Too diffuse research programm (too many projects).

- Different location of the two groups that compose the unit.

- **Recommendations:**

- Focus on the most promising and visible projects in fundamental Virology.

- Improve the funding sources.

- Enroll more PhD students.

- Reinforce local collaborations related to human cellular immunology.

- Define a strategy to recruit, in the short/middle term, a full-time EPST scientist in fundamental Virology.

- "Accord cadre" EFS/University to be signed (intellectual property, etc.).

- **Production results:**

(cf. http://www.aeres-evaluation.fr/IMG/pdf/Criteres_Identification_Ensgts-Chercheurs.pdf)

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	7
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	10
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	2
A5: Number of PhD granted during the past 4 years	2

3 • Specific comments

- **Appreciation on the results:**

The questions addressed are mainly related to post-transplantation complications and are therefore of clinical relevance especially in the context of the local clinical/research activities developed in Nantes. Clinical trials on HIV patients are also of medical importance. Thus, the research themes developed by EA4271 have a potential high impact in health.

Over the last three years, the quantity and the quality of the publications related to basic research are relatively low (11 publications, 7 with IF < 3 and 4 with IF 3-6 mostly on KIR receptors and NK alloreactivity including 1 J. Immunol. and 1 Eur. J. Immunol).

Joined publications with extramural collaborators (multicentric clinical studies) or related to "peripheral" clinical projects are numerous and of good quality (more than 40 publications including 2 J. Clin. Oncol., 1 Leukemia, 1 Clin. Infect. Dis., 2 AIDS and 4 J. AIDS). This denotes the dynamism and the strong relationships with the clinicians who compose the unit.

There is a lack of patent and of attempt to commercially exploit biological products derived from the research activities (e.g. specific KIR2D antibodies).

Two PhD students are currently in the unit. Three PhD theses and 2 HDR diplomas have been completed since 2008.

The unit is also strongly involved in clinical research based on local cohorts of infected/grafted patients. Three different clinical departments in Nantes Hotel-Dieu collaborate with EA4271. Members of the unit are also involved as principal investigators in several national (ANRS) and international multicentric studies. The quality of the networks in which the clinicians are involved is very good. In contrast, extramural collaborations related to basic/fundamental research projects are relatively low and could benefit from the local expertise in Immunology.

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

Invitations of PIs who compose the unit in international congresses are relatively scarce, thus denoting a lack of visibility of the research on the international scene. Clinical trials on HIV patients have raised a substantial number of grants from public organisations (PHRC, ANRS, European network). Although not detailed in the activity report, the team also benefits the contribution of private associations and pharmaceutical industries. It is noticed that no substantial grants for more fundamental projects (including ANR grants) have been obtained over the last three years. The attractivity (high level scientists, foreigner post-docs) is small. Clinicians of the unit participate to national and international networks/clusters. Long term collaborations with some foreign, as well as local, clinician partners exist. Although announced, there is a clear lack of visible collaborations with local groups working in the field of Immunology.

The concrete results of the research are of clinical importance and might be valuable to better harness HIV infection and opportunistic viral infection following transplantation. The impact of the fundamental research is less obvious.

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

Despite its recent creation, it is noticed that interactions between clinicians and scientists (University / EFS) composing EA4271 appear to be strong. There is also a real will to optimize synergies between researchers of the unit and those from the group working on HCV that will be joining the group (see below). The proposal is intended to deal with the respective priorities of the hospital, university and EFS.

The strategy to promote the emergence of cutting edge projects is nevertheless not clearly defined. Attempts to improve the visibility in the field of virology is clearly annouced but awaits results. Due to its composition, the contribution of the staff members to teaching is high. The implication of the team leader in the structuration of the research at the local level is strong. The objective in the middle term is to integrate an Inserm unit/center but the plan to integrate such a structure remains to be defined.

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

Main modification will be the incorporation of a new group working in the field of Hepatitis C (HCV) infection (1 PU-PH, 2 technicians, 1 PhD student, 1 post-doc). The research activities of this group concern the variability of HCV and its relationship with cellular tropism and pathology.

The team will be restructured into two groups (HIV/HCV and viruses/transplantation) to improve the synergy between lab members working on different projects within each theme (6 HDR).

The HIV/HCV group will maintain a strong element of clinical research and will develop fundamental research projects related to the consequences of virus genetic variability on the antiviral immune response, viral replication and tropism.

The Viruses/Transplantation group will conduct mechanistic studies and clinico-biological investigations.

As it states, the research program is too diffuse and sparse. There are too many separate/distinct projects without clear links between them. Clear choices should be taken to optimize the future impact of the research activities. Success in obtaining national (i.e. ANR) and international grants will rely on the ability of the scientific board to focus on the most competitive areas. The implantation of a unifying research project will aid to improve the visibility of the team.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
IMMUNOVIROLOGIE ET POLYMORPHISME GÉNÉTIQUE (IVPG)	B	B	A	B	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
Total	**42**	**5**	**20**	**26**	**36**	**59**	**5**	**17**	**29**	**239**
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**

UNIVERSITÉ DE NANTES

PRÉSIDENCE DE L'UNIVERSITÉ
DIVISION DE LA RECHERCHE
ET DES ÉTUDES DOCTORALES

Nantes, le vendredi 4 mars 2011

REF : JG/EP - 2011 RECH N°296
SUIVI PAR : Jacques GIRARDEAU
Objet : Rapport d'évaluation - S2UR120001445
- Immunovirologie et polymorphisme génétique (IVPG) - 0440984F

LE PRÉSIDENT

à

Monsieur Pierre GLORIEUX
Directeur de la section des unités de recherche
AERES

Monsieur le directeur,

Je vous prie de trouver ci-joint les observations de portée générale de Madame Berthe Marie IMBERT-MARCILLE concernant le rapport d'évaluation de son unité « Immunovirologie et Polymorphisme génétique (IVPG) », EA 4271, observations que j'approuve bien évidemment.

Je vous prie d'agréer, Monsieur le directeur, l'expression de mes sentiments les plus cordiaux.

Yves LECOINTE

UNIVERSITE DE NANTES * BP 13522 - 44035

1 quai de Tourville
BP 13522 • 44035 Nantes CEDEX 1
Tél. 33 (0)2 40 99 83 83 • Fax 33 (0)2 40 99 83 92
recherche@univ-nantes.fr

Comments on AERES report

We have read and carefully studied the report from the AERES visiting committee concerning the "Immunovirology and genetic polymorphism" research unit, EA4271. We agree with most of the positive points and negative items raised by the committee, all of which had been discussed during the visit.

We appreciate the comments on the high quality of translational research, which is one of our main goals, both in HIV and transplantation (allogeneic response, opportunistic viruses) medicine. This strategy relies on the high proportion of lab members involved in hospital activities, and our continuing efforts to develop research that can have a significant impact on patient health care. The committee also highlighted the unit's firm integration with clinical activities at the Nantes hospital site, leading to productive studies of well-defined local patient cohorts, and the unit's involvement in multicentric networks. These positive aspects are encouraging, as they should allow us to maintain a high quality of clinical research in the years to come.

We note that our main weaknesses concern the domain of fundamental research in virology. At the present time, our efforts in this direction are clearly not sufficiently competitive, and rather too dispersed. We fully understand this point, but we wish to provide some specific comments.

Projects specifically dedicated to fundamental aspects of virology started only at the creation of the unit, in 2008. They are mostly coordinated by three persons, one arrived in January 2008 and another was recruited to a permanent position in September 2008. In addition, the team lost two HDR members in 2008 and 2009 but the total number of HDR remains stable because of two new HDR were completed at the same time. This also partly explain the rather low number of PhDs completed since 2008. Finally, the development of such projects has been hamstrung by the absence of a technician working on fundamental virology. This will be partially remedied by the forthcoming recruitment (September 2011) of a university research technician dedicated to this activity. Furthermore, three studies are currently in revision before publication, including one performed in collaboration with one group of the U892 INSERM unit. Finally, our research capacities in fundamental virology will improve with the integration of the HCV group in January 2012, as clearly pointed out in the report. The arrival of this research group also indicates a potential attractiveness of the EA4271.

1 rue Gaston Veil
44035 NANTES cedex 01

Tel 33/240411116 Fax 33/240412952
e-mail : berthe-marie.imbert@univ-nantes.fr

The main threats that we have to overcome for the next few years are related to the high number of projects. This is again partially due to the youth of our team, which in 2008 incorporated researchers arriving with their own scientific expertise. We have already started to work on this problem, by selecting only projects that have obtained specific financial resources (one new contract for HIV research was obtained in January 2011 and three are currently under evaluation, including a collaboration with the U892). Only studies which lead to international publications and subsequent competitive projects will continue. We hope and expect that this strategy will provide "basic" data, which will serve to establish the scientific track record required to obtain additional funding, especially at the national level (ie ANR). In addition, the new organization of the unit, now based on HIV/HCV and virus/transplantation fields, will help us to focus on more convergent and unifying investigations.

Among the other points that we feel deserve comment, we do not consider that the physical separation of two parts of the unit represents a significant impediment to our research activities. The two labs are located on the same site, are easily and rapidly accessible, and it is not difficult to organize experiments and lab meetings so as to overcome this minor inconvenience.

In two years, our young team has succeeded in creating strong links between different members of the unit, as specifically mentioned in the report. One of our main strengths is that we have the means to develop original research programmes at the interface between cellular immunity, transplantation, and viral infection. Taking into account the recommendations that have emerged from this evaluation, we feel that we are able to improve on the weaknesses that the committee identified. The ongoing re-structuring of infectiology at the local level (emergent theme in infectiology within the SFR, and a specific course for infectious diseases in the Master 2) will also increase our visibility and subsequent attractiveness.

Nantes, 25th February 2011
BM Imbert-Marcille

1 rue Gaston Veil
44035 NANTES cedex 01

Tel 33/240411116 Fax 33/240412952
e-mail : berthe-marie.imbert@univ-nantes.fr